**Lancet Commission on the Future of Care and Clinical Research in Autism**

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## Executive Summary

Autism is a condition of global importance because of its prevalence across the world and the degree to which it can affect individuals and families. Autism awareness has grown monumentally in the last 20 years. Yet most striking is that much more could be done to improve life outcomes of the highly heterogeneous group of people who have autism. Such change will depend on investment in science focused on practical, clinical issues and social and service systems that acknowledge the potential for change and growth, as well as the varied, complex needs of autistic individuals and their families. The lives of the estimated 78 million people with autism globally and their families could be changed with such an effort.

The *Lancet* Commission on the Future of Care and Clinical Research in Autism took as its mission the question of what can be done in the next five years to address the current needs of autistic individuals and families around the world. Autism is a neurodevelopmental disorder that typically begins in early childhood and affects social communication and behaviours throughout the lifespan. Autism and other neurodevelopmental disorders have seen a tremendous influx of interest from the scientific community in the last 60 years. Significant progress has been made in many areas of basic and applied science, although the limits to our knowledge and understanding of autism are also very clear. For clinical purposes, reviews and guidelines have proliferated, even though the body of data on which many recommendations are based are typically from short-term interventions that address acquisition of specific skills that we hope – but do not confidently yet know – will contribute to long-term gains across development. However, very significant gaps remain in knowledge about key questions such as what interventions and supports are effective for whom and when, and which interventions lead to changes beyond their proximal outcomes. Underlying these outstanding questions is almost no information about what the active ingredients or mechanisms, behavioural or neurobiological, are for change. These issues are particularly important given that autism affects individuals from toddlers to elders and that autism is almost always accompanied by other developmental, behavioural and mental health difficulties or conditions that have major implications for lifelong outcomes.

On top of these issues is the recognition that autism affects individuals and families worldwide, most of whom are receiving no help outside of their own resources. If we are to develop evidence-based approaches to support the lives of autistic children, adolescents and adults who are living now (in contrast to the fervent hopes we have for neurobiological approaches in the future), we need to know what works for whom, when and at what intensity; in order to design systems that are cost-effective, affordable and scalable across the globe. We are nowhere near the ability to do this using existing data, but it could be done.

In response to this challenge, our Commission proposes a novel modified stepped care/ personalised health model of intervention and assessment for individuals with autism and their families. An important element, not always considered in such models, is that treatment and supports begin with the preferences, needs and costs, financial and otherwise, to individuals and families, and must take these into account at each step. These individual differences across autistic children, adolescents and adults and their families are nested within communities, cultures and social systems that must also be considered. Using data from a large-scale epidemiological sample (generously shared with us by the Norwegian Institute of Public Health), we provide initial examples of how and why such a stepped care/personalised health approach could be applied both to address the core features of autism and also co-occurring conditions.

Individuals with autism and other neurodevelopmental disorders are a valued part of our society and represent a prototype of neurodiversity. At the same time, many individuals with autism have high levels of need and are vulnerable, and societal attitudes to difference, inclusion and equity will impact their life experiences and outcomes. Social justice is a value we embrace. Autistic individuals and their families can show amazing strengths and persistence, patience and perception that can change development as well. Respect for this diversity and heterogeneity is key, as well as respect for the power of development and the possibility of change. This is a time for optimism with a focus on ways to move forward to make changes happen. It is also a time for realism, recognising the varied needs of autistic people, including those with severe intellectual disabilities and language impairments, as well as those with significant strengths in the same or other areas. It is also a time to recognise the scarcity of resources in LMIC and some HIC and to ensure that different underserved groups such as those who are minimally verbal, females, ethnic minorities and those with severe co-occurring conditions are included. Societies in every part of the world have a duty of care to all people with autism and those who care for them, and investment in research and services needs to be targeted wisely to help them achieve the outcomes and make the change that is possible.

Autism is a relatively specific disorder in some respects because it is defined by the intersection of social communication and sensory, restricted and repetitive behaviours and interests. Yet it is also one of many neurodevelopmental disorders, with which it shares a great deal. We believe there are times when it is important to consider autism as a specific condition and other times when recognition of the overlaps with other neurodevelopmental disorders is more appropriate. In the context of individual, family, cultural and regional diversity, we propose that stepped, personalised models of interventions and services based on focused research that tests them and their implementation, can change the lives of autistic individuals and those with other neurodevelopmental disorders throughout the world.

## Key Messages

1. At least 78 million people worldwide have autism; the majority do not get support or services.

2. Children and adults with autism can have happy and healthy lives but urgent action is required for this to happen.

3. Autism is heterogeneous and requires personalised, evidence-based assessments and interventions, accessible and affordable to every person, that will improve the lives of individuals and their families.

4. People with autism have complex needs. Meeting these needs requires government coordination across health, education, finance and social sectors across the lifespan and the active inclusion and participation of autistic people and their families.

5. A stepped care, personalised health approach to delivering services and monitoring effectiveness across time provides a framework for efficient, equitable distribution of resources to improve outcomes.

6. More information is urgently needed about the economic as well as personal consequences of autism, to inform the case for government and societal investment, action and support across the globe.

7. People with autism and those with other neurodevelopmental conditions have many similar needs. Developing appropriate systems of care for people with autism will also improve outcomes for those with other neurodevelopmental conditions.

8. Valuing autism and neurodiversity benefits society as a whole.

9. Research that will result in immediate improvements in the lives of people with autism and their families should be prioritised now.

# Introduction

This Commission brought together stakeholders in autism from a range of perspectives including clinicians and other providers, researchers, advocates, self-advocates and parents from six continents to address the future of healthcare in autism. One decision made early on was to focus on recommendations that could be put into effect in the next five years, with the potential to have immediate as well as long-term effects on the quality of life for autistic individuals and their families. Though there are a host of well-tried interventions and treatments for autism, we know much less than we should about which treatments or services should be offered when and to whom, for how long, with what expected outcomes and for what cost. These questions are outside the scope of most contemporary basic science or even translational research which currently is often prioritised over more practical knowledge, leaving autistic individuals, families and providers without evidence-based guidance.

The promise of basic science to positively affect clinical practice for autism and neurodevelopmental disorders remains distant for most people with autism. We support the ongoing need for basic science, but clinical practice cannot wait as we search for biomarkers and a clearer understanding of the genetics and neurobiology of autism which may lead to the development of biological first-line treatments, initially for highly specific subpopulations. We do not in any way wish to reject efforts in these areas but rather to stress the need to complement them with different systematic strategies and goals that will yield immediate results. Similarly, in these unique times, the COVID-19 pandemic has presented a pressing need to directly address human behaviour and practical service provision (e.g., social distancing, ensuring adequate protective equipment and hospital capacities) even as rapid advances in basic science have made a critical contribution to lessen the impact of the virus. Even more so in autism, we cannot wait for basic science to address the heterogeneity of potential causes and treatments of this complex condition, without addressing the current real-life needs of individuals and families globally. We argue in this Commission that it is possible for targeted research to change lives now, through improved mental and physical health and strengthening support systems. Clinical science should not be considered 'second class' compared to fundamental biological research which is simply unable to answer many of the questions that arise in considerations of human mental health and development.[1] While autism is a neurobiological condition, the clinical challenges raised for society and a very heterogeneous group of individuals are, for the most part, not ones that are likely to be solved by biomedical solutions for most people in the near future. How to fill this gap is the focus of this Commission.

In addition, reflecting that social justice is a recurrent theme in our conceptualisation of ways forward, we also made a decision that the same quality care should be expected for everyone everywhere. Therefore, we discuss pertinent information from progress to date even if it has only occurred in High-Income Countries (HIC), recognising the need to continue rigorous science and innovative clinical practice in HIC and Low- and Middle-Income Countries (LMIC). Our responsibility is to discern the most efficient, effective and economical ways to support change anywhere and everywhere for autistic people and their families, and help put such methods into practice across diverse communities, cultures and countries. For this reason, rather than following

a traditional approach to descriptions of clinical practice that begin with screening, assessment and diagnosis and then move on to interventions, we first emphasise the importance of valuing diversity and three other themes that are fundamental to a better understanding of the lives and needs of all autistic people: *heterogeneity*, *potential for change*, and *systems of care*. We then begin the discussion of clinical practice with a focus on interventions, supports and gaps therein that can make a real-life difference to those who live with autism today. The idea is that diagnoses and assessments should lead to information that contributes to decisions about interventions and services, and thus, the discussion of these issues then follows.

**Recognising and Valuing Diversity**

Autism is a complex neurodevelopmental condition and this complexity, in part, underlies why services and research have to date been inadequate to achieve the positive outcomes that are possible for many individuals. The complexity reflects several conceptually distinct aspects helpful in understanding the needs of each autistic individual. The term *heterogeneity* describes ways in which autism manifests differently between people who have the condition and within individuals across the lifespan; the *potential for change,* the recognition of which is not as widespread as it should be, is inherent in our use of the overarching term neurodevelopmental condition; individuals live within local and broader *systems of care* that include health, education and social care services that they will or could access; as well as within family, neighbourhood, cultural and global environments that differ widely in countries and continents across the world. We believe that autism allows us to appreciate and value difference and neurodiversity in ways that bring benefits to society as a whole. We describe first how each of these three themes, as well as cultural and global differences and neurodiversity, are important for an understanding of any one autistic individual, as well as differences between individuals who have the diagnosis.

Autism or, using the formal term from the American Psychiatric Association (APA) Diagnostic and Statistical Manual (DSM-5) and the World Health Organization's (WHO) International Classification of Diseases (ICD-11), Autism Spectrum Disorder (ASD), is a common, highly heritable and heterogeneous neurodevelopmental disorder that co-occurs with other conditions.[2] From Kanner's[3] first case series, autism is diagnosed based on observation and report of behaviour. The prevalence is estimated between 1 and 2% worldwide, meaning that at least 78 million people worldwide have autism.[4,5] We use the term autism to refer to the autism spectrum because it is briefer and more acceptable to many autistic people than Autism Spectrum Disorder or ASD.[6] It has been shown repeatedly that, though change can happen, the impairments in social behaviour, understanding and communication that characterise autism, accompanied by restricted, repetitive interests and/or unusual reactions to various environmental sensations, result in what are often lifelong difficulties that limit independence and community participation.[7] These difficulties often place extraordinary demands on families, as well as impacting the individual with autism.[8] Children as young as age two can be diagnosed with autism, but many children and adults are not identified until later, in part because symptoms may not be clear and, in part, because of a lack of recognition and understanding and poor access to appropriate services. Some individuals with autism have average or above-average intelligence and language abilities, are university-educated, in professional jobs and in a marriage or partnership with children. Others have severe intellectual

disability, little or no functional communication skills, limited social relationships outside the immediate family, and require round-the-clock lifetime care.

Fifty years ago research showed that autism is a neurobiological condition, often, but not always, associated with intellectual disability and epilepsy.[9] Autism is caused by a combination of many different rare as well as common genetic variants, though often the same genes are associated with other neurodevelopmental or psychiatric disorders, and to date most of the population do not yet have  profiles with known genetic findings.[10] While research into the neurobiology of autism is amassing intriguing findings, there is not yet a reliable diagnostic biomarker nor is there a psychopharmacological treatment for core autism features. However, there are many diverse behavioural aspects of autism, emerging during different points of development, that predict eventual independence and quality of life. Figure 1 shows when in development, in one longitudinal study, different factors became predictive of adult outcomes defined by objective measures of work / activities, independent living and social relationships.[7,11] These factors and the interventions and social systems that can support them are our focus.

Figure 1. Milestones listed at the age they became predictive of adult functioning from the Early Diagnosis longitudinal study from age 2 to 26

[Figure 1 here]

## Cross-Cutting Themes

### Heterogeneity

The presentation of autism changes over time, requiring different interventions across the lifespan from the point of first concern to later adulthood. Heterogeneity refers to the longstanding observation that there are individual differences in aetiology, clinical presentation and care needs over time. Failure to recognise heterogeneity in autism may adversely affect public awareness, assessment and diagnosis, clinical management, access to services, public policy and equity.

**Heterogeneity in the Diagnostic Classification Systems**

Over time, psychiatric diagnostic systems have tried to capture this heterogeneity. The term 'pervasive developmental disorder' was introduced in DSM-III/ICD-9, followed by 'autism spectrum disorder' in DSM-5/ICD-11.[12,13] 'Pervasive' highlights that autism affects more than one developmental domain and 'developmental' recognises that autism is a lifelong condition appearing in early childhood, though its manifestations change across the lifespan. The 'spectrum' notion acknowledges the breadth of individuals who qualify for the diagnosis, embracing both dimensional (from less to more severe) and kaleidoscopic ('colour spectrum') variation in diverse profiles of strengths and needs across individuals.

**Autism as One of Many Neurodevelopmental Disorders**

Autism belongs to a broader category of neurodevelopmental disorders; a group of overlapping conditions characterised by early onset of difficulties in developmental domains that produce functional impairments.[12,13] Neurodevelopmental difficulties range from domain-specific to pervasive across motor, language, learning, adaptive and social communication skills, and regulation of attention, activity, impulses, and emotions. Diagnostic subgroups such as autism, attention deficit/hyperactivity disorder (ADHD) and intellectual disability are distinguished from each other based on the profile of strengths and difficulties across these neurodevelopmental dimensions, although much neurobiological and phenotypic overlap is evident.[14] An individual's functioning can vary widely within and across these dimensions, and profiles of strengths and weaknesses may change with age, contextual demands, and interventions. Autistic individuals require different, and sometimes adapted, interventions that overlap with those for individuals with other neurodevelopmental disorders (e.g., communication-oriented parent mediated interventions for toddlers with autism and language delay; stimulant medication for a child with autism and ADHD; modified Cognitive Behaviour Therapy (CBT) for an adolescent with autism and anxiety).

**Co-Occurring Conditions**

All neurodevelopmental disorders, including autism, often co-occur with physical conditions (e.g., epilepsy, gastrointestinal disorders),[15] mental health disorders (e.g. anxiety, depression, ADHD),[16] and a range of challenging behaviours (e.g., self-injury, aggression, sleep difficulties). The presence of co-occurring conditions contributes to the enormous heterogeneity in individual presentation and can significantly impact everyday functioning, which, in turn, leads to differences in needs for support and services. However, many lives can be greatly improved by appropriate individualised intervention and treatment (*see Comorbidities section below*). Some of these co-occurring conditions, such as language delay or seizures, are more common in individuals with autism and intellectual disability.[17] Other problems such as aggression, oppositionality, anxiety, and emotional dysregulation cut across diagnostic entities.[18]

Heterogeneity is also evident in the number, severity and nature of the co-occurring conditions. For example, language delay shows a wide range from mild to severe. Limitations in receptive or expressive language unquestionably add to the social communication impairments in children. Delays in language are often parents' greatest initial concerns, and later, continue to affect many adults with autism, showing associations with daily living skills and disruptive behaviours across the lifespan.[19] For other autistic individuals, structural and functional language skills are intact, but difficulties with pragmatics (i.e., the social use of language) become apparent as they age and may interfere with communication with peers.[20] Similarly, as shown in Figure 2, people with autism vary in whether and to what degree they experience other neurodevelopmental disorders, such as ADHD or intellectual disability, as well as mental health conditions such as anxiety. As shown below, these differences interact. Across development their impact may be compounded, causing even more disruption over time.

Figure 2. Neurobiological and experiential influences on autism symptoms, mental health, and life outcomes across development

[Figure 2 here]

**Cultural Heterogeneity**

Heterogeneity is also reflected in diversity within family units, within cultures, and across countries (see *Global issues* and *Cultural diversity sections* below for more details). Families are the primary source of support for most autistic children and adults. They differ in composition, beliefs and priorities. Moreover, cultures, even within a region, differ not only in languages, beliefs and priorities, but in their access to and use of resources.[21] Research and clinical practice should pay careful attention to these differences, as well as to how scalable and sustainable models of care can be implemented for autistic individuals across the globe. Examples of different families in different cultures are illustrated in Panel 1 below.

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*Panel 1*
*Person portraits illustrating the variability in presentation, strengths and needs of autistic people*

*Adir*
Adir is an 18-year-old, nonverbal man with profound autism, intellectual disability and epilepsy who lives in a small town in the Midlands, UK in a close-knit family who were first-generation immigrants to the UK from Yemen. He was diagnosed with autism at age 4 and his parents enrolled him in a preschool that specialised in those with severe needs, with the hope that he could eventually participate in a mainstream classroom. There, Adir received behavioural interventions, speech and language therapy, and he participated in a social skills group. Adir took medication to manage his seizures. Later, he was given medication because his behaviour could become challenging to others when he was upset or agitated. By age 16 he was over 6 ft tall, weighed 275 lbs and his behaviour was challenging for others to manage. He was not fully toilet trained and had frequent accidents especially when frustrated. Adir's family could not find care that met his needs that they could afford, so his mother quit her job in order to supervise him. During outbursts he became physically aggressive towards himself and others, creating a safety risk for him and his caregivers. Several efforts at supported employment proved unsuitable and resulted in aggressive outbursts and his being fired. Much against their original plans to care for him at home, his parents are currently considering residential placement where he will receive 24/7 care.

*Franco*
Neither Franco's parents, who were white, conservative, working class people living in a small town in Kansas, in the midwest of the United States, nor his paediatrician observed any obvious early signs of autism and Franco reached most of his developmental milestones on time. However, his parents reported that he was a very fussy baby and did not want to be cuddled or held. At around 18 months of age, he began to interact with his parents less frequently, wander off, was no longer looking at their faces and stopped forming new words. At the time, his parents had just welcomed a sister to the family and the paediatrician thought that his change in behaviour might reflect these changes in the home. Franco spent most days walking in circles, trying to get outdoors and sorting his toys by size and colour. He insisted on eating only foods that were white and would start biting his own arm and pinching his caregiver if anyone tried to put new foods on his plate. Eventually his parents had him assessed and he received a formal autism diagnosis around age 3. For the next 2 years, he received general early intervention services

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at home two to three times a week. By age 5, he was making enough progress to be enrolled in a mainstream kindergarten with a full-time aide. At school, he enjoyed music and was well-mannered, but spent most of his time by himself continuing to play with toys alone or in parallel with other students. Franco had little awareness of danger and would wander off away from the family home. His parents added child-proof locks to all their gates and fences but with age he became more adept at climbing them. However, he was starting to show reciprocal smiles and his teachers and parents were pleased with his progress. He had a very strong and repetitive interest in being pushed on the swings at school and loved having his aide push him constantly at breaks. In fact, this is the one activity he clearly enjoyed and after school, he would constantly go to the door asking his mother to take him to the school playground where the 'good' swings were. One afternoon, at age 7, he wandered away from his home and nearly drowned in a nearby pond but was rescued by a neighbour. His parents have purchased an electronic tagging device and asked school to ensure an aide is with him at all times when he is out of class but they do not have the capacity for this to continue indefinitely.

*Sofía*
Sofía lives in Argentina with her husband and son. She has a PhD in renaissance art history. She is fluent in three languages, reads prolifically and has an IQ over 125. In college and graduate school, she spent most of her time at the library or at home reading. Sofía had a few friends that were part of study groups she participated in. She failed her oral examinations once before passing the second time. Before she was diagnosed with autism, she saw her problems as mostly consisting of restlessness, problems concentrating, and severe sensory issues that caused her physical pain. She also had problems on tasks that required her to think abstractly, however, she was able to quickly recite different trends in art, artists, styles, paintings and the evolution of painting styles across time periods. Since receiving her PhD, she has had difficulty obtaining and keeping a job because required meetings with her colleagues caused her extreme anxiety. She has been dismissed from three jobs and has been frustrated because she has not understood why. Finally, at age 30, when her 18-month old son's behaviours became overwhelming, they both were diagnosed with autism by her child's behavioural paediatrician. Today, Sofía works from home part time as an editor of an art journal. Her employer allows her to have flexible hours and she mostly interacts with her colleagues via the internet.

*Samir*
Samir is a 10-year-old living in a rural Indian village. His parents had a difficult relationship and his father, a farmer, was his main caregiver. Samir had always been a child who did not understand rules and his father had worried about him since he was young. When he was placed in the village school, the teachers raised a concern about him not learning anything and wanting to be on his own. However, his father felt he would 'grow out of this' and was reassured by relatives that 'boys often talk late.' A few months later when Samir did not develop like other children, his father took him to a traditional doctor where he was given a charm to tie on his wrist and complementary medicines. These had little impact except their cost to the family. Finally, on a schoolteacher's advice, Samir was taken to a child development centre where he was given the diagnosis of autism at 6 years. He was advised to return for speech and language therapy. However, the two bus rides each way were not sustainable, particularly due to the loss of daily wages and also due to the lack of any visible change in Samir over two weeks of attending the sessions. His father negotiated with his village school that Samir would attend some of the day with his peers. He has realised that his son may not finish school but is working toward the goals of Samir being independent with his self-care and being able to help with the cattle when he grows up.

**Autism and Neurodiversity**

Neurodiversity refers to the natural variability within human brains and minds.[22] Recognition of human diversity helps us better understand autistic individuals in ways that have far-reaching effects. These cut across issues as broad as human rights; equity and social justice; respect for difference; and the need to take account of individual and family preferences. Valuing neurodiversity has the potential to create stronger and wiser communities and positive social values.

The concept of neurodiversity is also the basis of an international civil rights movement that arose primarily as a response to marginalisation of autistic people. The neurodiversity movement considers autism as a neurological difference rather than a disorder, and is sometimes associated with challenges against efforts to find a cause or cure.[23] This movement also includes those with other neurodevelopmental conditions such as ADHD, bipolar disorder, dyslexia, and epilepsy, as well as those with differences in gender identity.[22–24] Individuals prefer to self-identify as a member of the neurodiverse community rather than with psychiatric and medical diagnoses that emphasise impairment and disorder.[23] Some emphasise that the term 'neurodiversity' includes all forms of neurodevelopmental diversity, including those with the highest needs.[22] Others within and outside of the neurodiversity community stress that the reality of disability for some people and some families not be underestimated.[25] There are also concerns about how access to services would be affected if autism were regarded as natural variation that does not need intervention.

Not all autistic people and stakeholders identify with this movement.[26] There is controversy about how those with the highest support needs, including those with significant intellectual disability and limited functional communication who are unable to advocate for themselves (i.e., those with 'profound autism'; see Panel 2), are represented by a non-medical model. Many autistic people struggle with their difficulties and feel excluded from society; some may seek a cure while others embrace autism as part of their identity, thankful for some aspects of who they are despite the challenges that come with difference; most are somewhere in the middle.[26] The ambition for full participation of autistic individuals in debates on issues ranging from service provision to setting research priorities is to ensure all views are represented, including those of individuals who cannot speak for themselves, which may require that a parent or other close contact speak for them. One sometimes overlooked aspect in ongoing debates in the autism community about neurodiversity is that there will exist a range of experiences, views and attitudes across stakeholder groups. In fact, it is possible to hold a plurality of views at one time. Another consideration for the Commission is that the current debates on medical vs. social models of disability can be quite different across social, cultural, and global communities.

From the neurodiversity perspective, diversity enriches and is a strength of societies, but requires adjustments from all sides. Even for autistic people who do not need much support, daily life situations can be exhausting, not only because of the excess of sensory stimuli but also because of a constant struggle to decipher social cues, to communicate and to deal with unexpected changes. Accommodations in the environment can make some disabilities become differences and even advantages (e.g., Roim Rachok Program[27]). Although individual factors contribute, and acceptance and accommodations do not always eliminate impairments, a significant proportion of the risk for poor outcomes is likely to be socially produced.[25] All developmental disorders hold up a mirror for society to reflect on the degree to which we help those with the highest

levels of need, make room for and include people who are different, and make an effort to build communities and institutions that function well for all citizens.

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*Panel 2*
*Profound Autism*

With DSM-5 and ICD-11, it was decided that autism should be considered as a single spectrum disorder defined on the basis of two core domains – social communication and repetitive, restricted, and sensory behaviours. These criteria, which can be met through history or observation, must be accompanied by a current functional impairment. The tremendous heterogeneity of autism is acknowledged in both of these diagnostic systems through the use of specifiers that include intellectual and language levels, the presence of co-occurring mental health conditions that may vary in severity, as well as genetic, neurologic, and other medical conditions, as shown in Figure 2. However, the DSM-5 clinical specifiers and the detailed sub-categories in ICD-11 (with and without a disorder of intellectual development and functional language impairment) are not easily or consistently used in practice or in research.

Until the 1990's, the majority of children and adults diagnosed with autism also had intellectual disability and were considered severely affected. However, reflecting the broadening conceptualisations of autism as a spectrum disorder, more recent prevalence studies in HIC have shown that the majority of children identified with autism do not also have an intellectual disability.[5] Despite genetic studies that have the greatest implications for more severely affected individuals, many other areas of research have focused on less severely affected autistic people. The media have also focused much of their attention on the growing proportion of autistic people without intellectual disability. Children and adults with autism and severe and profound intellectual disability have vastly different educational and long-term care needs that cannot be properly planned for if these individuals are not identified. Many are minimally verbal or non-verbal; most often they are not able to advocate for themselves and must be able to rely on family members to communicate their needs to policymakers, the media, medical professionals, and the scientific community. They and their families are at risk of being marginalised by a focus on more able individuals. Many of these individuals need constant monitoring, even as adults, because of safety concerns including higher risk for abuse and maltreatment due to their need for help with daily living skills and personal care.

For these reasons, our Commission proposes that the term 'profound autism' be adopted to apply to children and adults with autism who have, or are likely to have as adults, the following functional needs: 24-hour access to an adult who can care for them if concerns arise, cannot be left completely alone in a residence, and cannot take care of basic everyday adaptive needs. In most cases, these needs will be associated with significant intellectual disability (e.g., an IQ below 50) or very limited language (e.g., limited ability to communicate to a stranger using comprehensible sentences) or both. In order to represent the intensity of needs in a standard manner, profound autism is thus defined, not by autistic features, but by intellectual or language disability. The term "profound" was selected because it is less commonly used colloquially than severe and the term "low functioning" is disliked by many. Profound autism may be associated with complex co-occurring difficulties including self-injury, aggression, and epilepsy, but is not defined by these factors. Profound autism is not included in the recent revisions to the diagnostic systems but rather extends and amplifies the additional specifiers included in both systems; namely, the presence of intellectual and language impairment in addition to a diagnosis of autism in DSM-5 and "autism spectrum disorder with disorder of intellectual development and with absence of functional language (6A02.5)" in ICD-11. Someone who has some of these characteristics who is functioning well in a supportive setting may not choose to use this term, but we offer it for autistic people,

families, and clinicians for the purposes of advocacy and description. We hope that its introduction will spur both the clinical and research communities globally to prioritise the needs of this vulnerable and underserved group of autistic individuals.

The term profound autism is not appropriate in young children. It may begin to be useful, with the consent and participation of families, beginning in early school age (e.g., age 8 or older) for children with autism and severe to profound intellectual disability or minimal language, given the evidence that these factors are not likely to change. The term may be most helpful in adolescence and adulthood. It is not intended to describe other severe difficulties related to autism that may apply to individuals with extraordinary life circumstances, trauma, family conflict, lack of resources, or those with co-occurring mental health problems. We acknowledge that the word 'profound' may have different connotations and other terms may be more appropriate in other languages. For example, in Spanish 'severo' or 'grave' might be more appropriate because of different meanings of profundo (e.g., 'deep').

As part of this Commission, we analysed data from three samples: (i) 8 year-olds in the Norwegian Mother, Father and Child Cohort Study (MoBa)[28] a population-based pregnancy cohort study conducted by the Norwegian Institute of Public Health; (ii) 12 to 23 year-olds in the Special Needs and Autism Project (SNAP)[29] a British population-based study that identified children with autism and special educational needs; and (iii) the Early Diagnosis Study (EDX) a U.S. based longitudinal study shown in Figure 1 that has followed children referred at age 2 years up through age 30.[7] We used the criteria of either 1) verbal, non-verbal or full-scale IQ at or below 50, or 2), minimally verbal status as defined by Module 1 of the ADOS, or, in MoBa by the maternal response of 'no' to 'Is s/he now able to talk using short phrases or sentences?'. The proportion meeting the profound autism criteria was about 18% (95% CI 12-24%) in MoBa; 23% (13-28%) in SNAP; and 48% (37-58%) in EDX. The proportion of females was higher among those meeting profound autism criteria compared to those not meeting the criteria, though confidence ranges overlapped (MoBa: 45% [95% CI of 28-63%] vs. 17% [12-24%]; SNAP: 19% [5-42%] vs. 13% [6-21%]; EDX: 23% [10-36%] vs. 4% [0-11%]).

At age 25, in the EDX sample, none of the individuals meeting profound autism criteria were living independently; none had full time paid employment (though some had supported employment).[7] Of the 39 adults (of a sample of 82), who met these criteria at 25, 86% had met profound autism criteria at age 5 and 92% at age 9. Only 2 individuals moved out of profound autism between 9 and 18, due to improvements in language level and IQ to above 50. These data are specific to this cohort, defined by their early identification at a young age. Thus, although they are not representative of current prevalence rates, the findings support the stability and validity of the concept of profound autism. In the SNAP sample, of the 18 adolescents identified with profound autism at age 12 years who were reassessed at age 23 years 15/18 (83%) continued to meet criteria and 79% lived in specialist residential accommodation with a further 18% living with their family with high levels of support; again supporting the stability and validity of the concept in terms of high care and support needs.

The three samples reported here used different methods of sampling and recruitment. In addition, there were differences in methods employed to assess intellectual disability, language level, and autism symptoms, ranging from direct in-person evaluations to questionnaires, patient registries, and electronic health records, as well as length of follow-up. They range from an early clinic referred sample from nearly 30 years ago (EDX); to two population designs that involved screening and follow up of current cases for children with identified special needs (SNAP), and a nationwide cohort with screening and diagnostic assessment in combination with linkage to registry diagnoses and review of electronic health records (MoBa). This work lays the groundwork for an important area of clinical research and practice.

**Potential for Change**

## Change is Possible

Initially, autism was thought to be an intractable neurodevelopmental disorder with few effective treatment options, but a more optimistic view is emerging. Recent systematic reviews and meta-analyses of intervention studies for young children with autism have identified evidence-based psychosocial interventions which, when conducted in high quality university-led trials in HICs, resulted in change that can mitigate the impacts of autism on development for some people.[30,31] Furthermore, longitudinal research suggests that some individuals can compensate for difficulties associated with autism in ways that lead to very positive outcomes.[32] Although not all people will change to the same degree, people with profound autism can have lives with social contacts, meaningful activity and independence in some skills.[7] Consequently, the question is no longer, 'Is change and improvement possible for people with autism?' but rather 'What factors enable people with autism to live positive, fulfilling lives?', 'What are the key ingredients of effective interventions?' and 'What are micro- and macro-environmental barriers to change for this autistic individual?'.

## Evidence for Early Intervention

In many cases, autism and other neurodevelopmental conditions are apparent in the first three years of life. Accordingly, much intervention research has focused on reducing impact on early development. Developmental and behavioural intervention trials with young children are methodologically challenging[33] and a strong evidence-base requires an accumulation of evidence across multiple trials. Nevertheless, replicable results across studies indicate that early intervention can have positive effects on social communication, language, cognition, and adaptive behaviour in young children with autism.[30,31]

Historically, early intervention started with instructor-led, high-intensity applied behaviour analysis (ABA) and discrete trial training (DTT) that relied on external rewards to motivate learning and cognition[34] as well as to reduce problem behaviours. This approach, as originally implemented, has limited support from well-conducted, randomised controlled trials. However, it has been modified over the past few decades to be more naturalistic and developmentally appropriate, often with lower-intensity delivery and greater emphasis on the child as an active partner in communication.[35] In addition, other studies have focused on teaching parents to support the child in the development of early communication and social interaction.[36,37] There is emerging evidence that such programmes may be effective in LMICs such as India and Pakistan.[38] Based on a transactional model whereby behavioural symptoms signify the presence of autism and significantly impact subsequent development, early impaired social communication behaviours such as joint attention, symbolic play, or imitation are often targeted by interventions.[39] Thus, an intervention may teach particular skills that have immediate value (such as how to ask for help or how to say 'no'), as well as supporting pivotal skills (e.g., joint attention, imitation) that contribute to change in processes that have cascading developmental effects on language and cognition.[40]

**Why and When is Change Possible: Many Methods and Contexts Can Lead to Improved Quality of Life for People with Autism**

As depicted in Figure 3, the possibility of change follows from the hypothesis that, because of the plasticity of neurodevelopment, enrichment and modification of the environment and experience through interventions can have a significant impact on behavioural *and* neurodevelopmental processes over time.[40] Furthermore, as shown earlier in Figure 1, research has shown that different aspects of development emerge and perhaps, can be more easily modified, at different times.[11] Learning by enrichment of experience and/or modification of the environment to better address individual needs can have profound effects on typical and atypical neurodevelopment beyond childhood.[41,42] This may especially be the case for higher cognitive and executive functions associated with frontal cortical development[43] that play a role in an individual's capacity to compensate for some of the difficulties associated with autism.[44] Evidence supports the positive impact of interventions to enhance cognitive and emotional self-regulation and improve compensatory skills in children with autism.[45] Other evidence demonstrates reduction of social difficulties in school-aged children and young adults.[46] Thus, throughout development, interventions may affect both symptom reduction and enhancement of compensatory processes and quality of life in people with autism in middle childhood through adulthood. In common with other chronic and enduring health conditions, one-off, time-limited interventions will not be sufficient to enable lasting change for most people with autism. Rather, a developmentally-sequenced series of staged and personalised interventions will be required for any individual according to their developmental stage and profile of strengths and needs and the presence of co-occurring conditions (see Green[47]).

Awareness that change is possible is crucial to the development, study and incorporation of effective approaches into programmes in healthcare and education to support autistic people and their families across the lifespan. These interventions include appropriate, enhanced education programmes in schools and higher education settings, as well as community and clinic-based programmes that support peer interactions, leisure and social activities, adaptive skills and treat co-occurring conditions such as anxiety or depression.[42] Beyond the development and documentation of the efficacy and effectiveness of these programmes, issues related to how and when and who implements them must also be directly addressed to determine cost-effectiveness and feasibility both financially and in terms of individual, family and community burden.[48]

Figure 3. Influences on the path of typical development

[Figure 3 here]

**Systems of Care**

**Identity as a Service User**

We define 'system of care' loosely to include the set of health, education, social care, employment, financial and safety net services which families and autistic people potentially have access to in a given community, including informal networks or relationships. This definition includes both

general systems of health and education as well as systems, programs or benefits targeted to people with disabilities or special needs. The reality is that, if we change systems of care, we may improve the outcomes of many more autistic people than through focusing on individuals.

A defining feature of the lifetime of some people with autism living in HICs is engagement with service systems providing health and therapeutic interventions, material support, health insurance, education and training, community supports, and direct care. Some individuals and families have intense involvement with services at one time and much less or none later; others have never interacted with services much or at all. Getting an autism diagnosis can be a doorway into a social role as a potential lifelong service user, augmented by help and support from family members, neighbours and the community. Entry into, and use of, services from this perspective becomes more than a set of discrete events that happen to an individual. Service use for many people with autism and their family members can become a key element of their life stories that has a broad influence on the course, social identity, and meaning of their lives. However, in contrast to the situation for families with the most support in HIC, the majority of people with autism in LMICs and many in HICs live in communities with little to no dedicated infrastructure for people with developmental disabilities or special health care needs, resulting in families being left to manage on their own.[49,50] Many families in both LMIC and HIC assume primary caregiver roles and create their own informal systems of care involving nuclear and extended family and community groups, such as neighbours or church members.[50] Figure 4 shows the potential effect of differing levels of service, formal recognition of autism, active support, and community adaptation, on the outcomes and functioning of the heterogeneous population of autistic individuals.

Figure 4. Societal response and services can optimise outcome for all people with autism

[Figure 4 here]

As discussed throughout this Commission, the needs of individual autistic people and their families are heterogeneous and evolve over the life course. No single system of care delivers services across all domains or life stages. Many systems, for example, special education and paediatric care, end at a particular age. Other forms of social care may not be established in many regions and cultural contexts.[50] Care is sought from multiple sectors and providers, with integration, coordination and transition of care being major lifelong challenges for both families and providers.

**Fit between Individual Needs and Service Organisation**

Most community services are delivered through systems originally designed to meet the needs of other populations. For instance, in high-resource settings, many systems of services for people with autism and other neurodevelopmental disorders began in the mid-20th century as systems of care for people with intellectual disability. These legacy systems often use IQ thresholds for eligibility determination, which can exclude autistic individuals without marked developmental delays. Community mental health systems may not be well equipped to assist people with mental health issues *and* autism – again, leaving people with autism, with and without intellectual disabilities, to fall between the cracks of existing systems of care.[51] Even in contexts with strong legislative frameworks, where it is against the law for mental health services to discriminate

against people with autism (e.g., in the UK), it may still be challenging for people to access adequate support (see Panel 3 for examples of recent policy-practice interfaces in different countries).[52] Hence the need for patient navigation, a concept well-known in other areas of medicine, including primary care, in which there are explicit supports for patients' need for guidance in moving through health (and social service) systems.[53]

## Systems Level Solutions

Systems-level challenges require systems-level solutions as well as individualised care. This Commission recommends a blended approach to systems improvement that integrates evidence-based treatment practices into care systems along with the use of improvement science (the study of identifying, implementing, evaluating and disseminating strategies to bring about incremental, data-driven improvements in system performance).[54] Improvement science methods, including implementation, are widely used in school,[55] community,[56] and health care administration[57] but have not yet had much effect in care systems for people with developmental disabilities. The 'triple aim' of such methods is simultaneously to yield improvements in patient-perceived quality, population health, and per capita care costs.[58] For example, if criteria for entering into early intervention were changed from requiring an established diagnosis to 'possible' or 'likely' autism (whilst undergoing further assessment), earlier targeted intervention could begin for a greater number of children with autism and other neurodevelopmental disorders. In contrast, in some countries at some times, a diagnosis of autism led to exclusion from mental health services, which restricted eligibility from psychiatric and psychosocial services.

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*Panel 3*
*Policy and Practice in Diverse Settings*

Policy innovations can affect system-level performance and have an impact, both positive and negative, on individuals, often with a focus on access to care. In **South Africa**, there are no policies that are autism-specific but there is a National Early Childhood Policy that can allow access to early intervention in the preschool years; however, services are 'owned' by one agency with age-limited jurisdiction.[59] In **Argentina**, a National Autism Law complements a National Disability Law (2019) that obliges all health agencies to provide better access to primary care and diagnosis, and also raises the need for a comprehensive and interdisciplinary approach, training of health professionals and more research. **Peru** has a similar law and a National Plan for People with Autism. In **India**, autism was initially excluded from the Persons with Disabilities Act (1995) but was recognised in the National Trust Act (1999) after a hard-won battle led by parents and is now represented in the Rights for Persons With Disabilities Act 2016. However, the struggle for certification continued until 2015, at which point autistic children only received certification based on their IQ. It was only in 2016 that autism was certified using indigenously designed and validated tools, though implementation challenges continue as parents struggle to get certificates. In the **U.S.**, the passage of autism insurance mandate laws broadened access to autism specific interventions and shifted some costs from families to insurers.[60] Regional changes in rules also resulted in improved access to early intervention in some states and reduced racial disparities in others.[61] In countries with universal health care systems such as the **UK**, national guidance and online resources

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assist in development and implementation of quality standards and allow for comparison of service performance (National Institute for Health Care and Excellence (NICE)). National charities encourage families to refer to these guidelines and hold providers to account. Having a universal health care system does not always assure access to care. For example, in **Canada**, early intervention for autism is not covered under universal medical insurance and eligibility for public funding varies by province, making it very difficult to implement national guidelines. In **Australia**, the Helping Children with Autism (2008) initiative led to improvements in available early intervention for children up to 6 years. With the introduction of the National Disability Insurance Scheme in 2016, intervention and functional support is now available for people with disabilities, including autism, across the lifespan. However, it is important to note that the rollout of this ambitious scheme has been marked by flaws in implementation and controversy, with inequities identified in access.[62]

## The Importance of Transitions

Although primarily relevant in countries and contexts where adequate services exist, the theme of transition, defined as changes in contexts (e.g., leaving or entering school) or service eligibility (e.g., becoming a legal adult), is prominent in the life course framework. Transitions may also be critical starting points for the development of programmes in regions with few resources. Important to the concept of the potential for change in skills across the lifespan, transitions intersect with the theme of service experiences in two major ways. Service transitions occur when people change status from non-eligible to eligible, or transfer from one system of care to another. Service experiences during pivotal developmental periods may exert an especially strong influence on subsequent life outcomes,[63] establishing a foundation for continued achievement and healthy development. Several models exist for handling the transition from paediatric to adult health care, but issues of availability and access to quality care within communities persist.[64] For example, a lack of knowledge regarding the healthcare of young autistic adults among primary care providers, especially in rural or low resource settings, threatens their long-term health outcomes.[64]

Remote technology is one potential solution to empower and strengthen community-based healthcare for individuals with autism across the lifespan (see *Technology* section, below). Adaptation of the Extension for Community Healthcare Outcomes (ECHO) model enabled knowledge transfer from centres of excellence to primary care providers about the care of transition-aged individuals with autism, although it did not change providers' behaviour.[65] ECHO has also been utilised to promote best primary care practices by connecting autism specialists with primary care providers in remote areas of the world.[66]

## Major Issues in Clinical Practice and Research

### Intervention

An extraordinary amount of information about autism has accumulated in the last 50 years, with increased funding for research and an even greater increase, 30-fold, in the number of papers published.[67] We elect to start this section on clinical practice by focusing on interventions and

services known to effect change, and the kinds of changes we might expect to see. We propose that information about the effectiveness of various interventions has important potential to guide assessment, which is not often used. In addition, knowledge about evidence-based interventions and their documented outcomes can help identify targets for monitoring and review that would improve the usefulness of assessments across the heterogeneity of autism and provide better information for individuals and systems about what interventions have the greatest potential to yield useful and cost-effective change. We hope this order will result in readers considering more seriously how the results of assessments and diagnoses might be used to help individuals, and what the outcome of such a process should be, moving beyond the notion of the outcome of an evaluation as merely a diagnostic label.

In HIC, most children with autism are in school and many receive some form of preschool services.[68] Evidence supports interventions focused on specific needs, including the development of early social communication and language abilities,[30] social skills,[46] or co-occurring conditions, such as hyperactivity, disruptive behaviour or anxiety,[69,70] with a growing, though limited number, of independent replications.[71] Nevertheless, there are almost no comparisons across approaches.[72,73] Outside HIC, many children and adults receive little help beyond the efforts of their families.[49,74] Even in HIC, once children are school age, most of the help they receive comes from schools, where approaches vary from skilled to minimal.[75] After secondary school, even in HIC, there is a service/treatment 'cliff' in which many families and autistic individuals find themselves on their own.[63] In fact, this is the case all the way across development for most autistic people in LMIC.

Compared to several decades ago, more children with autism in HIC are now gaining academic skills and participating in higher education,[76] and a greater proportion of adults are living independent, happy lives.[77] Nevertheless, those with the most positive outcomes still remain a minority.[32] Because more people with average to above average cognitive ability receive diagnoses of autism in HIC now than 50 years ago, we do not know if improvements in some outcomes are due to higher abilities in more recently diagnosed cohorts or to improved interventions and services. Moreover, while it is difficult to measure trends over time, objective measures of quality of life for autistic adults have improved only minimally.[78] The importance of subjective factors, such as wellbeing and mental health, is becoming increasingly recognised and requires more research.[7] There is much evidence that mental health, as well as physical health, can be challenging in a significant proportion of autistic adults.[15,16] Thus, there is an urgent need for effective interventions and services across the globe and across the autism spectrum.

**A Novel Stepped Care/Personalised Health Model for Interventions in Autism**

Our goal is to propose approaches to clinical practice, including clinically oriented research designs, that can have real, immediate and lasting effects on the lives of children and adults with autism and their families. We outline a novel, adapted, precision health-integrated stepped care model for intervention, that includes aspects of personalised medicine approaches and recognises the wide range of strengths, needs, preferences and circumstances of autistic people and their families across the world. Our stepped care/personalised health model takes account of the heterogeneity of autism, by recognising that the profile of strengths and needs of each autistic

individual and their family should, in turn, determine the intervention and support priorities for them but also that these may change over time - and in a stepped manner - as initial interventions take effect and with development. We are aware that the terms "stepped care" and "personalised health" are used by different disciplines in different contexts with specific meanings. We are deliberately expanding the use of these terms in a new way to talk about the integration of both treatment and assessment using measurement-based care and shared decision making that takes into account patient and family preferences and resources every step of the way. Many of the issues raised are also equally relevant to other neurodevelopmental disorders, though there are a number of reasons why we continue to need the concept of autism, beyond the dimensions by which it is defined.

Given the heterogeneity of autism and of families, cultures and community resources, a diagnosis of autism does not directly lead to a single treatment plan. Nor is there any single intervention that is effective or even needed for all persons with autism. Personalised approaches are therefore crucial. Nevertheless, as shown in Figure 5, there are general principles which can be applied in our modified 'stepped care/personalised health' model to help organise the knowledge we have about interventions. This is not precision medicine based on biomarkers.[79] To date, valid biomarkers are not yet close enough to the behaviours and circumstances that need to be changed to be useful, though some day they may be. Our emphasis in this Commission is on changes to practice, systems, and research that can improve the lives of autistic people living now. In this time of the COVID-19 pandemic, we are seeing the results of a focused commitment to the development of vaccines through the efforts of science; we call upon systems to have a similar focus on how to improve the lives of autistic individuals and their families through evidence-based interventions and support.

Figure 5. Stepped care/personalised health intervention

[Figure 5 here]

Stepped care models arose to prominence in an attempt to address physical health in lower resource settings.[80] Stepped care approaches outline a system of delivering and monitoring treatment, so that the least resource-intensive service is offered and then gradually 'stepped up' to more intensive or specialist-delivered treatments if necessary. These approaches have been aimed primarily at improving access and reducing cost, which are of critical importance given the 'treatment gap' between people who currently receive adequate services and those who need them.[81] A key principle in stepped care is 'task sharing,' in which services are provided whenever possible by the least expensive and most accessible provider, with supervision and training provided by more highly trained professionals.[82] It is ironic that, in the U.S., it is often easier to get funding for the highest, most expensive clinician (e.g., a psychiatrist or neurologist) than for a less expensive provider (e.g., a behavioural technician supervised by a psychologist or an occupational therapist). Emerging models of stepped care for mental health have been proposed, though experience with long-term conditions such as autism is limited.[81,83]

In addition, for autism, as with other lifelong conditions, many factors beyond monetary considerations draw our attention to the 'life' costs to people, which informs our concept of

personalised health. These include the role of families, personal preferences and the possibility of using everyday experiences to support skill-building and mental health outside of a healthcare system.[83] The role of the family is almost always critical; thus, stepped care/personalised health models must take into account the needs, abilities and 'personal costs' (not just financial) to the family and directly to the autistic person. We propose that we need to move beyond the important concept of participatory research[84] to incorporate participatory decision making in each step of clinical practice and systems.[85] This means including autistic individuals and families, who make most of the decisions during childhood and for many, though not all, adults. What may seem like a less expensive intervention in monetary terms may have other costs. For example, a clinic-based CBT group run by non-experts, may require lower healthcare investment and be convenient for a health system but be costly for autistic people who are challenged by sensory aspects of transportation or for families who have to travel to the group that competes in time with other responsibilities.

Another challenge for stepped care/personalised health arises from the heterogeneity of autism. A stepped approach that is also personalised requires accounting for the widely-varying needs, skills, and circumstances of the autistic child, adolescent or adult and family.[47] A recent thoughtful review of maximising potential in autistic people organises different intervention approaches into three main categories: building skills, minimising barriers and optimising person-environment fit.[71] For example, a minimally verbal 10-year-old with autism whose nonverbal skills are more like that of a typical 3-year-old and who has significant eating problems will need the help of a skilled therapist to build a communication system that could be implemented by a more general interventionist or teacher. To address the feeding problem, using a stepped care/personalised health model, it may be necessary to employ a behaviour programme developed by an expert experienced in feeding difficulties in similar children, who demonstrates techniques and coaches the parents. Another 10-year-old with autism whose language and reading comprehension are approaching age level and whose mathematical skills are strong may benefit from an inclusive school programme with support to foster opportunities for peer interactions. If this is not sufficient to promote success, the school could organise a social group. Another child might benefit from CBT to alleviate anxiety and outbursts related to unpredictability. Put simply, the needs and strengths of autistic individuals and their families differ depending on their age, level of language, cognitive skill, autism severity, general mental health needs, and adaptive skills, and interventions should address the multiple components of needs and take into account personal preferences.[71]

Like other neurodevelopmental disorders, aspects of intervention for autism address building skills that are absent or diminished. These may include social interaction, such as shared enjoyment or taking turns, and communication, including spoken language, comprehension, and use of symbols and augmented devices, including reading, pictures or devices. For families, psychoeducation involving understanding where their children's skills fall developmentally, what are reasonable expectations for next steps, and learning techniques to support these aspects of development is critical.[86] Psychoeducation is an essential part of each step along the way. If a family or an individual with autism is actively involved in decision-making and treatment planning,[71] they need opportunities to learn about autism in general, the characteristics of the 'identified patient' in specific, and the potential benefits and limitations of what professionals and systems can offer

within locally-available care systems. This information should include potential harm associated with clinical interventions.[87]

In contrast to skill-building and supporting development, other interventions are aimed at supporting families or individuals to reduce behaviours or feelings that have negative effects, which Lai and colleagues[71] describe as 'barriers to progress.' These might include the development of alternative strategies for anticipating and dealing with behaviours such as aggression, tantrums or severe distress, as well as the treatment of depressive feelings, irritability or hyperactivity through medication or cognitive behavioural approaches. For many issues in mental health, treating both skill development and reducing difficult behaviours or feelings is a standard part of an intervention plan. For example, in CBT for depression, goals include reframing troublesome thoughts and providing alternative behaviours and ideas to replace them. Because the two types of difficulty can cascade, substantial evidence and developmental theory support early initiation of services as soon as symptoms are observed.[88] Studies to date have not yet provided strong support for pre-emptive interventions, such as working with younger siblings who have no symptoms or with infants showing early signs identified by community screening,[89,90] though interest in doing so is strong. Nevertheless, if families of very young infants are concerned about an infant, it is crucial that these concerns be taken seriously.

One implication for the integration of stepped care and personalised health approaches is that, for many children and adults, there will be multiple treatment goals. As shown earlier in Figure 1, longitudinal studies suggest that the factors that predict positive outcomes in terms of independence and wellbeing are cognitive and language skills, severity of autism symptoms, connectedness with peers, adaptive skills and mental health.[7,91,92] If these can be recognised and addressed together, or at least, taken into account jointly, outcomes may be improved, and services could be more effective and efficient. In addition, given the heterogeneity of autism, what works now may not work later for the same person, and what works later may not work now. Whether to step-up or step-down the intensity of an intervention or shift to a different approach should be based on data-informed progress monitoring and measurement-based care.[93]

**How Should a Stepped Care/Personalised Health Model for Autism Intervention Work in Practice?**

There are few models of how to build skills and minimise barriers beyond some of the earliest therapist- and parent-mediated interventions that combine approaches to improving social communication and helping self-regulation (e.g., Joint Attention, Symbolic Play, Engagement, and Regulation [JASPER];[39] Enhanced Milieu Teaching [EMT];[94] Early Start Denver Model [ESDM];[95] Social ABCs[96]). With the exception of the Early Start Denver Model, most of these methods are short-term and involve only limited re-adjustments of targeted behaviours within brief periods of time. SMART (Sequential Multiple Assignment Randomised Trial) models, as we will discuss below, provide useful information about the effects of different sequences of strategies (e.g., oral language only vs. oral language and augmented communication). This is a first step, but we still need data about the relationships between baseline features, initial rate of progress, type of intervention, and eventual outcome. The absence of this information means that we are dependent on the clinician, and the autistic individual if possible and the family, providing the first

impetus for a treatment plan and then for all decisions about what should happen next after what are primarily short-term treatments for a disorder with long-term implications.

Thus, as shown above in Figure 5, stepped care/personalised health begins with a definition of family and individual concerns.[97] We present this stepped care/personalised health approach to assessment to determine these concerns in the following section. For most individuals and families, there will be several needs or aims to be targeted at any given time. Next, factors related to the individual child or adult must be considered. These must begin with safety (e.g., a child who is wandering out of the house or has repetitive eye poking). Then we include preferences of the individual which have a significant effect on efficacy of treatment.[98] For example, does the autistic adult or a parent wish to avoid medication or, in contrast, seek a pharmaceutical treatment for depressive feelings or overactivity? Is the adolescent comfortable in groups or interested in participating in online interactions? Family circumstances, life events and family preferences – to be seen at home or in a clinic; to work in a group or individually; to use medications or not – are highly relevant to the potential effectiveness of a treatment, as are the family's acceptance of the diagnosis and resources to participate. Finally, as noted earlier, individual characteristics of the autistic person, including cognitive and language level, severity of autistic symptoms, strengths, interests, motivation to participate, and mental health all contribute to the likelihood of change over time.[8]

Having gathered this information, the idea of stepped care is to begin with the least 'costly' approach. However, as we said above in personalised health, costs include not just the budgetary impact on health and other systems, but also the burden on the family and the person with autism in terms of time, effort, financial cost and stress. Certain locations or modes of intervention fall relatively easily in the first step as shown in Figure 6. Priorities would include treatments at schools or preschools (e.g., Treatment and Education of Autistic and Related Communication Handicapped Children [TEACCH],[99] JASPER[100]) or home-based treatments (e.g., Social ABCs[96]). Yet, even with these obvious suggestions, important caveats remain which include that there is sufficient support and time for school staff in the first instance and for travelling therapists in the second. Supported employment programmes that take place in the workplace, such as Project Search[101] or Ready, Willing and Able[102] also fall in this category. Telehealth could conceivably fall in the first step, though this assumes that families have internet access and individuals are comfortable in this situation, which, as we discuss later (see *Technology section* below), is not necessarily the case.

A next step, more costly in terms of time, inconvenience or funding, would involve some travel by the family or individual to a nearby clinic, or a significant commitment of time from the family. This means not just greater financial cost but a greater demand on the family in terms of carrying out more intense parent-mediated treatments (Early Social Interaction [ESI],[37] Preschool Autism Communication Trial [PACT][36,103]) even if delivered at home. Treatment groups, generally conducted in clinics often by non-specialists, and common medications, which require regular visits to a local physician, might also fall into this category. The cost of these treatments is not negligible if they require time, effort or travel from an autistic person or parent, even if they are considered affordable for a health system. Variability in how families or autistic persons can and do use these treatments also needs to be recognised.

A third step would be highly specialised care that requires substantial travel to a tertiary care hospital or clinic, intensive hours whether at home or in the clinic or frequent clinic visits. This would include inpatient treatment, as well as some naturalistic developmental behavioural interventions (NDBIs),[35] or interventions such as Parent-Child Interaction Therapy (PCIT),[104] which typically requires clinic visits by multiple family members. A range of circumstances share different but significant 'costs' for families and to the health system but are necessary for progress in some cases. One of the concerns with stepped care models is that individuals and families may get stuck in an early step of care, without consideration of needs that should be addressed in later, more costly steps. This is why assessments and monitoring or progress through measurement-based care with shared decision making is crucial in avoiding waste while ensuring appropriate allocation of needed services.

**Shifting Roles over Time**

As shown in Figure 6, the roles of the family, the autistic individual and the community in provision of services and in decisions will change over time, with family involvement predominant in early years, in most cases decreasing during school years and often, but not always, increasing in adulthood.[64] The community, as represented primarily by schools for elementary age children, provides the greatest number of hours of potential focused support, with significant reductions in community resources available after these years.[63–65] Type and intensity of interventions available vary greatly both within and between countries across the world. For example, the number of hours of intervention that 'treatment as usual' preschool children received, varied from 3 to over 15 hours a week across different U.S. regions.[95] Similarly, a preschool child living in one city in India might have access to a parent-mediated programme, but not to an organised preschool available in another city.[38] A preschool child in Scandinavia may be in an inclusive child care programme, with services provided to support the childcare workers, though the family may not receive autism-specific support for years.[105]

Figure 6. Sources of support and locations of treatment

[Figure 6 here]

**The Evidence Base for Autism Interventions**

There are many published clinical practice guidelines (CPGs) for autism from governmental bodies and professional associations around the world[106] (see Table 1), although the quality, composition of such groups and the methodologies employed vary considerably. Recent articles also summarise the situation in a number of regions including China,[107] Indonesia,[108] Iran,[109] South Asia,[110] Sub-Saharan Africa,[21] and Vietnam.[111] Some of the methods of guideline development are similar, predominantly depending on the recommendations of an expert panel reaching consensus about appropriate interventions based on systematic and expert review of the evidence.[112] However, conclusions vary from those that only recommend approaches supported by meta-analyses of outcomes from multiple RCTs[113,114] to others that recommend a broader range of interventions and practices based on expert consensus reviews, including evidence from case-

control ('quasi-experimental'), single case designs and cohort studies.[115,116] Furthermore, there is little agreement among practitioners about what is evidence-based and what is not, which calls into question an assumption that clinicians - who may have very different assumptions about what is "good enough" or who come from different professional trainings with different biases - will automatically accept guidelines.[117] The utility of CPGs to guide practitioners in the complex often inter-disciplinary interventions and supports necessary to provide adequate care for the heterogeneous autistic population will vary depending on the particular intervention under consideration, the nature of the service or care setting, and social and cultural contextual factors.[112] The growing number of CPGs from different parts of the world is an important step toward creating international standards for service provision and offering benchmarks for quality service provision, but, without critical appraisal, is not a remedy in itself.

Table 1. Examples of guidelines for autism assessment and interventions

[Table 1 here]

Historical and local cultural factors play a role in the approaches and thresholds that are employed to judge levels of evidence of autism interventions. For example, in the U.S., autism intervention research began with behavioural approaches (e.g., ABA) that used the manipulation of the onset, offset and resumption of treatment approaches across single cases rather than randomised controlled trials as a way of comparing different conditions. Such research designs are systematic, inexpensive and flexible in the ability to address the needs of different children. Yet, they have clear limitations including biases associated with small sample sizes, lack of information on generalisation and the role of development, and often non-randomisation or non-blind outcome assessments.[118] Randomised controlled trials (RCTs), when well-conducted, provide the least-biased estimates of efficacy and often incorporate other rigorous methodological strengths including manualised interventions, pre-specification of primary outcomes, attention to blinding of assessors and conservative intention-to-treat analyses. However, they also have well-known limitations such as unrepresentativeness of highly-selected samples, an over-reliance on research-directed programmes that may not transfer to wider community practice, and restraints on individualisation and modification of an intervention based on responses, as would occur in clinical practice.[33] Despite differences in approaches to interpreting data, there is increasing agreement about particular intervention techniques that are helpful, such as using positive reinforcement, visual materials to support behavioural expectations, and matching level of difficulty in language and play to child ability.[117,118] Researchers have more consensus than clinicians as to the value of different interventions, typically adhering to standards for RCTs and blinded assessment. However, as shown in Figure 5, clinicians have to make daily decisions about what to recommend and deliver and so often have to move beyond the typically short-term, low intensity interventions that have the strongest evidence.[30]

Not all forms of intervention and not all clinical practice across the fields relevant to improving outcomes for autistic individuals can be tested in conventional 'medical model' RCT designs.[119] The absence of evidence from RCTs for a particular approach may not mean the approach is ineffective (or effective). Moreover, several well-intentioned attempts to introduce large scale changes in schools with random assignment to different classrooms have been unsuccessful for a

variety of reasons.[99,120] Despite calls for such research,[71] implementing double-blind 'gold standard' RCT designs may not always be feasible in evaluations of longer-term, multi-component complex services often involving populations where randomisation is either practically difficult or ethically contentious. For example, in psychosocial trials, parent report of adaptive function or child behaviour will be affected by parents' awareness of participation in the intervention, introducing potential bias. As shown in Table 2, the evidence for interventions is weaker when such studies are excluded.[30] In efficacy trials vs. care as usual in HIC, it can be difficult to find and sustain a randomly assigned 'treatment as usual' comparison group because families may be able to access similar and sometimes even more personalised treatments through other avenues.[95] In fact, over time, community services change such that comparisons to treatment-as-usual may vary considerably as treatment-as usual changes.

As shown in Figure 6, we list common approaches to intervention at different ages recommended in many different sets of guidelines. For children under 5 years, parent-mediated interventions such as JASPER, PACT, Pivotal Response Treatment (PRT), ESI, PASS (Parent mediated intervention for Autism Spectrum Disorders in South Asia), and therapist- and teacher-implemented versions of ESDM and JASPER are the most commonly studied. Some, as shown in Table 2 (listed under Naturalistic Developmental Behavioural Interventions [NDBI]), have been supported by RCTs showing changes most commonly in the specific social communication behaviours taught, such as joint attention, synchrony and social interactions (JASPER, PACT, ESI, Social ABCs).[121] General programmes of psychoeducation (e.g., Hanen More Than Words) are often used as well, though evidence supporting them is more variable.[122] Direct treatments, using similar approaches, usually involving a non-specialist (e.g., a graduate student, a childcare worker) for very young children report a range of intensity from one hour to 40 hours a week. Well studied programmes have reported effectiveness primarily in increasing cognition and/or language (ESDM;[95] ABA/DTT;[88] PRT[34]) or early social communication skills (JASPER;[39] Social ABCs[96]). The potential effectiveness of classroom-based interventions, using similar social-communication models, has been shown in several studies, but typically with less strong research designs (ESDM[123]). The World Health Organisation Caregiver Skills Training (CST) programme focuses on teaching caregiving skills to parents of very young children and older children with developmental delays and disabilities including autism, and is being evaluated in many sites across the world.[124] This is a very important first step but still does leave the primary burden of support and treatment on the family.

Table 2. Forest plot for robust variance estimation for outcomes by intervention type (adapted from Sandbank et al., 2020[125])

[Table 2 here]

For school age children and relevant to some older preschool children, there are a number of short-term targeted interventions either with parents (e.g., Research Units in Behavioural Intervention [RUBI][126]), directly with the child (e.g., Behavioural Interventions for Anxiety in Children with Autism [BIACA][127]) or with mental-health therapists (e.g., An Individualized Mental Health Intervention for Children with ASD [AIM HI][128]) that address common co-occurring difficulties such as behavioural problems, anxiety and fears with good evidence of effectiveness from RCTs,

systematic reviews and meta-analyses.[69,70,129] Techniques such as writing social stories about anticipated events are widely used,[130] as are strategies to increase communication in order to decrease difficult behaviours. Within schools, the TEACCH programme provides principles for classroom organisation that are aimed at increasing predictability and self-regulation,[42] though so far it has been difficult to support its specific effectiveness empirically. Evidence for the effectiveness of programmes to support social skills during school recess or breaks and increasing social interaction with peers is stronger and is supported with several multi-site trials.[131,132] Outside of school, many social skills programmes have been designed (e.g., Program for the Education and Enrichment of Relational Skills [PEERS],[133] summerMAX,[134] Social Skills Training Autism – Frankfurt [SOSTA-FRA][135]) that have empirical support. Most of the change seen is in short-term specific behaviours such as increased play and interaction with peers with limitations in generalisability to broader social and social interactions, such as in school.[46] Many children in HICs also receive specific therapies, most commonly speech and language therapy and occupational therapy,[68] which are sometimes addressed in CPGs.[113,136] Speech Language Therapy and Occupational Therapy employ a variety of techniques used in NDBIs, for which there is at least clinical consensus about their value.[117,118]

**Adolescents**

Adolescents with autism have particular needs and strengths and the development and evaluation of interventions for this group requires more focused research attention. During adolescence, there is a general reliance on education through schools. There is convergent data from a number of studies (though randomisation has been impossible) that older autistic children and adolescents who attend inclusive schools providing general education have better outcomes than those in special education settings, including greater increases in IQ,[29,91,92] higher educational attainment and better achievement,[76] even controlling for the likelihood that placement in an inclusive school is associated with different characteristics of the child. Psychopharmacology becomes a more typical component of treatment of co-occurring conditions in adolescence and later childhood, including ADHD, anxiety and aggression (see *Co-occurring conditions section*; below). Formal guidelines across countries, and not surprisingly across professions, differ in whether psychosocial approaches should always be attempted before medication is introduced (see Figure 5). Social skills interventions and CBT[127,137] have been shown to be effective in reducing anxiety though not yet depressive feelings. However, we know far less than we should about how to optimise mental health and develop independence across the heterogeneity of autism; this is another area where research is needed.

**Adults**

To address the needs of adults requires local community and stakeholder collaboration in the development of programmes by researchers and clinicians, as well as systemic change. The majority of autistic people are adults, yet there are far fewer services and supports available for them and very few adult programmes have been rigorously evaluated.[118] For adults, similar treatments to those used with adolescents, including CBT, medication and social skills groups (e.g., PEERS) have all been shown to have some effectiveness.[138–140] Supported employment and job coaching programmes are available in some regions and there is growing evidence of their

effectiveness.[101,141] Programmes and systems to support adult development of adaptive skills exist but are seldom documented in research.[142] Behavioural programmes for adults with autism have been described for many years, although few are RCTs and many involve individuals with more severe intellectual disabilities. The use of behavioural approaches is also controversial among some neurodiversity advocates.[26] Adult services for people with profound autism and across the range of abilities are the area of greatest need in HIC areas and require systemic support. For LMIC, because few services are available at any age, needs are even broader across the lifespan. More widely, the need for awareness and training about autism, and in some cases specific support for individuals, has become increasingly recognised in statutory services in many communities, ranging from unemployment and job support services, to the police, the courts and prisons.[143]

Finally, many interventions developed for autism, for example, for social communication, could be useful for children, adolescents and adults with other neurodevelopmental disorders;[144] not having a diagnosis of autism should not be an exclusionary criterion for accessing an effective intervention. Similarly, interventions developed for other populations may be helpful with autistic people, sometimes with adaptations that recognise the particular social impairments or sensory challenges in autism. For example, CBT for anxiety with autistic adolescents has been modified to account for differences in cognitive style, communication and insight.[69,137] Interventions for autism cannot depend on being offered only by autism experts. The reality is that most treatment for autistic people of all ages, even in HIC, is not offered by specialists; most care is provided in educational and community settings which may or may not have consultation or support from experts.[145] Thus, as discussed later in the *Workforce capacity* section, training and supporting non-experts must also be part of research and systems planning. Critical factors include understanding what works with whom and when; and what are some of the predictable needs and variations that need to be considered to support autistic individuals. This information, as well as training and supervision, needs to be made available in an accessible way to non-specialist providers, from preschool and school teachers, to job coaches, to school or community professionals and to families.[146] This is another reason for measurement-based monitoring; if progress on goals is not occurring, ask why not.

Panel 4 summaris    es intervention recommendations for clinical practice across the lifespan.

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*Panel 4*
*Recommendations for Clinical Practice – Interventions*

1. Appropriate personalised health interventions in a stepped care model for a given child or adult requires integrating information from previous assessments, current providers and teachers, the family and the individual within the context of existing or possible local care.
2. Identifying appropriate formal treatments, community resources and everyday activities that may address goals and ways to support use of these resources, as well as reducing or eliminating services that are not effective or no longer needed, should be part of each treatment plan. Health care systems must support this communication, navigation and continuity.
3. Interventions must take into account the preferences of individuals and families and the implications of implementation in culturally diverse contexts. Evidence-based interventions in lower resource settings should be implemented, though adaptations and innovative strategies may

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be required.

4. Families and autistic adults who can speak for themselves should be involved at each step, but should never be expected to assume societal and community responsibilities for individuals who need support.

5. Families and people with autism are a vulnerable population, sometimes receptive to false claims of effectiveness and unstudied treatments that may have significant adverse effects.

6. Across the globe, psychoeducation and interventions for families and individuals with autism, that promote autonomy and personal choice and decrease vulnerability through knowledge, are essential components of equitable global and local models to support decision making across steps of care.

7. Intervention as soon as difficulties are identified is essential.
   a. Early problem-focused intervention for neurodevelopmental disorders should be accessible, based on screening and identified needs following a stepped care model, without waiting for an appropriate comprehensive assessment or formal diagnosis of autism.
   b. Co-occurring conditions including medical, developmental, behavioural and psychiatric should be addressed with adequate treatments as soon as they are recognised.
   c. Stepped care models based on personalised data and systematic monitoring should allow rational, graded increases or decreases in intensity of intervention when needed.
   d. Systems should prioritise evidence-based interventions, recognising that most of these treatments are short-term and focused, and that other ongoing approaches including education and employment support are also necessary to support autistic individuals over time.

8. Modifications to existing evidence-based treatments, including cultural adaptations, may be necessary to optimise both behavioural/psychological and medical approaches together and separately for co-occurring conditions in autism and to increase effectiveness and participation.

9. Adolescents with autism have particular needs and strengths; the development of clinical practices for them, most notably interventions, requires more focused research attention.

10. Typical lifespan involves more years in adulthood than childhood. To address the urgent needs of autistic adults requires collaborative participation by researchers, clinicians, self-advocates and families in the development of intervention programmes, as well as systems change.

## Screening, Assessment and Diagnosis

The primary aim of a diagnostic assessment is to inform treatment planning with an individual and a family. Given that there is no single 'autism treatment', the assessment should not only be a description of autism features but also should describe an individual's profile of strengths and needs and the family circumstances, resources and motivations that affect outcomes and care.[147]

## What is an Adequate or Appropriate Assessment?

Although the statement that we need more than a diagnosis sounds simple, there are more complexities to it than one might predict. Understandably for many families and adults, the primary concern at the point of an initial expert diagnostic consultation is a diagnosis, but in part, this may be because they are not yet aware that there is no single treatment for autism and that the course of an autistic individual's development is as much determined by other factors as by the

autism. Nevertheless, in some countries and regions, having a formal diagnosis of autism results in access to services and funding otherwise not available, a reflection of the influence of systems.

Beyond providing documentation that allows access to services within systems of care, the primary recipient of most assessments is the family or for verbally fluent adolescents and adults, the individual. Diagnostic assessments need to consider what the family already knows, what they want to know and what information will help them understand, support and advocate for their child. These factors can be lost when a provider makes a quick diagnosis without more information or sometimes even in long detailed written reports with little attention to questions raised by the family (e.g., including long lists of expensive treatments a family could not afford). For verbally fluent adolescents and adults, the same concerns hold true.

Many formal guidelines propose a multi-disciplinary assessment in order to address the basic characteristics of the child (or adolescent or adult) and family (see Figure 7). There is widespread agreement about gathering a history, observing the individual clinically and carrying out a broader evaluation of current functioning and family contexts. However, the practical outcome from this process, beyond arriving at a diagnosis and how to do this (e.g., by standardised or informal methods, by questionnaires or interviews or medical record review or direct testing) and in what context (e.g., in a standard office visit, in a waiting room, in a formal observation in clinic or school) is seldom delineated. For most guidelines, a 'clinical consensus' diagnosis by expert diagnosticians is considered the gold standard, but there has been little attempt to test the reliability over time or between clinicians of such judgements, or even how this would be measured. Studies that have addressed these questions within autism (comparing various previous subtypes of ASD) have found much variation.[148]

Some factors that have been repeatedly identified as major moderators of outcomes, such as language level, cognitive ability, adaptive skills and co-occurring mental and physical health conditions,[29,91,149] are specified as crucial in some guidelines, but not in others, in part depending on the region and the profession of the guideline-writers. In some CPGs, the assessment of such variables is considered as extraneous and either the responsibility of schools or social services outside of the healthcare system, which may not exist in some contexts. Research has established that lifelong outcomes are affected by factors beyond diagnosis, including cognitive or language level or co-occurring conditions, yet there are few systematic studies of how these variables contribute to responses to different treatments. This comes back to questions raised in our intervention section about the need to know which interventions work for whom and when, which in turn have implications for what needs to be evaluated.

It is also reasonable to raise the question of when a formal diagnosis of autism makes a difference, beyond consideration of other factors such as cognitive or language delays, mental health issues and other features. There are clearly many times when diagnosis does make a difference, for example, in obtaining early intervention for young children who are verbal but clearly autistic, or in creating an appropriate CBT programme for an anxious adolescent with autism, or in selecting a suitable medication for an older child with autism and ADHD. However, sometimes it may not. A valid diagnosis is a necessary step in developing an adequate treatment plan, but it should be considered a beginning, not an end. The lack of a diagnosis should not prevent the initiation of

intervention, though, in the long run, adequate assessments are important, as we have outlined above in matching the needs of a child or adult with autism and their family with services.

Contributing to the question of how important is the formal diagnosis of autism versus the provision of an individualised evaluation is the question of whether single-provider assessments are sufficient or multiple disciplines are necessary. Single provider assessments are less expensive, more realistic for LMIC, and even in HIC easier to organise and reimburse. In some studies, families prefer them.[150] Multiple providers participating in the same assessment require time to maximise team efficiency and maintain clear communication with each other and the family or individual, and often also result in families and autistic individuals having to repeatedly offer the same information. On the other hand, whether most single providers have the skills necessary to observe, measure and discuss with families the range of issues affecting individual children or adults is unclear.[151,152] Kanne and Bishop[147] highlight that, despite a 'waitlist crisis' in many countries and communities for evaluations at particular centres, short-cuts to speed up the diagnostic process, such as remote video capture or biological tests, do not actually address the problem. The shortcuts overlook the fact that the critical outcomes of a diagnostic assessment are fed back to the individual, family and other providers about the individual's profile of strengths and needs and the provision of individualised recommendations on intervention and care across development (for an example of research concerning the provision of feedback for a different condition see Schechter *et al.*[153]).

Moreover, there is much evidence to indicate that diagnoses with standardised information are more reliable across sites and more valid over time than single clinician judgments.[154] Including information from both caregiver report and clinical observation increases the reliability and validity of diagnoses.[155,156] The intention of any diagnostic instrument, like the use of many medical instruments (e.g., a thermometer, a stethoscope), is not to deliver an inarguable answer, but to provide standard data to a clinician who can use the data, together with other information, to make a diagnostic formulation and appropriate care plan over time. Thus, requiring clinicians to use at least one standard instrument in the documentation of severity of autism symptoms, with an awareness of the strengths and limitations of that instrument, seems an appropriate minimal standard, particularly if the instrument can be used as a benchmark in later assessments. Knowing there is a potential for change places responsibility on the provider to be able to document what improves, which currently happens relatively rarely. This presents a challenge to LMIC, particularly those with many different languages, but is beginning to be addressed by the development of indigenous instruments which can be translated at least into the major languages used by providers, if not all the families.[157]

Figure 7. Assessment flow and standardised instruments

[Figure 7 here]

**Stepped Care/Personalised Health Approach to Assessment**

Accompanying the stepped care/personalised health model we proposed for intervention, we also recommend an integrated stepped/personalised approach to assessment of the developmental and

functional profiles of neurodevelopmental disorders with a focus on individual and family needs (See Figure 7). This approach allows inclusion of a broader, more heterogeneous group of children and adults beyond only those who receive an autism diagnosis and avoids sequential disorder-specific assessments (e.g., one assessment pathway for autism; followed by one for ADHD) with a focus on developing a personalised intervention plan and monitoring change. This links to our stepped/personalised intervention approach that moves from matching assessed needs for broad-level entry interventions to increasingly intense and specific interventions according to identified priorities for the individual and family.[158]

Many children with autism are first referred for difficulties characteristic of other neurodevelopmental disorders, such as language delay or attention problems.[159] Conversely, children who are referred with concerns about possible autism may have other neurodevelopmental disorders without autism. A stepped/personalised approach allows consideration of these overlaps from the start. This is different than systems in which individuals with autism and other neurodevelopmental disorders are tracked into different types of service (e.g., education versus mental health services, or social versus medical services, depending on their diagnoses or needs) from an early age. We propose a stepped/personalised care model that can be adjusted as heterogeneous needs change with development and overlaps emerge across diagnostic categories and intellectual ability levels. In contrast to our intervention section, first we provide descriptions of empirical findings about surveillance and screening and assessments and then we return to consider the stepped care/personalised health assessment model in more detail.

### *Diagnostic Criteria for Autism*

The DSM-5 and ICD-11 diagnostic criteria are applicable at any age and level of language and intellectual functioning, with a range of possible manifestations. Social communication difficulties should be greater than those expected given the individual's general developmental level. Several different repetitive or restricted behaviours are required, but these, as with the social communication deficits, can be obtained from a developmental history. A diagnosis of autism also requires evidence of clinically significant impairment in current functioning, such as limited daily living skills, psychological distress, or need for support in everyday settings such as nursery, school, employment or the community.

A significant change in the current DSM-5[12] and ICD-11[13] was the removal of ASD subtypes (e.g., Autistic Disorder, Asperger's Disorder, PDD-NOS), folding them under the single diagnosis of Autism Spectrum Disorder or autism. Instead of unreliable categorical subtypes, the DSM-5 and ICD-11 require profiling of individual strengths and weaknesses, including the level of intellectual, language and adaptive functioning, and any co-occurring neurodevelopmental, mental health and medical conditions (see also NICE CG128[160]). These changes have the potential to radically re-conceptualise the field, as we have said earlier, in that the primary aim of a diagnostic assessment is to inform needs-based treatment planning and service provision, and to provide data for monitoring of progress and anticipation of later needs, rather than to provide a categorical diagnosis, with the assumption that needs change and improvements can occur. The introduction in this Commission of the term 'profound autism' (see Panel 2) is intended to further extend and amplify the 'clinical specifiers' that are included in both diagnostic systems, with a similar aim to

inform and help individualise intervention, support and care for some of the most vulnerable autistic individuals, who, nevertheless, still have the potential for better lives.

## *Early Identification and Surveillance*

Early identification of clinical signs is the first step to facilitating prompt referral for an assessment and diagnosis. In many cases, features of autism and other neurodevelopmental disorders are apparent early in development, though the specificity of these signs is still unclear. Retrospective and prospective studies, including those utilising high-risk sibling designs,[161] have shown that onsets of autism symptoms are variable across the first years of life, with suggestive, neurobiological group differences potentially measurable earlier[162] and clearer behavioural differences emerging from 12-months of age onward.[163] Some children show delayed and atypical development from early in life, others a plateauing of development over time, whilst some show a loss of skills already acquired. Incidents of such regression (mostly in social skills, including language) at about 15-18 months seem to be relatively unique to autism and some rare genetic neurological conditions such as Rett Syndrome.[164] Other children show symptoms which only become clearly visible later, usually during more complex social interactions with peers and unfamiliar adults.[165] Thus, heterogeneity is present from an early age including in patterns of symptom onset and progress.

Screening is the administration of a brief questionnaire or examination, usually at a single or a few predetermined ages, to rapidly identify individuals in need of in-depth assessment. A wide range of screening instruments for autism, general developmental delays and emotional and behavioural problems (see Figure 7 for examples) is available. However, there are contrasting views, both strongly supportive[136] and unsupportive,[166] on the strength of the evidence for their use in *universal* autism-specific screening in the absence of any parental or clinician concern. A recent meta-analysis of the parent-rated Modified Checklist for Autism in Toddlers - Revised with Follow-up (M-CHAT-R/F),[167] the most researched autism-specific screener, reported an overall sensitivity of 0.85 (95% CI 0.79-0.92) and specificity of 0.99 (95% CI of 0.99-0.99).[168] Nevertheless, whilst it is possible to identify some children with autism before parents or professionals have expressed concerns, in studies with systematic follow-up to mid-childhood, autism is missed in many screened children.[169]  Positive predictive values are low in general population studies (15% in Guthrie *et al*[169]; 6% in a meta-analysis by Yuen *et al.*[168]), with higher, but still moderate values (e.g., 53%) in 'high-risk' samples already identified with developmental concerns.[168] On the other hand, the process of screening, even when there are  'false positives,' may result in primary care physicians making earlier and more referrals that lead to intervention and support, including for children with other neurodevelopmental disorders but not autism who are identified by the screen.[170] There is a balance between the relative costs and benefits of screen false positives and false negatives; false positives may lead to unnecessary assessment and parental concern, whereas false negatives may lead to under identification, late diagnosis and delay in intervention.[136]

Developmental surveillance, a broader concept, in countries other than the U.S., is the ongoing, systematic monitoring of development over time, including the integrated use of clinical observation, asking parents about their concerns, family history and use of screening instruments such as those described above, repeated over time.[171] Autism screening instruments also identify

children with broader neurodevelopmental disorders.[136,166] Universal developmental surveillance of infants is common in some countries and regions.[114,172] Variability in the emergence of early signs of autism, another example of its heterogeneity, highlights the utility of surveillance in which children are monitored at regular intervals during their early years[171] and families can be referred on for help. However, access to universal healthcare is limited or even absent in many places, especially in low-resource settings and LMICs;[173] in such circumstances opportunistic contacts, such as immunisation visits can be utilised as a means of identifying early atypical development.

It is important, however, to recognise that many health practitioners (including community physicians and paediatricians) lack specialised skills and training regarding neurodevelopmental conditions, including autism, in infancy. Thus, the training of professionals on early signs of atypical neurodevelopment remains a high priority if we are to identify, diagnose and intervene in a timely fashion.[136] Descriptions of early signs and symptoms of autism are available to support professionals, as well as to help raise public awareness.[114,174] In addition, well-established risk factors for autism have been identified, including parents expressing concern that their child might have autism,[175] preterm birth, a family history of autism, and a number of genetic syndromes such as Tuberous Sclerosis Complex and Fragile-X Syndrome.[176] It is also important to be aware of referral and recognition biases related to gender, ethnicity and social disadvantage that impact the timely identification of neurodevelopmental concerns, an autism diagnosis and access to provision such as education support.[177,178]

Despite the availability of this information, the reality for many families is that children in both HIC and LMIC countries are not identified early and only recognised when they enter formal educational settings such as kindergarten or school, if at all.[179,180] Often, later manifestations of autism coincide with periods of transition, for example, entry into high school or leaving school. These are therefore important developmental stages at which professionals involved in these systems should know the signs and symptoms of autism in order to refer families for advice (see NICE[160]). At whatever age an individual is identified as having concerns regarding neurodevelopment, in accord with the belief that lives can be improved with help, they should be promptly referred for assessment.

### *Assessment of Functioning and Support Needs*

At the point of initial recognition of difficulties, the priority should be to identify the areas in which the individual (and their caregivers) has needs and to identify services within the community that can provide support and intervention. As shown earlier in Figure 7, a needs assessment can be brief, but should identify key strengths, concerns, and functional impairments. A clinical interview with caregivers (and individuals able to self-report), or standardised instruments that cover a range of symptoms, strengths and challenges and provide red flags for follow-up about support needs can be used. Findings from all these sources should be summarised in a written report, available to the family and appropriate for their level of language and understanding. Although standardised instruments can be useful to structure a clinical interview, they are no substitute for in-person, open-ended questions about concerns and needs. Professionals should be aware that parents vary in their understanding of their child's needs, particularly when it is a first child, and/or when the child is very young.  Questioning must take account of the families' socio-cultural background.[181]

Most important is to recognise that evaluating needs is an ongoing process, which in current systems is often overlooked. For example, some families at the time of diagnosis believe that, once their child can speak, everything will be fine; yet as the child develops or as they encounter more information about autism, they become aware of other needs and challenges. Other families may begin with many identified areas of need and narrow them down as they prioritise particular issues of greatest current relevance in the context of the resources of the family, the person with autism and the wider community.

### Diagnostic Assessment and Treatment Planning

Whereas a brief needs assessment can be used for access to broad-level services, a more in-depth assessment is essential to give families and individuals information and to develop a personalised plan for targeted interventions, as exemplified in Figure 5. Core components of a diagnostic assessment for autism, and neurodevelopmental disorders more broadly, are to document relevant aspects of the individual's developmental history and to construct an individualised profile of treatment-relevant strengths and difficulties. These will include verbal and nonverbal skills, adaptive functioning, social communication difficulties, behavioural flexibility, and emotional, behavioural and medical functioning. Stepped/personalised assessment can be used for each component. This means that the clinician can consider what information is already available (e.g., achievement tests or IQs from school reports) and what is lacking (e.g., a detailed assessment of receptive language if this is in question or a description of peer interactions); conduct a brief assessment or screening to check for issues, and, then if indicated, carry out more comprehensive evaluation. Clinicians from many disciplines (e.g., physicians, psychologists, speech-language pathologists, social workers) can lead the assessment process, if they have training in autism and related disorders. Due to the need for assessment of multiple domains of functioning, input from clinicians of multiple professional disciplines is ideal (see CPGs in Table 1). If multidisciplinary assessment is deemed unnecessary or is not possible (e.g., in low-resource settings), the lead clinician is responsible for being sure that all other components are addressed, if appropriate. For example, if a child is seen only by a physician or nurse practitioner, they should attempt to determine verbal and nonverbal level for the child if they have the training or refer for additional testing.

### Core Assessment Components

### Assessment of Social Communication and Restricted, Repetitive or Sensory Behaviours

Diagnosis of autism requires integration of information across multiple contexts (e.g., in daily life at home, in the clinic setting, or at school). An array of standardised diagnostic instruments allows evidence-supported documentation of autism symptoms in social communication and restricted, repetitive or sensory behaviours and can provide benchmarking for later re-assessments of change over time (instruments that provide this are marked with an arrow in Figure 7), though putting together this information still depends on a competent clinician. Examples are listed in Figure 7, some of which are open source (marked with an asterisk). Evidence supports use of a combination of instruments based on parent account and direct clinical observation.[155,156] The Autism Diagnostic Interview–Revised (ADI-R)[182] and the Autism Diagnostic Observation Schedule–2nd

Edition (ADOS-2)[183] have been most widely used in clinical practice and research studies (mostly in tertiary healthcare settings, larger school systems in the U.S. or research) in HIC. The need to take a global perspective on autism is driving attempts to develop scalable (usable in different places and situations), open access tools, which are not limited by their proprietary costs, but this work is currently in its infancy.[173] A validated open access diagnostic tool was developed in India and has now been made available but would benefit from being evaluated across diverse populations and compared to gold standard approaches.[157]

### *Language, General Developmental Level, and Adaptive Skills*

The diagnosis of autism entails assessment of social communication skills and behavioural flexibility in the context of the individual's developmental level and language skills. An estimate of overall developmental level should precede assessment of social communication and repetitive behaviour. Studies show that standard cut-offs on many instruments for autism have low ability to differentiate between individuals with autism and individuals with severe global developmental delay without autism.[155] The ADOS-2 provides age- and language-standardised cut-offs and dimensional scores for social communication difficulties and repetitive behaviour patterns (separately and combined). These features allow the clinician to consider developmental level,[184] which may be especially important in the differential diagnosis of intellectual disability or identification of a co-occurring diagnosis.

As shown in Figure 1, language and intellectual functioning are also among the reliable predictors of prognosis in autism. For example, first words by age two and flexible phrase-speech by age three are predictive of better social functioning in adolescence and adulthood.[185] Further, nonverbal IQ within the average range by age three years is predictive of a more positive developmental course and outcomes in adolescence and adulthood[75] and may be related directly or indirectly to differential treatment responsiveness. Assessments of the individual's receptive and expressive language skills, nonverbal problem-solving, and adaptive skills are necessary to assign DSM-5 clinical specifiers, relevant to ICD-11 subtypes and have implications for prognosis and treatment planning.[136] Informal estimates do not provide the same information as standardised assessments and may limit reliable and valid focused follow-ups, which should be a priority even in LMIC.[152] Efforts are underway to develop more scalable methods for LMIC countries.[186] Brief, norm-referenced tests of non-verbal and verbal ability are available to provide a rough estimate of developmental level; these can be administered by providers experienced in clinical assessment who are not psychologists in as little as 10-15 minutes.[187]

### *Screening for Emotional and Behavioural Problems*

Given the frequency and the importance of co-occurring problems, assessment of potential difficulties beyond autism is essential (see *Co-occurring Conditions* section below). Several questionnaires and norm-referenced screeners are available to detect signs of emotional and behavioural disorders. These measures are available in versions for parents, teachers, day care staff, and self-report, some are free, and some are available in many languages (Figure 7); though they do not generally have empirically validated cut-offs for autistic populations, so should be used descriptively. Identification of symptoms calls for further assessment to evaluate severity and

diagnosis of a co-occurring condition. For example, parent reported hyperactivity may be an indicator of concomitant ADHD and this can then be further assessed using a range of questionnaires and more structured observation and interviewing.[188]

*Medical Evaluation*

As shown in Table 3, the purpose of the medical evaluation is to identify potential aetiologies and co-occurring medical conditions that require further assessment, inform recurrence risk, or integration into intervention planning. Several organisations have published guidelines for medical evaluations (see CPGs Table 1). What constitutes an adequate medical examination of a child or adult with autism varies widely across countries and professional associations. There is agreement that a medical history, family history, and a physical examination are essential to document growth parameters, physical and neurological abnormalities including tics, motor function, and dysmorphic features/congenital anomalies suggestive of genetic syndromes in need of further testing (see *Co-occurring Conditions* section below). If there are any concerns about a lack of previous standardised assessment of hearing and vision, these should be recommended. Additional workups, such as blood tests, EEG, or MRI are pursued only if indicated by presenting symptoms or history. Oral hygiene should also be addressed in every person with autism on a regular basis. In some, but not all countries, genetic tests are a standard part of a medical assessment.

Table 3. Medical evaluation for autism

[Table 3 here]

## Assessment Process and Diagnostic Formulation

Similar to treatment decisions, a stepped/personalised approach can be used for time- and resource-efficient assessments. In some cases, the presentation of autism is clear, and a standardised instrument may only be needed to benchmark the severity and types of social communication difficulties and repetitive behaviour patterns for treatment planning. In other cases, the presenting symptomatology is unclear or complex; for example, a child who clearly has ADHD but also other difficulties, requiring further assessment of autism symptoms. A study of sequential assessment strategies showed that about two thirds of toddlers referred to an autism specialty clinic received sufficiently high (52%) or low (20%) ADOS-2 scores with high probability that another autism symptom measure (ADI-R) was unlikely to provide incremental diagnostic prediction.[189] We further examined the performance of this decision rule for this Commission and found that of 448 toddlers screening positive in the population based Autism Birth Cohort Study in MoBa,[175,190] 6% had sufficiently high scores and 80% had very low scores on the ADOS, respectively, thus potentially reducing the need for further autism testing beyond an ADOS to 14% of at risk children.

Scores and diagnostic classification derived from standardised assessment instruments (e.g., scores, classifications, likelihood ratios) should be integrated with other relevant clinical information, including consideration of factors known to influence instrument performance (e.g., gender, level of intellectual ability, emotional and behavioural difficulties, cultural context). However, clinicians should use at least one standardised instrument and use it over time, even

though none of the available instruments are perfect. An important clinical question is whether the pattern of symptoms is better explained by another condition. For example, a child with language impairment but developmentally appropriate social communication may warrant a diagnosis of a developmental language disorder.[191] A child with social impairments characterised by impulsive behaviour or discordant relationships but insufficient social deficits otherwise may be diagnosed with ADHD. When the diagnostic conclusion is autism, relevant diagnostic specifiers, such as language delay, are warranted and will inform treatment planning.

Dimensional scores, such as the ADOS CSS (Calibrated Severity Score) and the Social Responsiveness Scale (SRS) T-scores, are useful to benchmark the degree of social communication difficulties and repetitive behaviour patterns.[76] Even if the diagnostic conclusion is not autism, the degree of autism-related symptoms may be important to document because of relevance for treatment planning and tracking potential changes over time.[184] When a clinician is uncertain about a diagnosis, additional information can be gathered (e.g., home videos, teacher reports, parent observations) and another visit within weeks or months may be necessary. A second visit, occurring in a reasonable length of time (i.e., weeks) or after a transition (e.g., starting school) may be particularly valuable for very young children or older children and adolescents with complex difficulties to rule in or rule out a diagnosis of autism. Continued surveillance and re-assessment may be necessary, but, even in cases for whom the diagnosis is not yet confirmed, supports and interventions addressing the child, adult, and family's needs should be initiated.

### Communicating the Assessment Results

Guidelines for communicating information about a diagnosis are available in numerous sources (see Table 1). Most guidelines include meeting in person with the individual/child and family to describe the profile of strengths and challenges, the diagnostic conclusion, what it means for prognosis, as well as individualised recommendations for supports and interventions. Acceptance and understanding of their child's 'difference' will vary according to family, community and cultural perspectives. A second meeting with consideration of the family's cultural perspectives and views on child development may be necessary. For families, learning to work with providers and systems is a process that evolves over time. Participation in a thoughtfully conducted assessment and feedback can make a key difference and increase continued engagement.[192]

### Focused Follow-Up Evaluations

The strengths and challenges of individuals with autism change across developmental periods and over time[29,193] and it is the clinician's responsibility to ensure that families have ongoing care. In many countries, including HIC, there is an emphasis on initial diagnostic assessments with minimal follow-up. Focused follow-up assessments should be used to monitor progress and to anticipate vulnerabilities, social difficulties (e.g., bullying) and disorders (e.g., depression) as well as family circumstances, particularly at times of transition (e.g., entry into high school, move from paediatric to adult services). Theoretically, within a stepped/personalised care model, the primary care provider could assume the lead in ongoing care, monitoring risk, advocating for families' needs and referring to specialty care as needed,[136] though how often this happens currently is not clear.

**Adolescents and Adults**

Adolescence is a unique period in development that shares some issues with adulthood, such as sexuality and others with childhood, such as parental interactions. As with typical adolescents, the adolescent with autism may assert a desire for more privacy and independence. However, parents are still responsible for their care and are usually the instigator of evaluations and primary reporters. In adolescence, assessments will be very different for young people with profound autism than those with average or higher intellectual ability and those in between. To the extent possible, attention to the questions and priorities of the young person as well as their caregivers is warranted. Referrals are often made because of immediate difficulties related to co-occurring disorders or transitions such as into or out of secondary school. It is possible, but difficult to determine appropriate cognitive and language tests for intellectually disabled adolescents and adults depending on the purpose of the evaluation. Assessment of adaptive skills is particularly important.[193] Parents' memories of early histories may be limited. At this age, teachers may know students less well than teachers of younger children. However, diagnostic measures do exist, as do assessments of potential co-occurring conditions such as ADHD, limited executive functioning, depression, anxiety and irritability.[188]

General expectations for assessments of adults seeking a possible diagnosis of autism are similar to those for children and adolescents but differ in the reason for assessment and the parties involved (e.g., if the impetus for the evaluation came from the adult individual, spouse, family member or a social/legal service).[194] Assessments of children and adolescents depend heavily on parent reports, which are often not available for adults. Siblings, with permission of the adult, may provide important historical information if parents cannot. Typically, self-reports of autistic adults may yield discordant information from standardised clinical observations or reports of others close to them;[195,196] this calls into question research that relies solely on self-reports and highlights the need for supportive information. On the other hand, Patient-Reported Outcomes are a major interest in many HIC.[197] In HIC, adults coming for first a diagnosis usually do not have intellectual disabilities,[198] and often have other mental health conditions including anxiety, depression, ADHD,[15] vulnerability to sexual exploitation and learning disabilities,[199] as well as disorders that are less commonly associated with autism but have some overlapping features, including schizophrenia.[16] Thus, the diagnostic assessment of adults requires familiarity with autism and other adult mental health conditions as well as knowledge of associated services. Standardised measures have lower specificity and sensitivity with adults, but in some studies have been very helpful.[200]

**Autism in Females**

Another aspect of heterogeneity is reflected in the current interest in whether autism presents differently in females compared to males. This is to be welcomed, not least because in one UK population-based study girls with similar levels of symptom expression to boys were less likely to receive a diagnosis of autism from clinical services.[201] This might reflect sociocultural factors in the application of the diagnostic criteria, differential sensitivity in the commonly used screening and diagnostic measures (though this has been fairly consistently disproven in large scale studies),

or greater resilience or protective factors in girls that appear to reduce the need for clinical services at a given symptom level.[202] In epidemiological studies the prevalence of autism is three-to-four times higher in males than females, although the ratio is lower in those with severe intellectual disability.[5,203] Under-recognition and under-diagnosis in females may account for a proportion of this difference. Findings on age of diagnosis are not consistent but where sex differences have been found females tend to receive the diagnosis later than males.[5,204]

Much of what we have learned about autism has been largely based on clinical presentation and scientific investigation in males, notwithstanding the fact that Kanner included descriptions of girls in his seminal early accounts.[3] In studies that have examined sex differences in phenotypic presentation, the most consistent finding is lower severity of restricted and repetitive behaviours in females with, conversely, in some but not all studies greater social-communication impairment in females, though effects sizes are small.[205,206] In addition, some studies have reported higher levels of externalising behaviour in females than males.[205] Clinicians need to be aware of the potential for under-recognition of autism symptoms in females and different expressions in particular symptom clusters. In the social communication domain, potential female advantages mean that the presentation may be somewhat different from that seen in males, with higher social attention or motivation for friendship.[207] In the domain of rigid and repetitive behaviours and interests, symptoms may be misinterpreted if viewed through the cultural lens of activities that are typically considered gender appropriate. For example, young autistic girls may, like their peers, have a large collection of dolls (rather than trains for boys) but these are only played with in an isolated, repetitive and non-imaginative manner. Few replicable findings on cognitive differences have been reported, although the notion that females with autism may in some ways 'camouflage' or 'compensate' for autistic difficulties has attracted much attention, including from autistic women who identify with the concept, but requires further empirical validation.[208] Personal accounts from females describing their experiences of growing up with autism are helpful for clinicians, carers autistic females, and provide models of female autistic self-identity.[209] Questions of how some interventions may have different effects with females than males have seldom been addressed and should be taken into account by clinicians and families.

### *Gender Nonconformity*

Gender nonconformity, or 'gender variance', including transgender gender identity and non-heterosexual sexual orientation, is more common in autistic individuals (and those with other neurodevelopmental conditions) than in the general population.[24] This may be part of a different self-concept, less reliance on or reference to social norms and/or part of a neurodiverse experience of, and outlook on, the world. For some individuals in combination with an autistic self-identity gender nonconformity is an example of social and cultural 'intersectionality'. Clinically, recognition and assessment of these issues is important with respect to identifying individuals - both male and female - who may be vulnerable to (sexual) exploitation and bullying from peers. There is also an elevated prevalence of DSM-5 gender dysphoria (called 'gender incongruence' in ICD-11) in autistic individuals.[210] Recognition of possible autism in this clinical population is important as this would indicate the need to tailor interventions that can be used to ameliorate potential resulting distress and self-harm or neglect, as well as potential medical interventions including puberty suppression and cross-sex hormone intervention. Clinicians and parents may

sometimes dismiss gender dysphoria as an autistic trait, as an unusual or over-focused interest. Conversely, there is potential for under-recognition of possible autism in an adolescent if their social difficulties are ascribed to gender dysphoria in isolation instead of potential signs and symptoms of autism.[210]

**Barriers to Access and Global Differences in Approaches to Assessment and Diagnosis**

Certain groups, within HIC and LMIC, are more vulnerable to late identification and diagnosis of autism; these include females, children with age-appropriate language and cognitive skills or ADHD symptoms, and children in families of low socioeconomic status, ethnic minorities or those living in non-urban areas.[211,212] Most individuals with autism remain undiagnosed in LMIC[213] and other low-resource settings, where developmental surveillance is rarely performed for any neurodevelopmental disorders. Parents with concerns about developmental delays may struggle to obtain a referral to a service with capacity for developmental assessment. Many LMIC have low levels of literacy that restrict families' abilities to access appropriate services. Children may be brought to clinics by adults other than their biological parents, limiting historical information. In spite of parental concerns about their child's development, many families do not start the journey to assessment and diagnosis due to lack of awareness, stigma or financial barriers. Indeed, families may receive false reassurance in primary care settings due to a lack of knowledge among staff about neurodevelopmental disorders such as autism and may then face long delays to reach a specialist level of care due to the limited numbers of specialist centres. In LMIC, and low-resourced regions within HIC, children who finally receive a diagnosis tend to be those with more complex clinical presentations including intellectual disabilities or epilepsy. Children with milder social communications delays may not come to clinical attention, if at all, until adolescence.[214]

**Summary of Stepped Care/Personalised Health Approach**

We advocate for a stepped, personalised, transdiagnostic approach that addresses development and multiple dimensions in identification, assessment, and treatment. This approach moves away from an emphasis on a categorical diagnosis as an endpoint toward a focus on treatable problems that affect the quality of life of the individual and families within their communities. In HIC and LMIC, this model recommends that assessments focus on information that is relevant for treatment planning in collaboration with families. Follow-up care should consider mutual goals set out by the clinician and the autistic individual and/or family to monitor progress and ongoing service needs. In addition to an emphasis on family and individual priorities, personalised stepped care can employ brief caregiver reports, validated screening measures to identify the need for further investigation, to rule out particular concerns (such as developmental delays or co-occurring conditions), and to highlight ways to use community resources within the context of the family and community.

Below Panel 5 summaris      es screening, assessment and diagnosis recommendations for clinical practice.

| *Panel 5* |
| --- |

*Recommendations for Clinical Practice - Screening, Assessment and Diagnosis*

1.  Developmental surveillance within healthcare and education systems can identify young children with autism and other neurodevelopmental disorders whose difficulties have not previously been recognised or characterised. Screening instruments can provide useful information but should not form the sole basis for triage for further assessment and support. Parental concerns should always be elicited as part of ongoing developmental surveillance.
2.  The aim of a diagnostic assessment is to inform intervention and service planning for the individual and family.
    a. The assessment must be more than an enumeration of autism features and a formal diagnosis and include the identification of strengths (e.g., visual-spatial skills, attention to detail) and difficulties (e.g., language, motor), general delays, adaptive skills (e.g., toileting, dressing), behaviour problems (e.g., temper tantrums, aggression) and overall health that may not fit into formal diagnostic categories but are relevant to short-term and long-term outcomes and care decisions.
    b. Co-occurring conditions, including intellectual disability, should be considered with the same diagnostic and treatment standards in people with autism as in other children and adults.
    c. Personal and family concerns, preferences, resources and needs should be considered right from the start in any evaluation.
3.  Use of at least one standardised instrument for documentation of the severity of autism symptoms and to provide a benchmark for later re-assessments is recommended when empirically tested instruments are available that are appropriate for the culture and community. Clinical consensus is indeed the gold standard in many countries, but available evidence for the reliability of these diagnoses is seldom reported and other data strongly suggests that clinicians make more reliable decisions when they have access to standardised information from caregivers and observations.
4.  Because needs and skills change over time, re-assessments are essential for adjusting interventions and services. In addition to reviewing original treatment goals and overall functioning, validated measures of behavioural problems and adaptive functioning allow evidence-based monitoring of progress. Given the rapid developmental changes in preschool years, focused re-evaluations within a year of first diagnosis are strongly recommended. In school age, adolescence and adulthood, follow-up visits should address transitions, specific concerns and progress.
5.  Medical evaluations identify potential aetiologies and co-occurring medical conditions that may require further assessment or specific treatments. The medical evaluation may also prompt genetic testing that may not affect treatment but may inform recurrence risk and families' access to information.
6.  Evaluations of adolescents and adults may require adaptations from traditional approaches to address the role of parents and families and recognition of the rights and desires of the teenager or adult, and the somewhat differing concerns (e.g., sexuality) and co-occurring disorders that arise in this age group (e.g., anxiety or depression) is also warranted.
7.  Females, children with co-occurring disorders, those with age-appropriate language and cognitive skills, and children from socially disadvantaged backgrounds, ethnic minorities or living in non-urban areas are at elevated risk for late diagnoses. Increased clinical awareness and policy changes are needed to improve detection in these subgroups.

**Designing Research that Has Meaning for Practice**

**Prediction of Treatment Response; From Assessment to Intervention**

With a better understanding about who is most likely to respond to which interventions, when, and at what intensity and for what duration (e.g., the interaction between heterogeneity and treatment response), resources could be allocated more equitably to those most likely to benefit. In addition, more input is needed from autistic individuals and their families about their experiences, needs and aspirations. This information is also relevant to prioritising capacity building to provide different sorts of interventions in LMIC and underserved communities. Some studies have shown that children with better skills at baseline make the greatest gains.[88,215] In contrast, other studies found that children with the fewest skills progressed while more skilled participants did not improve.[122,216] This is especially relevant in clinical trials where investigators are expected to define the minimal level of change needed to justify the treatment. The number of adequate measures is limited, but even more limited is our ability to identify mediators, which are very rare, and moderators, including the factors above that affect individuals' responses to various treatments. The specification of minimally meaningful improvement may be more straightforward for medication studies than, for example, teaching parents who begin with different levels of skill or knowledge to support their children's communication, which also varies. It is possible to compute these metrics for many autism treatments, but this is seldom done.

Matching treatment type (e.g., parent-mediated or direct, CBT or medication or both) and intensity (for preschool children 5 or 20 hours a week in a structured program) to need and benefit is particularly important in planning services in low-resource contexts, but also in HIC where expensive, intensive treatments may be used when not needed or when unlikely to result in the promised change. Analyses in autism studies that identify factors that predict greater treatment responsiveness (i.e., moderators) are rare due to insufficient sample sizes, variability in measuring informative predictors (e.g., some studies do not include language level or IQ; others do not include family factors), and because randomised clinical trials often deliberately impose stringent entry criteria to control variability. For example, participants with very low IQs or severe behaviour problems are excluded from many studies.[217] Studies that have the power to address actual mediators are even more rare.[218] An area of increasing interest that may in future improve precision of measuring potential moderators is the identification of relevant stratification biomarkers (e.g., biochemical indices, genotype, EEG or neuroimaging signature).[79,219,220] However, these measures first need to meet basic standards for replicability and validity and then be tested in trials to provide evidence that biological differences do relate to different intervention mechanisms and responses. Such work is currently underway in a number of international consortia (European
Autism Interventions—A Multicentre Study for Developing New Medications [EU-AIMS-2];[221] Autism Biomarkers Consortium for Clinical Trials [ABC-CT];[219] Province of Ontario Neurodevelopmental [POND] Network[220]) but translation to routine clinical practice, even in expert centres in HICs, is at least several years in the future.

**Using Evidence-Based Approaches to Streamline Assessments**

A more efficient approach for moving from assessment to effective treatment in the face of heterogeneity is based on the psychometrics of diagnostic and dimensional assessment instruments that make use of what we already know about treatment-related issues such as presenting problems,

referral concerns, developmental level or age (see Figure 7). This approach recognises that we are often dealing with more than one disorder and, if we can use relatively brief questionnaires to rule out some conditions, more assessment time can be spent on critical matters. In line with stepped care/personalised medicine, this approach is focused on supporting the clinician in offering the most appropriate services given a child, adult or family's needs.[222] Here we again present new epidemiological data from the Norwegian Mother, Father and Child Cohort Study (MoBa) in order to illustrate how to apply these strategies.

Figure 8. Probability-based approach to assessment

[Figure 8 here]

Figure 8 illustrates how the pre-test probability that an individual has a given diagnosis or treatment need can be estimated. A likelihood ratio (LR) is then used to combine this probability with information from risk factors and with results from standardised instruments to ask if the probability is high enough to 'rule in' or 'rule out' a particular diagnosis or treatment need. This is a more sophisticated version of the earlier discussion on whether the ADOS alone is sufficient or if the additional time for an ADI is warranted.[189]

In the Norwegian MoBa population sample of 679 35–47 month-old children assessed in the Autism Birth Cohort Study clinic,[155] likelihood ratios of diagnosis of autism were derived for single and combined instrument criteria[175] for children who were diagnosed with autism (n=66) or other neurodevelopmental disorders (*n*=303).

Figure 8A shows the likelihood ratios of autism based on results from single instruments (left columns) and combinations of parent-based instruments and the clinician-based ADOS (right-most four columns), which can help estimate the post-test probability of autism in an individual case. Positive likelihood ratios are informative for 'ruling in' diagnosis or treatment need, with a LR+ of 2, 5, and 10 corresponding to around 15%, 30%, and 45% increases in probability. Negative likelihood ratios, on the other hand, are informative for 'ruling out' with LR- of 0·5, 0·2, and 0·1 corresponding to around 15%, 30%, and 45% decreases in probability.[223] In this approach, the recommendation is to start with a broadband screener, and move to more specific and comprehensive instruments as necessary to increase or decrease the probability sufficiently to rule the diagnosis/treatment need in or out.[222]

Figure 8B shows an example of a toddler with a 50% starting probability of autism. An SDQ-Prosocial score of 6 or below would increase the probability of autism to 63% when considered alone (lightest pink), and to 88% if combined with an ADOS result above the ASD cut-off (medium pink). In contrast, an average-range (>6) SDQ-Prosocial score would reduce the probability to 29% (light green) when considered alone, and to 7% if combined with an ADOS score below ASD cut-off (dark green). In some cases, a single instrument result could change the probability sufficiently to exceed the rule-in or rule-out threshold. For example, in this case, an ADI-R Toddler score that meets the more stringent 'Research' threshold would increase the autism probability to 92%. If this exceeded the personalised probability threshold, and the clinician's

interaction with and observations of the child also supported a diagnosis of autism, the individual, family and clinical team could decide to finish the stepped/personalised assessment.

The clinician needs to 'personalise' the threshold for ruling in and out a diagnosis/service need (Figure 8C), taking into account the benefits and costs associated with the diagnosis, intervention and the family's perspectives and preferences (see Figure 5).[224] For example, a moderately high probability threshold might be sufficient when the goal is to evaluate if a child with anxiety is in need of autism-adaptations in CBT treatment; or in deciding if a language delayed preschool child should receive a low intensity parent-mediated early intervention aimed at improving social communication. On the other hand, in a diagnostic evaluation for long-term treatment planning or beginning an intensive autism-focused behavioural treatment, the clinician and the individual or family may together decide on a high probability threshold.

This approach is common in evidence-based medicine. In mental health, published papers using similar approaches are available for bipolar disorder[225] and ADHD.[226] Printable visual probability nomograms (e.g., Figure 8B), online calculators and apps are freely available within the academic clinical psychology world to calculate post-test probability.[227] These probabilities are not necessarily something a clinician would calculate for an individual patient, but rather a way that clinicians could use group data to make recommendations for sequences of assessments and potential cut-offs (which would depend on the context and the characteristics of the individual). As in Figure 7, clinicians must integrate information beyond reading scores on instruments to move through personalised steps.

**Mechanisms of Change**

Despite the growing body of empirical support for a small number of treatment approaches that work in autism, and the use of interventions with clear or probable evidentiary support, we know relatively little about how or why evidenced-based treatments work, either in terms of mechanisms of change or active ingredients. The focus lately of many research funders in HIC has been on the identification of neurobiological factors that could contribute to positive treatment response (as summarised above).[219–221] To date, however, the usefulness of these research efforts to families and clinicians has been tantalising but less fruitful.[1] In particular, the difficulties of identifying the role of biomarkers in treatment response are manifold. First, because of the heterogeneity of autism, the putative biomarker may only be present in a subgroup and miss detection. Second, the developmental nature of autism suggests that a given biomarker may be relevant at certain stages of development but not others. Third, the replicability of neurobiological measures and their applicability to individuals beyond specific subgroups remains in question.[228] More focused consideration of behavioural factors that mediate change, which can be reliably measured and are more accessible to most providers, might provide more immediately useful information.

Moreover, the effectiveness of an intervention in an RCT may be affected by known or unknown (and measured or unmeasured) intervening variables (e.g., improvement in co-occurring sleep problems or decreased parental stress during an intervention study may contribute to improvements in disruptive behaviour).[229] In these examples, it may be difficult to determine the time sequence or the direction of change: did a decrease in the child's disruptive behaviour reduce

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parental stress, which then contributed to improved parental efficacy and further reduction in disruptive behaviour or vice versa.[230] Collectively, these considerations indicate the need for more tailored intervention approaches with a priori hypotheses about mechanisms of change, including psychosocial factors as well as neurobiological measures, built into research designs with sufficient sample sizes to detect them.[216,218]

In the meantime, studies of environmental and active behavioural ingredients do exist. There are replicated findings on the importance of changes in parental behaviour for social communication outcomes and core diagnostic features in the child.[103,231] In fact, the documented feasibility of many parent- mediated interventions even provide "implementation" data that are sorely needed for interventions in the community. Proximal improvements in joint engagement have been linked to downstream effects on social communication skills and language development.[40] Successful engagement in school playground activities predicts positive response to social interventions.[232] Parental and caregiver preferences and beliefs in a treatment may be relevant to child treatment response and potential change.[98]

**Intensity and Duration**

Our knowledge about *how much* and *how long* a given intervention should be delivered remains limited. To date, there have been few systematic comparisons.[39,95] A recent study by Rogers *et al.*[73], conducted across 3 different sites, compared two relatively high intensity conditions (i.e., 12 vs. 20 hours a week) of two types of intervention (i.e., ABA and ESDM) for two-year-olds with autism. There was no overall effect of treatment intensity on autism symptoms, although greater improvement was found at 1 of the 3 sites with greater intensity. This is a start: A next step would be to determine if regular, relatively intense. face to face interventions of this kind have different effects than typical clinic visits or low intensity parent-mediated interventions that occur even less frequently.

Current public policy debates in many countries on the format and resources for early intervention are occurring in the relative absence of reliable data. In both HIC and LMIC, decisions about timing and intensity of treatment should be based on evidence, rather than whatever is most avidly promoted, recognising that change is possible but cannot be taken for granted. Questions about the timing and intensity of intervention are not just relevant to early childhood. As discussed earlier in *Potential for Change*, these concerns extend to adolescence and adulthood because developmental changes are still occurring, and individuals continue to be vulnerable to the onset of co-occurring conditions. As stated earlier, concerns about the timing and intensity of intervention are highly relevant to designing programs in low resource environments where selection decisions about resource management are critical. Where such gaps exist, systematic studies are needed to provide evidence on which decisions can be made.

Another important but often overlooked factor is the matter of post-treatment follow up. Post-intervention booster sessions have been offered in some cases and may be helpful,[36] but have not yet been formally evaluated in autism trials. Some studies have shown continued benefit for up to six months post-treatment.[126,128] However, many empirically supported interventions, such as parent mediated early social communication programmes, parent training for behaviour problems,

social skills trainings and CBT for anxiety are short-term,[69,70] and we know relatively little about longer term outcomes.

**Issues in Research Design and Outcomes**

In the midst of these quandaries, it is striking how little is known about the practical issues involved in implementing the most common and well-studied interventions beyond a few parent-mediated interventions. The number of review papers, meta-analyses and guidelines far exceeds the number of high quality RCTs (see Lai *et al.,*[71] Sandbank, *et al.*[30] for additional information). Randomised controlled trials remain essential to expand the evidence base for short-term specific interventions. However, the recommended, and trusted sequence for developing and testing complex interventions (i.e., model development; pilot feasibility; efficacy and tolerability; effectiveness in a wider sampling frame and implementation into community settings) has rarely been achieved in autism.[233] It is widely recognised that combinations of psychosocial and pharmacological treatments are often beneficial but there is almost no research about such.[71] Although fundamentally rational, the traditional pathway with RCTs is time-consuming and expensive; indeed, it is likely that few interventions in autism could go through this entire sequence. Some researchers have called for a massive investment in high quality, systematic, well-designed multi-site RCTs for the many different interventions currently being employed. The assumption is that an individual child or adult or family will move from one short-term modular intervention to another throughout life.[71,103]

Yet this approach to creating a clinically useful evidence base is unrealistic. Even if funding were available for the many very large-scale trials, particularly if an aim was to test for mediators, that would be needed for interventions at different ages and for different subsets of autistic children and adults, most psychosocial interventions last 3 or 4 months and have limited generalisation effects.[234] As the child or adult faces new demands and requires different approaches, other modular interventions would be put in place which could be effective. However, the practical challenges of carrying out brief RCTs at each point in time for different groups of people with autism are immense. Modular interventions make sense if we assume they teach a specific, generalised skill or evoke a cascade of learning (e.g., that helping a family of a young child play and communicate with the child leads to improved later language or social skills).[40,103,235] However, to our knowledge, there are no funding mechanisms for such research programmes even in HICs with the largest research spending; nor is it likely that such a programme would be feasible to implement over a long period of time without shifts in priorities in funding agencies. Moreover, there are few follow-up studies that document the 'cascade' that shows continued progress beyond the immediate goals of such interventions, and even then, causal connections are very difficult to identify.[236]

Demonstrating the efficacy of an intervention does not guarantee adoption or sustainability in the wider community.[237] The recognition that implementation of approaches is separate from empirical support is at the root of implementation science.[238] Recent evidence that effect sizes in university-based interventions are larger than those in the community[239] is not surprising, but also does not mean that interventions cannot be effective. Rather, it should be an impetus for refining methods on how to implement interventions in the community.[240] The gap between what research

currently offers and the needs of individuals, families and the community concerned about autism, calls for action and re-thinking the science of clinical practice in this field. More systematic consideration of essential intervention components and adaptations required to promote adoption in the community is a pressing matter to improve the lives of people with autism and their families.[48,71] Perhaps more so than in other fields of psychiatry and paediatrics, the majority of RCTs of psychosocial interventions in autism have remained closely tied to the University-based programme developers. Whilst this has the advantage of ensuring expert supervision and fidelity of each 'bespoke' treatment model, it has limited the number of independent replications of different approaches and also the identification of common (and effective) components - that are shared in common between many programmes - that can be tested more broadly in community services by non-expert practitioners and that are necessary for the study of wider implementation, as we call for above.

RCTs are the gold standard of evidence and the most recognised approach for studying interventions. Yet autism research could benefit from alternative approaches developed in other areas of public and mental health.[241] This would require that systems that currently rely on traditional standards for high quality research, such as guideline-producers, need to shift. There is a range of approaches that can be used to assess causality. Engaging stakeholders (e.g., consumers, clinicians, administrators, family members and autistic people) in the development and adaptation of interventions is a starting point. Building the capacity of systems to receive the intervention and strategies to facilitate successful introduction and sustained adoption of a new programme are other essential steps.[124,242–244] To build an evidence base and test interventions in real world conditions, with due consideration of human resources and cost, a wide range of research designs will be needed. Efficacy can be tested with implementation by researchers in the practice setting, such as peer-mediated approaches in schools.[132] Implementation can be carried out by community personnel (teachers, child care workers) with monitoring and outcome measures collected by researchers.[131]

Psychosocial RCTs often compare a study intervention to treatment-as-usual. As noted, usual care varies widely and its effects may equal or exceed the benefits of the study intervention.[95] Designs can test the order of interventions using a series of sequenced randomisations of study participants based on initial response such as the Sequential Multiple Assignment Randomised Trial (SMART). These have begun to be applied in autism[39,93] to show the benefits of different treatments (e.g., direct therapy only vs. use of speech-generating devices) and are an embodiment of stepped care/personalised health in some ways. However, they could be used even more efficaciously, with deliberate planning and sufficient sample sizes, to show which treatments worked best with which children and how much early response to a treatment predicts eventual outcome with that intervention and/or another approach. SMART designs hold promise but require large samples and sophisticated data analysis.[229] Many interventions share common elements, some of which may be essential and others not. Studies focused on testing of active ingredients or combinations of components such as Multiphase Optimisation Strategy (MOST) designs may be used to test a streamlined treatment package that is scalable and less expensive.[241] Another application of MOST designs could involve a randomised evaluation of implementation strategies with a focus on scalability.[245]

Observational, non RCT studies are vulnerable to many methodological limitations, including unmeasured confounding, reverse causation and other biases. However, because the long-term follow-up required to establish effects from RCTs can be too expensive or too difficult to achieve due to attrition, they may be a practical way to identify treatment targets and evaluate interventions. There is a range of approaches that can be used to assess causality such as natural experiments and instrumental variable analysis. A further approach to reduce the lag between efficacy and implementation is the application of hybrid study designs that combine effectiveness and implementation.[246] In a hybrid design, a study may test specific implementation strategies in the context of an effectiveness study. For example, in a region with limited access to mental health professionals, an implementation/effectiveness study could compare two approaches for training parents to train other parents in behaviour management.[242] The results could reassure policy makers, clinicians and consumers which implementation strategy is ready for wider application.

Systematic epidemiological studies, careful single case studies with systematic efforts to reduce biases, and designs such as stepped wedge offer ways to approach the inherent challenges of research with a heterogeneous and developmentally changing population.[247] Yet, currently, most practice guidelines would not include such studies. In addition, there is great interest in the use of novel modalities to deliver and assess interventions and training in hard to reach communities, including the use of digital technology and remote monitoring (see *Technology* section, below).[248] However, to date, there is limited evidence that such methods reduce the time lag from research to practice or reduce disparities in access between higher and lower income countries.

**Schools**

Schools are a system that provides a unique opportunity to bridge research and practice, though how often, or how well, this occurs is variable. In most higher income countries, public schools cannot legally exclude children with special needs. In LMIC, parents may struggle to have their children included in mainstream schools and advocate for appropriate services for students who need more structure.[249] The mandate to include children with autism in schools should be a primary public policy focus. In addition to academic skill building, appropriate teaching in school should increase adaptive skills and promote independence. Schools provide daily environments that can be incredibly helpful or difficult (for example, when bullying occurs) depending on the person-environment fit. Barriers to school-based research include difficulties in obtaining buy-in from administrators and community personnel, which is essential to support school providers' use of a novel intervention. There are also challenges of training providers to deliver interventions with fidelity.[48,250] Notwithstanding the difficulties, if school-based research is properly designed and supported, the large number of children with autism served in schools provides a natural context to test interventions at scale with a focus on relevant outcomes. These outcomes include retention in the classroom setting, acquisition of life skills, and better peer interactions. School-based research may be particularly useful in underserved communities and LMIC.

**Intervention Research across the Lifespan with a More Targeted Focus on Adolescents and Adults**

Intervention research with adolescents and young adults with autism has primarily focused on social skills or social cognition[133,251] and co-occurring anxiety.[127,137] Some newer programmes, however, have addressed executive functioning[45] and practical issues such as employment.[101] Most of this research has not included individuals with intellectual disability. Future research is needed that tests interventions for autistic adolescents and adults to promote achievable independence, such as employment;[101] meaningful, generalisable social skills; improvement of common co-occurring mental health conditions;[141,252] and broader functioning and wellbeing, for example as captured by the WHO International Classification of Functioning, Disability and Health.[253] Research in general on autism in adulthood is relatively recent and limited, that on older adults is almost non-existent, and there is a pressing need for funding agencies and researchers to prioritise intervention and evaluation research across the whole ability range and across the lifespan. In addition, the inclusion of people with lived experience in autism in the planning and conduct of such research is increasingly recognised as critical. Overall, the brevity of this paragraph reflects the limited data available in this area, not its importance.

**Inclusion of Underrepresented and Under-served Communities and Individuals**

Most of the evidence derived from intervention research in autism is based on research in middle- and high-income countries with majority white children.[21,254] The growing evidence for transportability of adapted versions of well-documented approaches is encouraging.[38,124] More research in low-resource countries is clearly needed (see *Global* section, below). Research on moving effective interventions into underserved areas, culturally and linguistically diverse communities, and socioeconomically disadvantaged locations is limited. Research efforts in LMIC and underserved communities require cultural adaptation as well as documentation of intervention implementation and effectiveness.[86] Finally, more research attention is warranted for subgroups of under-served individuals with autism, such as minimally verbal children, individuals with profound autism, adults, females, minority ethnic groups, immigrants and refugees.

**Cautions for Research in LMIC**

Although we encourage and aim for research to occur across diverse settings and communities, these nascent research efforts need to be conducted with mandated ethical guidelines. In some LMIC settings, there may not be ethical review boards. Power imbalance may exist between researchers and participants. Some families and individuals may be unfamiliar with the meaning of informed consent and their right to refuse to participate. To ensure that vulnerable families are not subjected to unethical practices, research oversight of the highest quality is imperative. As is true in any context, research in LMIC should embrace a participatory approach that includes autistic people and their families as well as potential providers, to maximise the utility and relevance of the research.[255]

**Understanding the Relative Cost-Benefits of Empirically Supported Interventions**

There are never enough resources to meet all the needs or satisfy all wants, and so decisions about which interventions to deliver are usually informed not only by whether they are effective, but how much they cost. This is a pressing public policy matter in high- and low-income countries

(see *Economic Costs of Autism* section, below). Unfortunately, the cost-effectiveness of autism interventions is dramatically under-studied (see Byford *et al.*,[256] for rare exception) and we recommend this as a priority for future clinical research (see Panel 6). Furthermore, both short-term and long-term perspectives warrant consideration. For some interventions, small initial effects, for example, in social communication may translate into longer-term gains, whereas the effects of other interventions may be limited to the immediate context. These could, in turn, have very different economic implications. To advocate for the needs of autistic people and their families wherever they live, the challenge is how to implement scalable strategies for the delivery of evidence-based interventions or best practices in a manner so as to improve access to care within the constraints of available human resources and budgets.

**Measuring Outcomes**

Current empirical data on interventions is beleaguered by the lack of comparable outcome measures across studies. Although many measures have been used in autism treatment research,[257] only a few have been validated as outcomes[258] that reflect meaningful changes in the lives of people with autism. We lack standard measures specifically designed to be meaningful and sensitive to change over time for core symptom domains or co-occurring conditions that can be compared across treatments.[4,259–261] Patient Reported Outcomes Measures (PROMS) - often completed by parents or other proxy raters for children - are important,[262] but many autism interventions are psychosocial, making it difficult to mask allocation to participants, parents and teachers who are best placed to report on meaningful everyday outcomes. It is well recognised that placebo effects are strong. In other neurodevelopmental disorders such as ADHD, unblinded outcome measures, such as parent reports of the benefits of parent training, produced biased (higher) estimates of effect sizes than blinded, objective, performance-based measures.[263] In contrast, more objective measures, such as the ADOS, are less susceptible to bias, but are expensive and relatively insensitive to short term changes. Other measures lack ecological validity. Practical outcomes, such as participation in school, or parent stress measures are less often reported, even when available. To conduct large-scale trials in community settings, outcome measures are needed that can be used across different studies and are inexpensive, accurate, unbiased and relate to treatment targets, as opposed to changing diagnoses. Poor outcome measurement, the presence of placebo or expectancy effects[264] and the difficulty in HIC of finding untreated control groups has made it more difficult to sort out ineffective treatments from invalid measures.

There is also a need for measures that allow for mechanistic analyses and more ongoing progress monitoring.[218] The use of formative (and not just summative) measures also fits within current advanced methodological approaches being used to examine treatment efficacy in autism, such as MOST and SMART designs.[39] In some areas of mental health, there has been a push within clinical research to develop ways to document progress regularly in standardised ways, often digitally, and provide feedback to the provider and the family or an adolescent or young adult during treatment.[265] Applied behaviour analysis has a long tradition of documenting children's responses in detail, with those data sometimes shared with the family. Other approaches, such as Youth Top Problems and Parent Target Problems,[235] and other Patient-Reported Outcomes engage the parent, and the youth when possible, in nominating the most pressing problems. Progress on these

problems is reviewed at follow up visits. Both the act of reporting and the providers' review of the information have been shown to be linked to better progress,[266] though this is complicated in a heterogeneous disorder where sometimes progress is slow. However, there are some examples in autism of measures that could suit the dual purpose of providing formative and summative data, including the Autism Behavior Inventory.[267]

Another need is to develop outcome measures that can be scaled for larger samples within the complexity of existing systems (e.g., schools, community-based mental health centres), including low-resourced communities and LMICs, perhaps by leveraging the use of technology. The BOSCC (Brief Observation of Social Communication-Change) is one example of a new measure developed for use with young children with autism, that allows for more frequent re-administration, and thus potentially could fill this role.[268] It consists of a 12-16 minute videoed interaction (e.g. on a cell phone) with a family member, teacher or naïve research assistant that can be done at home, school or in a clinic, with instructions but no formal training. However, it requires human coding that means training 'blinded' coders or using coders from existing centres. The intention is to find automatic methods of coding the video and audio-recordings that would minimise costs and burden across the lifespan, but this is still in development.

There is interest in the use of iPads or other commonly-available technological devices to support data collection and outcome measurement, but to date without clear meaningful results of their impact[269] (see *Technology* section, below). Eventually, audio recordings might yield automatic codings of language; videos might be used to code proximity to others; and information about sleep, activity level or arousal may eventually be interpretable. However, these will need to meet standard psychometric standards (e.g., test-retest reliability on an individual basis), safety standards of security and validation against more recognised outcomes. Linkage of data across databases for education, health and social care is also important and has provided evidence supporting longer-term benefits of intervention in other neurodevelopmental disorders such as ADHD.[270] Finally, outcome is more than the patient's' response to intervention but also the potential for implementation and the fidelity with which the intervention was carried out.

*Panel 6*
*Recommendations for Clinical Research*

    1.The most urgent questions involve what works for whom, when, and how much.
    a. Answers to these questions would allow appropriate development of scalable interventions across the globe and are critical to improving the science underlying practice decisions in LMIC. Future research in HIC and LMIC must be sufficiently powered to address these questions.
    b. Research with adolescents and adults is particularly needed, though a better understanding of developmental differences in early years (where changes are more rapid) and their relationship to interventions (as a moderator and as predictors) is also important.
    2. RCTs for short-term interventions, including medication and behavioural trials, are a priority but the field needs to move on from basic two-arm trial designs comparing a targeted intervention against 'treatment as usual' to test the relative effectiveness of different types or intensity or

combinations of interventions.

3.Implementation and effectiveness trials are needed to address gaps such as effectiveness outside of clinics, effectiveness with diverse populations across age ranges, developmental levels and socioeconomic and cultural backgrounds, and the implementation of required training and systems changes required to make them scalable.

4.RCTs should assess generalisation beyond treatment-specific assessments and parent reports of short-term changes to address long-term follow-up of focused intervention, including cost-effectiveness and budget impact analyses in their design. Potential mechanisms of change, including child, family and social factors, and moderators of outcomes, should be prioritised as much as proving that a given short-term intervention is effective.

5.Alternatives to traditional RCTs should be developed and supported in order to address other challenges, including difficulties in finding comparison groups in 'treatment as usual,' circumstances where randomisation is not feasible, studies of use of already-in-place approaches and tools, and therapies commonly used in clinical practice e.g., speech-language therapy or occupational therapy, and educational approaches. Systems supporting guidelines should address the need for such designs and consider how to evaluate them beyond traditional standards.

6.Along with predictors of progress and outcomes, research should address factors that drive resiliency and capabilities in some families and individuals and those that serve as barriers and challenges to others.

7. Inclusion of stakeholders in the development of clinical trial designs and outcome measures is critical, including how to best use Patient-Reported Outcome Measures.

8. Research on early identification in preschool children should shift focus from short-term evaluations of the accuracy of autism-specific screening instruments to test the effectiveness of broader surveillance strategies, tailored to local models of service provision. These should aim to identify both autism and other early-emerging and commonly co-occurring neurodevelopmental conditions; and include longer-term follow-up and evaluation of costs and benefits to the whole population.

9. It is possible to carry out high quality research in LMIC. Support for such studies is crucial and should address implementation and feasibility as well as outcomes.

10. Technology has the potential to reduce disparities and improve clinical care and quality of life for individuals and families who live with autism and other neurodevelopmental conditions. To realise this potential for autism, rigorous scientific scrutiny in partnership with the autism community plus infrastructural developments will be required to bridge the digital and knowledge divide around the globe.

**Evaluation and Management of Co-Occurring Conditions**

A significant aspect of the heterogeneity of autism is that the majority of people with autism have co-occurring conditions, i.e., developmental, physical, behavioural or psychiatric, across their lifetime. These conditions are treatable and often affect quality of life at different points of life as much as autism core features. Evidence-based treatment can result in increased wellbeing for autistic people and their families and may enable better access to other services and supports.

For example, new epidemiological data analysed for this Commission from the Norwegian MoBa cohort show that the proportion of autistic children with elevated emotional (e.g., anxiety) and behavioural difficulties (e.g., hyperactivity, aggressive behaviour) even from 18 months to 5 years far exceeds the proportion of these concerns in the general population. In many cases, concerns

increase with age (Figure 9). In early childhood, parents reported that over 70 percent of children with autism experienced some kind of co-occurring emotional or behavioural difficulty; early trajectories of emotional and behavioural difficulties were also associated with mid-childhood outcomes such as daily life impairment, school enjoyment and friendships.

Figure 9.    Heterogeneity in early childhood trajectories of emotional and behavioural difficulties and mid-childhood outcomes in a population-based sample of children with autism

[Figure 9 here]

Many people with autism are initially referred for symptoms of co-occurring conditions rather than core autism symptoms. Indeed, anxiety, aggression, and sleep problems are often the greatest focus of parents' concerns.[271] These conditions adversely affect quality of life, from the young child all the way up through adulthood, including friendships and difficulties at school or work. Thus, identifying and treating co-occurring conditions is an essential component of personalised intervention planning and the formulation of short and long-term intervention targets from assessment. In the initial diagnostic evaluation and follow-up, the presentations of other behavioural and psychiatric conditions are considered as differential diagnoses. The same diagnostic and treatment standards for these disorders should apply to people with autism as to other children and adults, although the manifestation of symptoms may vary. Once the diagnosis of autism is made, integration of co-occurring conditions as well as core features is essential in the stepped care approach.

As shown in the stepped care/personalised health figures for assessment and intervention (Figures 5 and 7), the same system of decisions needs to be applied to co-occurring conditions as for an autism diagnosis. Because many putative autism symptom rating scales are confounded by other behavioural conditions (e.g., the SRS[272]), specific screening and diagnostic assessments of the differential behavioural and psychiatric disorder diagnoses need to be performed during evaluation.[155] Stepped care/personalised health procedures and data from novel systems, such as that described earlier in Figure 8, that use probabilistic data from autistic samples can be applied to streamline choices for areas of focus. A clinical environment with knowledgeable providers, that is culturally appropriate, adapted to the needs of the stakeholders, and that allows sufficient time for assessment, discussion, and participatory decision-making, is necessary to support a successful diagnostic evaluation of co-occurring conditions.

Table 4 shows the prevalence of common co-occurring conditions, according to population-based or clinical studies. The wide range of prevalence for many conditions (also evident in meta-analyses[16,273]) results from ascertainment biases and measurement differences across studies, as well as real differences across age, sex and populations. Because similar factors vary in studies of the general population, we do not show comparative prevalence rates but rather indicate where there is robust evidence that rates are higher in autistic people. Despite these confounds, it is clear that heterogeneity in the prevalence and incidence of these conditions is associated in different ways with different ages, resulting in higher rates of ADHD in children and increased rates of depression, schizophrenia, and bipolar disorder in adulthood.[7,16]  The underlying shared risk for

autism and co-occurring conditions can be related to shared genetic risk, as for ADHD, intellectual disability (e.g., fragile X syndrome) or different forms of epilepsy (e.g., Tuberous Sclerosis Complex).[15,16] Shared psychosocial risk is a possible factor for other conditions, but there is limited evidence about this.

Table 4. Common co-occurring conditions in people with autism

[Table 4 here]


## Conceptualising Co-Occurring Conditions

Whenever two conditions occur at rates that exceed chance, interest is inevitably prompted in the nature of the association. The term 'comorbidity' is typically applied to the co-occurrence of two conditions (e.g., autism and anxiety) with the implication that they are independent, but it may be that the two conditions are not separate but overlap or are associated in complex ways. For example, noncompliant, irritable and oppositional behaviour can be related to rigidity or impaired verbal communication; the latter may also mask anxiety as the underpinning driver of externalised behaviour.[295] Anxiety can be related to aspects of cognitive style that are more common in autism, such as poor executive function[296] and intolerance of uncertainty.[297] Similarly, depressive symptoms can follow social interaction problems with peers, but also may be related to other environmental risk factors. Thus, we use the term co-occurring conditions with the understanding that the relations between autism and other conditions may be complex.

Symptom overlap between autism and other mental health issues is a clinical challenge for both assessment and intervention. For example, social avoidance may be a manifestation of either an anxiety disorder or of autism; apparent separation anxiety may reflect a child's strong reaction to a change in routine rather than separation; and an emotional outburst in a novel environment may reflect rigidity and intolerance of uncertainty and not generalised anxiety. Regardless of whether these issues are truly additional conditions or part of autism, they must be addressed. Alternatively, co-occurring symptoms such as those related to anxiety may be missed, especially if using standardised instruments, because of their atypical presentation.[298] They therefore require careful assessment and corresponding intervention formulation. From a practical standpoint, however, clinicians should avoid either attributing all maladaptive behaviours to autism or, on the other hand, failing to take into account the role of core aspects of autism in treatable co-occurring conditions.


## Infants, Toddlers and Preschool Aged Children and Issues Addressed at First Diagnosis

Co-occurring physical conditions must be diagnosed and addressed as a first priority within the heterogeneity of autism. Among these are hearing and vision problems, epilepsy, and medical conditions associated with some genetic syndromes (such as in Tuberous Sclerosis Complex, Prader-Willi or Klinefelter Syndrome).[136] In cases of behavioural or cognitive regression in autism, the potential for epilepsies and related conditions, such as Landau-Kleffner Syndrome, must be considered. Different forms of epilepsy and seizures frequently co-occur with autism, with one

peak of incidence in early childhood and a second in adolescence and young adulthood.[17,291] The presence of intellectual disability, as well as female sex, is associated with higher rates of epilepsy in autism (see Table 4).

Sleep problems in autism are also frequent, affecting all ages, and have adverse effects on daily functioning, learning and behaviour in the individual as well as on the whole family.[299] Diverse problems related to the gastrointestinal (GI) tract, such as selective eating, constipation, diarrhoea, and gastro-oesophageal reflux, are more frequent in autism (see Table 4) and may cluster with behavioural problems.[300] Researchers are currently exploring possible associations with altered microbiomes[301] serotonin levels,[302] cytokines,[303] and stress response.[304] Nutritional deficiencies can occur and possibly lead to decreased bone density and increased fracture risk.[305] Individuals who are underweight, have symptoms of dysphagia or food allergy may benefit from further medical investigations.

In general, the characteristics of each of these problems are varied and not specific to autism but commonly co-occur in all children with neurodevelopmental disorders. For sleep problems, empirical support is available for parent education, sleep hygiene and other behavioural interventions as first line therapies,[306] as well as the use of melatonin when other therapies are not effective.[307] Other medications are often prescribed in some countries but with limited evidence to support their use (see Table 5). Standard treatments are often effective, but may require adaptations, a longer duration of intervention and more frequent follow-up by providers. Practice pathways and consensus guidelines for evaluation and treatment of common GI and sleep conditions in autism are available.[308]

The most common co-occurring behavioural and emotional difficulties during preschool and school age are hyperactivity, irritability, oppositional problems and anxious behaviours[309] as well as elimination disorders.[277] These conditions can be measured using standard approaches, whether they represent distinct conditions or elevated behavioural symptoms associated with autism. Parent training strategies using psychoeducation, positive parenting and behavioural techniques[70] have been effective, especially regarding irritability and oppositional behaviour. Behaviours such as peering at objects, unusual movements, talking to oneself or fixated interests and unusual preoccupations that used to be described as 'psychotic' in children are now generally considered part of the core features of autism.[310]

**School Age and Adolescence**

'Wandering' is the propensity of 25-50% of children to leave a supervised, safe space, or to escape from the supervision of a caregiver.[311] Wandering, which is not a diagnosis but a behaviour that causes much concern, is associated with risk for accidental drowning and traffic injuries.[312] Younger age, intellectual disability and behavioural/psychiatric conditions in children with autism increase the risk for wandering.[311] Bullying, beginning in childhood but continuing on through adolescence and beyond, is also a serious concern.[313] Dyslexia and dyscalculia are often not identified in autism but are common and can be addressed with standard educational approaches adapted for autism.[76]

Other behavioural issues in this age range overlap with those emerging earlier, but treatment options are greater. These include the direct treatment of children and adolescents, often in groups (including caregivers in most successful treatments), adaptation of CBT approaches for anxiety,[69,127,137] and more common use of medication. ADHD is typically addressed with psychostimulants.[314] Irritability, aggression, oppositional behaviours, and severe repetitive behaviour are not diagnoses, but symptoms which need to be carefully evaluated and considered in relation to physical and environmental issues. They can be addressed with parent training (see above). Antipsychotics like risperidone or aripiprazole,[315] are sometimes prescribed, ideally after other approaches have been tried, although effectiveness and side effects are more variable in autism than some other conditions. Thus, prescribers should utilize a "start low and go slow" approach when initiating and titrating medications to treat co-occurring behavioural and psychiatric conditions. Additional expertise may be required when considering dosages outside the usual ranges (see Table 5). Even in adolescence and adulthood, psychosocial, environmental and sometimes physical issues can contribute to problematic behaviours, so it continues to be important to consider these factors in an initial assessment. In general, it is recommended that psychosocial approaches be used before psychopharmacological interventions in children (see CPGs in Table 1).

The recent explosion of genomic and system neuroscience findings have provided several targets for psychopharmacological manipulation of underlying biology, with the hope that targeting such aetiological pathways may have broad effects across domains, including core symptoms. Potential compounds targeting excitatory:inhibitory (E:I) balance and synaptic plasticity (e.g., GABA and glutamate modulators) and neuropeptide systems involved in social perception/cognition/affiliation are currently in clinical trials in children, youth and adults with autism.[316]

Table 5. Commonly used medications in children and adolescents with autism

[Table 5 here]

**Older Adolescents and Adults**

Youth and adults with autism are at elevated risk, increasing with age, to be overweight or obese.[15,331] However, research often groups adolescents either with younger children or with adults (e.g., Seltzer *et al.*[332]). Lower physical activity, prescription of atypical antipsychotics, autism severity, sleep problems, and family history of obesity all contribute to risk. This is accompanied by increased risk for metabolic sequelae including diabetes mellitus, hypertension, and non-alcoholic fatty liver disease.[331] These, in turn, may contribute to the nearly three-fold increased risk of premature mortality in autism, highlighting the urgent need to focus on preventive care interventions.[287] Nutritional counselling, behaviour modification, physical activity and adjunctive metformin for young people taking antipsychotics can be effective in reducing body mass index.[320]

Adolescence is a time when a number of mental health disorders first become apparent and adolescents with autism may be even more vulnerable. Hence, eating disorders, depression (especially in females), anxiety, suicidal ideation, non-suicidal self-injury, and psychotic symptoms all occur in adolescents[129] and in adults[16,252,284] (see Table 4). These symptoms must be taken seriously and addressed. Psychotic and psychotic-like symptoms occur in typically developing adolescents,[16,129] especially associated with depressive episodes.[333] Some people with autism show formal thought disorder, such as restricted thinking, and others may have psychotic-like episodes, which can sometimes be incorrectly interpreted as psychosis.[176] Better primary health care and mental health services, as well as evidence-based guidelines on the evaluation and treatment of co-occurring conditions are needed. There is also a huge knowledge gap about co-occurring disorders in older adults, including dementia and Parkinson's disease.[334]

Overall, modifications to existing evidence-based treatments are often necessary to optimise both behavioural/psychological and medical approaches for co-occurring conditions in autism to ensure effectiveness and participation. Modifications range from the provision of multi-modal information and materials, including visual guides; work on emotional literacy and understanding; the critical role of engaging and joint working with of parents/carers and ideally across environments (e.g., school and home); and consideration of the role of sensory atypicalities and their impact. Until evidence is generated for these modified approaches, autism-informed and autism-friendly modifications to existing evidence-based practice should be employed. Systematic efforts to reach non-autism specialist therapists with information about these adaptations are important, as most intervention will not be delivered by autism experts; again, stepped care/personalised health approaches may be particularly valuable (see Figures 5 and 6).

## Economic and Personal Costs

Alongside the social justice and social equity values which underpin our approach, more information is urgently needed about the economic, as well as personal, consequences of autism, to inform the economic, social and political case for action across the globe. The pervasive scarcity of resources – in HIC as well as LMIC – means that difficult decisions must be made. It is necessary to know not only which interventions are effective, but which are affordable given budget constraints, and which make best use of society's scarce resources. Economic evaluations, such as cost-effectiveness analyses, compare the outcomes and cost implications of two or more interventions.

Costs can range widely across many sectors. Buescher *et al.*[335] estimated the lifetime costs of supporting an individual with autism and intellectual disability to be $2·4 million in the US and $2·2 million in the UK; and $1·4 million in both countries for an individual with autism without intellectual disability. In childhood, special education services and parental productivity loss are the highest costs; in adulthood, highest costs are residential or supportive living costs, individual productivity loss and medical costs. Although in HIC, costs are often discussed in the context of early intervention over an individual's lifetime, adult costs far outweigh childhood costs, in part because adulthood is a far longer phase of life than childhood.

Cost-effectiveness analysis examines whether the outcomes achieved by one intervention compared to another are sufficiently important (in scale and relevance) to justify the extra resources needed to generate them. An intervention could be cost-effective even if it costs *more* than the comparator because the beneficial effects for autistic people and their families are viewed by the decision-maker (such as a government) to be 'worth' the higher costs. This is a value judgement: how much is society (represented by government in this case) willing to pay to improve the lives of autistic people and families? This is rarely an easy judgement.

If the task is to decide which is the better of two interventions for autistic people, then a measure of, say, social communication or adaptive functioning would be appropriate to measure effectiveness, but if the task is to decide how to allocate across different clinical areas (such as interventions for autistic children, or adolescents with depression, or adults with cancer), then generic outcome measures are needed, such as quality-adjusted life years (QALYs) or disability-adjusted life years (DALYs). A significant challenge for the autism field is that these generic outcomes might not be sufficiently sensitive to measure change in autistic people, which then leaves autism in danger of being overlooked in the perennial battle for resources.

The situation is not helped by the paucity of cost-effectiveness evidence. A systematic review focused on children and adolescents[336] identified only two robust studies: one RCT-based evaluation suggested that the PACT intervention did not appear cost-effective in the short-term when added to treatment as usual (Byford *et al.*[256]); and the other used modelling to estimate potential costs and benefits to age 65 of developmental early intervention programmes (Early Start Denver Model), concluding that there would be cost savings as well as effectiveness gains.[337] Another recent modelling study concluded that, even under optimistic assumptions, ABA was not cost-effective.[338] Other studies using modelling methods point to economic gains for some interventions such as CBT and supported employment.[113,339] However, the very small number of valid and reliable cost-effectiveness studies highlights the need for future intervention studies to incorporate rigorous health economic analyses in their design from the outset.

The under-recognition and under-diagnosis of autism already noted, combined with the lack of evidence on the economic costs and benefits of interventions and services, exclude autistic people and those with other neurodevelopmental conditions from access to an equitable share of public and private resources that would improve their life choices and outcomes. More information about the economic and personal costs and consequences of autism is required in every country and region across the globe. A requirement to record individuals with an autism diagnosis within healthcare, education and social care systems would inform local service planning and provision and also contribute to our future ability to estimate the 'real world' costs, and the personal and societal consequences, of autism relevant to each community, as well as to monitor equity of provision.

**Family Experience**

**Historical and Cultural Context**

In the 1960s, autism was thought to be the result of poor parenting. Mothers were singled out as bad parents and called 'refrigerator mothers,' too cold to provide the love and warmth a child needs

to thrive.[340] They were told the best they could do for their children was to send them to live in an institution and were pressured to undergo psychoanalysis to determine why they (the mothers) were such bad parents. As a result, there was a tremendous stigma associated with having a child with autism. We now know that autism is not caused by parenting style. Nevertheless, in some parts of the world there is still significant stigma associated with a diagnosis of autism and families are often reluctant to take their children to be diagnosed or to seek help.[341] This varies widely by region, culture and availability of services. A recent review included studies of caregivers (predominantly mothers) across three cultural regions – East Asia, the Middle East and Western societies – and reported a negative impact of autism-related stigma upon caregiver mental health.[341] In some cultures, those who are identified as deviating from group harmony are vulnerable to being devalued, rejected and stigmatised. Families fear such stigmatisation and consequently hide their circumstances (and sometimes their child with autism) from their community, leading to a range of harmful consequences.[341]

In addition, culture influences explanatory models for autism, for example in some African cultures autism is conceptualised as resulting from witchcraft and poor parenting.[342] Similarly, Alqahtani[343] has shown how Saudi Arabian parents may rely on cultural interventions involving religious healers. In some countries there is still a psychoanalytic approach to autism or a strong cultural belief that early diagnosis is equal to prematurely 'labelling' the infant and so autism diagnosis is delayed.[344] These variations emphasise the importance of creating partnerships and using language that can synthesise cultural and biomedical views so that families can engage in services. The situation for parents today, at least in many parts of the world, is much improved and they are rightly seen as the primary carers and key advocates for their child. Nevertheless, many community care systems inappropriately place an over-reliance on parents to negotiate, coordinate and sometimes even assume the role of the primary service provider, bringing additional disadvantage to those with the least personal and financial resources. Families are also vulnerable to unproven fads and false treatment claims for non-evidenced 'alternative approaches' (see Panel 6).

### Impact of Autism on Family Members

When an individual is diagnosed with autism, the entire family is affected. Parents of children with autism experience higher levels of stress and depression compared to parents of typically developing children and those with other types of disabilities.[8,345] Contributory factors include, parental mental health, resilience and support, severity of autism symptoms and behavioural problems, extensive care needs, financial difficulty, problems with school, low satisfaction with health care providers in many communities, and concern about their child's future.[8,345] In some cases, parents' greatest concerns stem from a poor acceptance of autism by society and sometimes by other family members; worries over the permanency of the condition and long-term care; feelings of isolation, and the impact on siblings.[346]

### *Siblings*

Siblings of children with autism are at higher genetic risk for autism and other mental health conditions than typically developing children.[347] Growing up in a household with a brother or sister

with autism also confers unique environmental stressors, with siblings showing higher levels of internalising and externalising disorders, social and behavioural problems, and distressing emotions such as guilt and embarrassment about their sibling's behaviour.[348] In cultures where there is stigma linked to disabilities, autism in the family can impact the marriage prospects of siblings.[50] On the other hand, some siblings have a positive response to growing up with a sister or brother with autism, including greater empathy, resilience, maturity and self-confidence.[348] Having a sense of control and understanding of autism, access to time–alone with parents, supportive and inclusive environments, and the chance to relate to other siblings are protective factors that facilitate positive psychological outcomes in siblings of autistic people.[348]

*Grandparents*

Having already raised children, grandparents are often in a unique position to spot early signs of autism and encourage developmental screening. Findings indicate that frequency of interaction with a grandmother may reduce the age of diagnosis.[349] A study of 1,870 grandparents by the Interactive Autism Network in the USA indicated that a majority played a role in the diagnosis and treatment of autism in their grandchild.[350] These ranged from being the first to raise concerns, supporting others who raised concerns, involvement in treatment decisions, to providing financial support and even moving closer to their grandchild's family so they could help 'manage all that is involved with autism.'

**Vulnerability to Non-Evidence Based Treatments**

Caregivers may be particularly vulnerable to poorly evaluated fads and false treatment claims in the popular press, social media and on the internet. Many of these interventions have subsequently been shown not only to be ineffective but some to have adverse effects. Clinicians have a responsibility to be informed on what are evidence-based and non-evidence-based treatments and to advise and guide parents through the ever-changing minefield of misinformation about autism and specifically autism treatments that are available (see Panel 7). At a systems and societal level, one protection against unevidenced 'treatments' is the equitable provision of evidenced-based care through existing health systems.

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*Panel 7*
*Vulnerability to non-evidence-based treatments*

Despite research advances in the neurobiology of autism, many unanswered questions remain regarding causes and effective treatments. In this context, many families of individuals with autism have turned to unproven medical treatments, and to complementary or alternative medicine (CAM) treatments.[151,351] In some cases, unscrupulous providers may prey on a family's desire for a 'cure' or urgent needs to address challenging behaviours such as aggression or self-injurious behaviour, or those in low resource settings where there is no access to evidence-based approaches or advice.

CAM approaches include natural products (e.g., herbal remedies, homeopathy, vitamins, minerals), mind and body interventions (e.g., music therapy, yoga, meditation) and specialised diets (e.g., gluten free, casein free (GFCF) diet). There has been little rigorous testing of the efficacy of some of these approaches

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(e.g. homeopathy). For others that have been tested in controlled trials, there is no evidence of effect (e.g., GFCF diets[352]). For facilitated communication (as distinct from the independent use of augmentative devices), consistent evidence emerged of manipulation by the therapist (e.g., Hemsley *et al.*[353]). However, there is emerging evidence of modest benefit, both for associated behaviours and autism symptoms, for omega-3 and vitamin supplementation,[352] although the mechanisms of effect and the specificity to autism vs. other neurodevelopmental disorders are not well understood.

Of greater concern are a number of non-mainstream biomedical therapies (e.g., antifungal treatment, ayurveda, chelation, hyperbaric oxygen, leuprolide (Lupron), secretin, stem cell treatments) that have been advertised as 'autism treatments' by word-of-mouth, social media or the internet with sophisticated marketing, unsubstantiated testimonials and unproven claims. Most of these lack evidence, some are costly or take time away from potentially more effective therapies (e.g. stem cells[354]), and others have been shown to be potentially harmful to the health of the individual (e.g., secretin,[355] chelation[356]).

Healthcare providers, by evaluating evidence and potential for harm, fulfil an important role in helping families make responsible decisions about CAM and non-mainstream biomedical approaches.[357] Several studies indicate, however, that autistic people and their families frequently do not disclose CAM use to their healthcare providers, often due to a fear that their providers harbour negative attitudes about CAM.[151] Studies of healthcare providers indicate lack of knowledge about CAM treatments for autism, concerns about the potential for harm and the burden of time and cost that unproven therapies place on families.[151] There is a need to strengthen the partnership between providers and families in order to reduce decisional conflict and foster treatment plans that are safe and effective. Providers who gain trust by providing longitudinal primary care within a 'medical home' can have a positive impact on helping families make responsible decisions about treatment and gain access to therapies that are evidence based and safe.[358] As discussed earlier as part of a stepped care/personalised health approach, the concept of shared decision making provides a framework for the respectful discussion of potential treatments with families and providers to engage in bidirectional exchange of information, review potential risks and benefits of treatment options and ultimately arrive at decisions that respect the knowledge and values of both parties.[151] Our Commission recommends that providers gain knowledge of the evidence base behind benefits and potential harms of CAM non-mainstream biomedical treatments; ask families about the use of CAM; and partner with families by providing information about potential risks and harms to enable responsible decisions about treatment.

## Parent and Family Advocacy

Parents and families have played a critical role in policy, practice and research advocacy across the globe over many decades, and because of their work, autistic people today benefit from earlier diagnosis and have more evidence-based treatment options. In many countries, parent and voluntary groups have successfully lobbied for legislation, e.g., the National Autistic Society in the UK for the 2009 Parliamentary Autism Act, and Autism Europe with the European Commission. In the U.S., parents lobbied for IDEA (Individuals with Disabilities Education Act), which guarantees individuals with disabilities the right to a free and appropriate public education. Parent advocacy groups such as Cure Autism Now, the National Alliance for Autism Research, Autism Speaks and the Autism Science Foundation were the driving forces behind the Combating Autism Act and the Autism Collaboration, Accountability, Research, Education and Support Act which nearly doubled National Institutes of Health (NIH) funding for autism research. In Germany, parent advocacy groups were the driving force to establish any kind of intervention in the 1980s

and work jointly together with professionals in developing national clinical guidelines on diagnosis and intervention. In Argentina, autism advocacy groups joined to create RedEA, an autism network involved in awareness campaigns, and advocacy to create political and social changes; and 150 organisations formed the group 'artículo 24' that promotes and guarantees educational inclusion. In Australia, the Helping Children with Autism initiative, introduced by the federal government in 2008, was a direct result of parent lobbying and provides support for children under six with autism, their families and caregivers. In South Africa the 'Right to Education Campaign' was led by the Western Cape Forum for Intellectual Disability (WCFID). Children with severe disability were deemed not to be 'educable' but after many years of lobbying, the parent-led WCFID launched and won a court case enshrining the right to education for all children, specifically those with severe to profound intellectual disability. A similar story played out in India where the Persons for Disabilities Act of 1995 did not recognise autism as a distinct disorder. Parents lobbied the government to pass the National Trust for Autism, Cerebral Palsy, Mental Retardation and Multiple Disabilities Act of 1999, the first ever legislation to be passed in India that recognised autism as a distinct condition. It allowed the setting up of State Nodal Agencies across the country to support families, and in 2009, the Right of Children to Free and Compulsory Education was passed. Continued pressure from families and other stakeholders led to their inclusion in the committee that drafted the Rights of Persons with Disabilities Act of 2016, which includes autism and expands the right of individuals to education and social care benefits. In Bangladesh, a parent advocate chaired a National Advisory Committee for Autism and Neurodevelopmental Disorders which played a key role in the development of a Strategic and Convergent Action Plan on autism and other neurodevelopmental disorders, the result of inter-ministerial collaboration to provide an integrated framework for action in Bangladesh. In Canada, where health care and education are provincially managed, autism organisations partnered under the umbrella of Canadian Autism Spectrum Disorder Alliance (CASDA), to advocate for a National Autism Strategy and to develop Canadian-wide standards. Together, these examples highlight the importance and impact of parents and, increasingly, self-advocacy worldwide, as well as the difficulties individuals and families have faced in accessing services over time.

## Global and Cultural Diversity

Assuming a minimum prevalence of 1-2%, a figure that varies by region,[274] currently at least 78 million individuals around the globe have autism. Outside urban areas in most countries, families have virtually no access to either assessments or evidence-based interventions. The 'assessment and intervention gap' seen around the globe is compounded by a 'knowledge gap' in LMIC and other low-resource settings.[74] 95% of all children under five-years old with developmental disabilities (including autism), live in LMIC.[359] However, little research is conducted outside of HIC. For example, though sub-Saharan Africa (SSA) and South-East Asia showed the greatest rise in recognition of developmental disabilities over the last 30 years of all global regions, a recent scoping review showed that less than 1% of the world's autism research originated from SSA.[21] In addition, this research was mostly conducted with families already receiving services, so was not representative of the other ~90% of families who received none. Table 6 shows how our main themes of heterogeneity, potential for change and systems are particular challenges in LMIC.

Table 6. Particular challenges for families who live with autism in LMIC and other low-resource settings


[Table 6 here]

The World Health Organization (WHO) has recognised autism as a global health priority and passed a resolution calling for 'comprehensive and coordinated efforts for the management of autism spectrum disorders' with key recommendations for all member states to implement.[213] The needs of families who live with autism around the globe are universal: to understand their child's developmental differences; to seek support that may improve and optimise outcomes; to be included as active members of society; and to receive appropriate support to be empowered for their child's journey into and throughout adulthood.[360,361]

**Platforms of Care**

The Disease Control Priorities[362] have recommended platforms of care for the delivery of evidence-based interventions for mental health and neurological problems, including autism and other neurodevelopmental disorders. These expand beyond the 'vertical levels' of health, education and social welfare, which too often leave families stranded between these levels, and create roadblocks in transitions. These platforms are 'the level of the health or welfare system at which interventions or packages can be most appropriately, effectively, and efficiently delivered.'[363] Matching our 'systems' theme, the population level platforms aim to inform policy to support the development of cross departmental community strategies, as well as healthcare approaches. Within the healthcare platform, specific delivery channels are centred around individuals (or families), primary, secondary or specialist care. These can guide resource allocation while also directing best practices at various levels of care.


Many of the priorities for global action have been highlighted during this report. These include families as key stakeholders; remembering that most autistic people are adults; addressing the need, particularly in LMIC, to find scalable models of raising awareness, identification, assessment and care that in most cases will take place across a lifetime; recognising the importance of systems and economic implications; and acknowledging the continual need to take into account heterogeneity and diversity not just in individuals with autism but in their cultures, contexts and personal preferences.

**The Importance of Cultural Diversity in Global Settings**

Cultural diversity encompasses broad social constructs including gender, race/ethnicity, class, income, language, religion, sexual orientation and gender identity (see *Autism in Females* and *Gender nonconformity* sections above). Many autistic individuals will have 'minority' or non-dominant status across several of these social and cultural factors and there is increasing recognition that the intersectionality of these makes individuals vulnerable to both discrimination

and exclusion from appropriate services. Autism is defined by a recognisable pattern of behaviours and symptoms across the globe, but the cultural context in which these are interpreted has great impact on the awareness of difference, identification, access to care, development of care systems, and individual and family interactions within such systems.[342] Cultural context may foster acceptance of autism, or alternatively, may induce stigma or harm. People with autism or other neurodevelopmental disorders are more vulnerable to maltreatment, sexual exploitation, neglect and other human rights violations,[364] along with inequitable access to health care and education. Stigma associated not just with autism, but with mental health and neurodevelopmental conditions, is a significant concern in many cultures.[49,362,365] For example, in a comparison of Swedish and South African caregivers of autistic children, participants from both countries identified their families as sources of support, but caregivers from South Africa also reported that sometimes families were barriers to progress because of fathers' attitudes and family members' expectations for children's behaviours.[366] In contrast, Swedish parents were more negative about health professionals, reporting concerns about providers' levels of knowledge and the degree to which they were supportive, whereas this was rare in South Africa.

Two examples of cultural differences in the explanatory models which could impact engagement with services, are illustrated by Shaked,[367] who describes mothers' struggles to get their autistic child's behaviours accepted in an ultra-orthodox Jewish community. In Pakistan, parents found comfort from spiritual healers' explanation that looking after their child was a 'divine duty'.[49] Despite increased initiatives to address cultural diversity, we are only just beginning to explore approaches that could work well for individuals with autism across culturally diverse settings.[365] This is most obvious in the dearth of evidence from LMIC. However, it is also an important factor within and across many HIC countries, where there are substantial ethnic/racial and socioeconomic disparities, with minorities and disadvantaged socioeconomic groups (and in some studies females) receiving fewer services and later and less accurate diagnoses.[201,368,369]

**Developing High-Quality, Scalable, and Sustainable Clinical Services**

Making services scalable should not compromise standards of evidence, meaningful outcomes and efficacy.[370] As we have noted, we lack basic knowledge about what treatment or assessment strategies in autism are most effective, when and with whom. A better understanding of the 'key ingredients' and mechanisms underlying change (as discussed above in *Mechanisms of Change* ) will better allow us to determine appropriate treatments, assessments and methods of monitoring for all autistic people and their families. However, there are also practicalities in LMIC in terms of the availability of specialists who, at least in urban environments in HIC, are often sought out for care or at least consultation. Even in urban HIC, the reality is that most interventions are not conducted by specialists, but by teachers and education staff, early intervention workers and social service providers.[371] In a few LMIC settings, stepped care is in place, but often not to the degree it could be, nor in a well-supported or supervised fashion. In LMIC, there is a great need for task-sharing approaches (see *Workforce capacity* section below) where specialists train and supervise community-based healthcare and education workers so as to optimise their inputs to individuals with more complex support needs.[81,370,372]

Another question is the degree to which research and programmes developed in HIC countries can and should be applied, with appropriate cultural and contextual adaptations, in other settings, including both LMIC and other HIC countries. Panel 8 provides an example. Use of strategies and tools developed in HIC for screening and diagnosis have been employed in a number of other regions,[173,373] including Jamaica,[374] Africa,[375] and South Asia.[110] In addition, studies have examined specific instruments, such as the ADOS in South Africa.[376] These studies have found general applicability across countries[173] and also in diverse populations within the U.S.[377] Simultaneously, efforts have been made to develop and validate open access tools which can be used with minimal contextual adaptation, for example, the INCLEN Diagnostic Tool for Autism Spectrum Disorder (INDT-ASD) in India.[157]

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*Panel 8*
*PASS Plus: An example of an adapted intervention for autism: Supporting low resource settings to deliver evidence-based care*

The only way to provide equitable care for children and families in India is to consider innovations and systems that can deliver evidence-based interventions in settings with scarce specialist resources. One such innovation is the Parent mediated intervention for Autism Spectrum Disorders in South Asia Plus [PASS Plus], an expanded version of the Pre-school Autism Communication Therapy [PACT],[36] which was systematically adapted and evaluated over two pilot trials in South Asia.[38,244] The adaptation process took an intervention delivered by specialists in a high income setting (the UK) and developed a package that could be delivered by non-specialists with no prior exposure to autism, while still maintaining fidelity. While PACT, and the adapted PASS focused only on social communication; the need to support co-existing behavioural and mental health difficulties for families, resulted in the development of a manualised clinical decision algorithm and expanded the package with the Plus component.

The key strengths of the PACT intervention that permitted the adaptation process were 1) the development of a clinical decision algorithm and careful manualisation, which allowed it to be translated into three languages and provided content for the non-specialist counsellors to communicate to parents of varying literacy, and 2) its parent-mediated approach, which permits the PASS Plus counsellor to deliver strategies to the caregiver without requiring expert knowledge beyond the intervention components itself. The non-specialist counsellor facilitates the parent to build on their strengths and recognises the caregiver as their child's expert, sharing strategies for them to adopt in a systematic phased manner. The direct work with parents results in quicker generalisation and more 'therapy time' across routine activities and supports the low intensity (fortnightly sessions) which in turn increases acceptability and engagement for families and scalability for the health system.

The adaptation and expansion aimed to preserve the mechanistic component of the original social communication intervention identified as parent synchrony; this was facilitated by the use of personalised video feedback, a key component of the original intervention. Each session is centred around a short episode of play between the parent and their child, which is recorded. During feedback, clips of the play are reviewed by the parent and the non-specialist counsellor; the parent is encouraged to identify moments in the play when their behaviours supported their child to communicate. This use of video requires the counsellor to personalise their inputs to meet the needs of individual parents, allowing a reflective discovery of their own efficacy in supporting their child's social communication.

An important part of the adapted PASS Plus package is the training and supervision cascade which includes an objective competency measure, ensuring the fidelity of delivery of a quality session while also ensuring that more complex problems are supported by the specialist who leads the service. This package is currently being evaluated in a cost-effectiveness trial in India.

Research about 'home-grown' vs. 'transported' models of intervention in children's mental health generally[378] suggests that transported models can be adapted and implemented in different cultural contexts with good clinical outcomes. However, this requires sustained attention to adaptation processes, supervision to maintain fidelity over time and a clear understanding of implementation challenges.

Successful applications of adapted interventions developed in the UK and the US to other countries have been made in research settings, most notably the PASS and PASS-Plus adaptations and expansion of PACT (see Panel 8), and the Chinese[379] and Australian[123] adaptations of ESDM. Evaluations of well-established behavioural techniques have also been reported for parent-mediated interventions in Nigeria[380] and rural Bangladesh.[381] Effect sizes from the most well-controlled trials were in fact sometimes even larger than when similar interventions were employed in HIC, potentially because 'treatment as usual' in the comparison groups was less available.[370] Notably, for these studies and others conducted in preparation for similar trials,[59] similarities and differences in implementation barriers and facilitation factors were not always as predicted. For example, in India, families preferred the delivery of parent-mediated interventions at home, whereas in Pakistan, families preferred to come to a local centre.[38] South African caregivers were positive about the opportunities to watch parent-mediated strategies provided in videos of other parents with their children,[382] though African providers were sometimes sceptical about using American videos.

The most successful projects in LMIC, and elsewhere, have consistently welcomed families as active participants not only in service design, evaluation and development, but also in interventions. One issue, across all contexts, but particularly relevant to LMIC is general public awareness of autism and neurodevelopmental disorders. Earlier, in our stepped care/personalised health model (Figures 5, 7), we emphasised that diagnoses should be followed both by provision of information to families about autism, as well as discussion with families about the needs they perceive. For families in LMIC, evidence-informed parent education, training programmes and early access to information online can also connect them to other families, teach skills to support their child, and empower them as advocates for their child, contributing to self-management.[86,230,360] Capacity-building (see below) and implementation of evidenced-based programmes of care in LMIC is critical to support the rights of people with autism and other neurodevelopmental disorders to have their needs met within the context of the Universal Declaration of Human Rights (UDHR), United Nations Convention on the Rights of the Child (UNCRC) and Sustainability Development Goals (SDGs). A recent scoping review outlines a framework to overcome barriers to universal health care for autistic children in LMIC that includes recommendations for practice, policy and research.[383]

Based on the available evidence showing the benefits of parent-mediated interventions delivered by non-specialist providers,[145] the WHO Caregiver Skills Training (CST)[124] is an evidence-informed parenting intervention to support caregivers, both tapping into their existing competences and developing new skills that can foster their child's learning, social communication, and adaptive behaviour. The programme was designed to be implemented by trained non-specialists and adopts a family-centred approach that fits within a stepped-care model for caregivers of children with developmental delays (not only those with autism). CST can serve as a transdiagnostic first step to support families who have developmental delays and neurodevelopmental disorders.

## Technology

Technology has been explored for various purposes, including screening, diagnosis, intervention, outcome monitoring, assisting autistic people to participate in society, and to provide information, training or remote consultation to families and providers[384] (see Table 7). A wide range of technologies has been developed, including personal computers and mobile technologies, shared activity surfaces (e.g., sensing technologies to measure sounds or distances, robotics and virtual reality, aimed at different users in different settings[384,385] and many of these are now available to the autism community.[386] Digital technologies provide opportunities to address geographical inaccessibility, delayed provision of care, and low adherence to clinical protocols. However, digital technologies should enhance and complement functioning health systems and cannot replace important skilled human resources and adequate financing.[80,81,387]

Table 7. Potential applications of evidence-based technologies for autism (adapted from Kumm, 2018[388])

[Table 7 here]

The recent COVID-19 pandemic provided a powerful impetus for families, professionals and businesses across the globe to move towards digital technologies for communication, information, education and healthcare, including in the autism community.[389] Working remotely, treating remotely and coming together through Zoom meetings and other technologies have become more much more commonplace in some regions. However, most relevant to autism, technologies have often been developed without rigorous scientific evidence and without active participation of key users.[384,390] Little consideration has yet been given to the feasibility of implementing such technologies, particularly in LMIC, where the greatest potential impact may be seen.[389] Limitations in feasibility include affordability, accessibility, cultural appropriateness, and sustainability.[391] A 2016 report by the World Bank highlighted that the rise in access to internet and mobile connectivity has been far greater in HIC than in LMIC, risking that the existing 'digital divide' may increase unless concerted efforts are made towards 'universal internet' and mobile access across the globe.[392] The COVID-19 pandemic certainly magnified these pre-existing digital disparities.[389] In addition, somewhat unexpected factors, such as gender differences in access to both smartphones and computers, will be important to consider as assumptions are made about the usefulness of different approaches.[393] In the context of these implementation challenges, Table 7 shows the likely feasibility of a range of technologies for autism.

**Current and Future Uses of Technology for Autism**

The WHO recently generated a classification of Digital Health Interventions organised around four key user groups – those living with health conditions and their families, healthcare providers, health systems/resource managers, and data services[391] - each of which is relevant to the use of technology in autism. Here we propose five pragmatic uses of technology for autism in the coming years:

*1. Technology for connecting people to people*
Contemporary social media technologies (e.g., Whatsapp[TM] and Facebook[TM] and similar systems) may be powerful tools to connect families and individuals who live with autism to one another (; http://www.thinkingautismguide.com). Online platforms can also connect families and individuals with autism to professionals (e.g., through electronic appointment bookings for someone with autism who would struggle to do so over the phone or in person), while also supporting the formation of user groups (e.g., a group of trained therapists for a specific intervention).

*2. Technology for connecting people to knowledge and for training*
An increasing number of online resources are available to individuals with autism and their families, offering research summaries, state-of-the-art information updates and 'toolkits' on a range of topics. These include information about specific tools, suites of local and national resources for families and practitioners about young children, and an e-textbook from an international association of providers of children's mental health services.[394] Formalised training and certification courses for specific interventions can also leverage technology. Virtual and Augmented Reality is also being explored for both interventions and training purposes.[395]

*3. Technology for screening/surveillance, diagnosis, consultation and clinical care*
Complex electronic systems for medical records, surveillance, targeted communication, decision support and data management, as well as affordable, accessible tools for webinars and video conferencing, are now available. This has allowed for new models of clinical care such as for screening and surveillance[396,397] and the ECHO model for remote peer-on-peer consultation.[65] A recently developed series of digital tasks, using eye-tracking and fine motor coordination has shown promising early results to differentiate typical and delayed development in Indian 2-6-year-olds.[186] Electronic health records will continue to gain in sophistication and will support further improvement in data management and communication.

*4. Technology for Alternative and Augmentative Communication (AAC)*
There are a range of AAC devices and therapeutic tools[398] and many innovations possible in this domain. These include speech-generating devices[93,399] and less high-tech methods of communicating using pictures (e.g., the Picture Exchange Communication System [PECS][398]).

*5. Technology for new types of data collection and analysis*
Technological advances may become particularly transformative in the collection of new types of data, including behavioural analyses (e.g., through wearable devices[400]), potentially with the use of increasingly sophisticated artificial intelligence and 'big data' methodologies. Data are needed to support their validity and reliability.

**Risks and Pitfalls of Technology for Autism**

Despite the increasing potential benefits of technology for autism, there are also multiple risks and pitfalls to be considered. These include technical challenges such as calibration of tools (e.g., tablets, eye-trackers, smartphones); the need to validate and generate an evidence-base for the technology, including how is it actually used; the risk of false claims, misinformation and predatory commercial practices; privacy and confidentiality issues and ownership and curation of data; safeguarding and protection against exploitation of potentially vulnerable users; and screen addiction. Cost and accessibility of the technology, as well as acceptability to different users, will remain a significant risk to be considered to ensure that the 'digital divide' that currently exists between HIC and LMIC does not become larger, thereby increasing rather than decreasing current the disparities.[392]

## Workforce Capacity, Competency and their Role in Implementation

The WHO set out key recommendations for building capacity to support individuals with autism and other neurodevelopmental disorders across several levels from institutional and academic activity, to civil society and government, that support our proposed models of stepped care/personalisation health in both assessment and treatment/support.[401] Whilst utilising the relevant evidence, interventions must match local contexts.[383] In LMIC or sparsely populated contexts, one strategy is the development of broad skills to equip staff to work with the population within their specific context.[82] Such 'task sharing,' as discussed earlier within the stepped care/personalised health model, requires reconfiguring tasks between professionals; ensuring that complexity of the work demands matches the skill level of the provider; and task sharing between professionals and non-professionals, each of which is critical in LMIC settings where the number of professionals available is limited. As highlighted above in our *Recommendations for Clinical Research* (Panel 6), we need more trials that study effectiveness and implementation factors rather than simplistic efficacy trials of one intervention compared to 'treatment as usual', in order to inform how evidence-based interventions can be scalable and adapted for use in LMIC and other under-resourced settings.

In rural Australia, for instance, researchers introducing a Rural Allied Health Generalist, delineated 337 discrete tasks across 6 allied health professionals (AHPs), with 45% of the tasks already delivered by more than one profession and 38% by more than two. Reconfigured tasks were repackaged into 13 categories based on functional and diagnostic categories, rather than traditional professional repertoires and made available to all AHPs.[82] Increased skill flexibility is achieved in several ways: by enabling one professional to do tasks traditionally allocated to others in order to cover a wider range of care needs (e.g., Rahman *et al.*[38]); delegating tasks requiring less training so that the highest skilled individuals can do the most complex activities; task-sharing between professional and non-professional groups (e.g., parents) while expecting experts or professionals to retain particular responsibilities, and broadening skills horizontally to support more integrated care.[401]

In HICs, well-established systems and competency frameworks established by professional regulatory bodies may act as barriers to flexible working and task sharing.[82] Radical and more controversial solutions include shortening professional training, focusing on specific skill acquisition in incremental phases with a 'step on – step off' curriculum with several exit points in training,[82] sometimes referred to as micro-credentialing.[402] Programmes such as Increasing Access to Psychological Therapies (IAPT) in the UK have been able to teach core skills and recruit practitioners from a range of backgrounds.[403] In all contexts, sustainability requires ongoing supportive supervision, ideally with a local implementation champion, and ensuring local ownership of the programme[394] and the knowledge that more expectations cannot just be added to the roles of non-specialists without recognition and allocation of resources. Systems improvement, active engagement of healthcare managers and users, and consideration of performance-based financing are all necessary to improve the application of knowledge to delivery.[404] In neurodevelopmental conditions such as autism, proactive, developmentally phased life-span system models of management that recognise periods of increased or decreased need in the individual or their family are appropriate.[47] Across the globe there is a very limited skilled workforce with expertise and experience of working with autistic adults across all levels of identification, diagnosis, intervention and support. Thus, systems are needed to support more skilled workers at both non-speciality and speciality levels.

**Conclusions**

Autism Spectrum Disorder is a heterogeneous human condition that affects how people interact with others and with their world across the lifespan. It is both relatively specific in some of its characteristics (e.g., particular repetitive movements and interests, aspects of communication, effects on relationships) and also general in its association with cognitive strengths and limitations, difficulties in self-regulation, mood and attention. It is a prototype of a neurodevelopmental disorder in that it arises from early emerging differences in brain development that affect many aspects of behavioural, social and cognitive development and functioning across time. The experiences and lack of experiences associated with autism, affect brain and behavioural development. Autism affects both the people who receive the diagnosis and their families across the world. Yet individuals and their families can show amazing strengths in persistence, patience and perception that, in turn, can change development as well. Continued respect for this diversity and heterogeneity is key. We also believe that there are times when it is important to consider autism as a specific disorder and other times when recognition of the overlaps among neurodevelopmental disorders is under-recognised and needs to be more carefully considered.

The goal of this Commission was to identify what can be done to improve and support the quality of life for children and adults with autism and their families across the globe. We built on what we already know to identify strategies and goals for future research and clinical practice, and to promote more equitable and broader dissemination and implementation of resources and services. We are aware that the evidence base that informed our recommendations is not perfect. However, one of the major premises underlying our recommendations is that we can do much more than we are doing, noting the need for social justice and a responsibility to those living now as well as to future generations. Individuals with autism are a valued part of our societies. We urge commitment to greater investment in what we can do for them and their families now, with a focus on how we

can build on existing information to answer specific practical questions that will then better inform interventions and services to help autistic individuals achieve their fullest potential.

This is a time for optimism with acknowledgement of the potential for change that is present in different ways at different times within autism. However, this is also a time for realism about what we can do across contexts, including HIC and LMIC, and across the lifespan. In this context, we have proposed the use of the term profound autism to describe individuals who are very likely to need significant support throughout their lives, but still have opportunities for improved quality of life through positive daily activities, supported independence in everyday actions and social contacts. We also need realism about the scarcity of resources, inequities and the need for social justice, and the kinds of system developments that will be required to make these changes happen.

Autism is a neurobiological disorder. We have not dwelt much on biology here, not because it is unimportant, but because the likely benefits of basic science and even translational science to autism, for the most part, are for very particular populations (e.g., rare genetic disorders) or are someway distant. We recognise the importance and future promise of basic science, but argue that deliberate investment in clinical research *now* is equally important in achieving goals of improvements in the quality of life for autistic persons and their families.

Social justice is a theme we embrace beyond heterogeneity, the potential of change and the need for systems change. The proportion of autistic people and families who receive adequate support is small even in high-income countries and very small in LMIC. This occurs because of lack of knowledge about what is necessary for whom and when; and lack of prioritisation in systems of social, health care, and research funding. If we better understood the answer to relatively obvious questions about for whom, how much and when interventions are needed and efficacious, as well as more about the active ingredients behind changes, resources could be allocated more appropriately and effectively. For much of the rest of the world though, issues start with a lack of resources and quickly circle back to even greater knowledge gaps, stigma and systems that do not value human life and persons with disability. In general, our recommendations for both clinical practice and systems change are based on beginning with needs and methods of change considered within models of stepped care/ personalised health for intervention and assessment – and with continual involvement of stakeholders including autistic individuals, families, supportive community members and providers at each step of the way. Capacity building is critical to strengthen care systems, particularly in LMIC, and for under-resourced populations in HIC. In the contexts of cultural and regional diversity, research and service approaches that employ dimensional approaches to factors that influence development yielding personalised, dynamic models of intervention and services, will be the key to a better future for individuals with autism and other neurodevelopmental conditions.

### Actionable recommendations

1. Autism affects at least 78 million people around the world, yet formal documentation of their existence is limited to a subset of countries. Formal documentation through governmental health, education and social care systems of people affected by autism would

be a first step in determining needs and addressing potential inequalities in these individuals.

2. Autism is a complex though common neurodevelopmental disorder which requires personalised assessments and intervention strategies. A stepped care personalised health model for assessment and determination of interventions can increase the effectiveness and efficiency of approaches. Governments and healthcare systems must recognise the need for integration across systems to support the needs of autistic individuals and their families across development.

3. Autism is a neurodevelopmental disorder that changes with development and in turn affects development. A single assessment or a single treatment is never sufficient. Follow-up assessments and personalised treatment plans that focus on individual strengths, difficulties and changes in contexts and expectations across the lifespan are needed.

4. Interventions for autism and for co-occurring conditions should begin as soon as symptoms are noticed and then monitored with more comprehensive assessment once begun. No one should wait months or years to start treatment because they are unable to find an appropriate assessment. However, during some reasonable period of time (i.e., no more than several months), assessments do need to be supported and carried out to identify personalised needs.

5. Focused research strategies at a government or institutional level should be prioritised with an emphasis on clinical practice that can increase our understanding of what interventions work, for whom, when, how, with what generalised outcomes and at what cost. National and international infrastructure should be developed to help such projects move beyond single-investigator led, albeit multi-site studies to more integrated attempts that take into account individual differences within autism, support studies that build on each other and provide evidence for broader community implementation and effectiveness, rather than simply show an intervention is better than a waitlist or treatment as usual.

6. Governments and services should monitor access to provision to ensure that underserved groups, including those who are minimally verbal, females, ethnic minorities, those from social disadvantaged backgrounds and those with severe co-occurring conditions, have equitable access to appropriate services.

**List of Figures, Tables, and Panels**

# List of Abbreviations

Terms and Abbreviations
- ADHD = Attention deficit/hyperactivity disorder
- AHP = Allied health professionals
- ASD = Autism spectrum disorder
- BMI = Body mass index
- CAM = Complementary or alternative medicine
- CPG = Clinical practice guideline
- CI = Confidence interval
- CPG = Clinical practice guidelines
- DALY = Disability adjusted life years
- DSM = Diagnostic and Statistical Model
- EEG = Electroencephalogram
- GFCF = Gluten free, casein free
- GI = Gastrointestinal
- HIC = High income countries
- HR = Hazard ratio
- ICD = International Classification of Diseases
- IQ = Intelligence quotient
- LMIC = Low and middle-income countries
- LR = Likelihood ratio
- MOST = Multiphase Optimisation Strategy
- NDBI = Naturalistic developmental behavioural intervention
- NDD = Neurodevelopmental disorders
- RCT = Randomised controlled trial
- RR = Relative risk
- RVE = Robust variance estimation
- SMART = Sequential Multiple Assignment Randomised Trial
- SNRI = Serotonin-norepinephrine reuptake inhibitor
- SSRI = Selective serotonin reuptake inhibitor
- YLD = Years lived with disability

Policies and Institutions
- AHRQ = Agency for Health Research and Quality
- APA = American Psychiatric Association
- AWMF = Association of Scientific Medical Societies (Germany)
- CASDA = Canadian Autism Spectrum Disorder Alliance

- CDC = Centers for Disease Control and Prevention
- HCWA = Helping Children with Autism
- IDEA = Individuals with Disabilities Education Act
- NDIS = National Disability Insurance Scheme
- NICE = National Institute for Health Care and Excellence
- NIH = National Institutes of Health
- RTE = Right of Children to Free and Compulsory Education
- SDG = Sustainable Development Goals (UN)
- SIGN = Scottish Intercollegiate Guidelines Network
- UDHR = Universal Declaration of Human Rights
- UN = United Nations
- UNCRC = United Nations Convention on the Rights of the Child
- UNESCO = United Nations Educational, Scientific and Cultural Organisation
- USPST = US Preventive Services Task Force
- WCFID = Western Cape Forum for Intellectual Disability
- WHO = World Health Organization

Programs and Interventions
- AAC = Alternative and Augmentative Communication
- ABA = Applied Behaviour Analysis
- AIM HI = An Individualized Mental Health Intervention for Children with ASD
- BIACA = Behavioural Interventions for Anxiety in Children with Autism
- CBT = Cognitive Behavioural Therapy
- CST = Caregiver Skills Training (WHO)
- DBT = Dialectical Behavioural Therapy
- DTT = Discrete Trial Training
- ECHO = Extension for Community Healthcare Outcomes
- EDX = Early Diagnosis Study
- EIBI = Early Intensive Behavioural Intervention
- EMT = Enhanced Milieu Teaching
- ESDM = Early Start Denver Model
- ESI = Early Social Interaction
- JASPER = Joint Attention, Symbolic Play, Engagement, and Regulation
- IAPT = Increasing Access to Psychological Therapies
- IS = Interpersonal Synchrony
- LEAP = Learning Experiences - An Alternative Program for Preschoolers and Parents
- MoBa = Norwegian Mother, Father and Child Cohort Study
- PACT = Preschool Autism Communication Trial

- PASS = Parent mediated intervention for Autism Spectrum Disorders in South Asia
- PCIT = Parent-Child Interaction Therapy
- PECS = Picture Exchange Communication System
- PEERS = Program for the Education and Enrichment of Relational Skills
- PRT = Pivotal Response Training
- RUBI = Research Units in Behavioural Intervention
- SNAP = Special Needs and Autism Project
- SOSTA-FRA = Social Skills Training Autism – Frankfurt
- TEACCH = Treatment and Education of Autistic and Related Communication Handicapped Children

Assessments
- ADI-R = Autism Diagnostic Interview–Revised
- ADOS-2 = Autism Diagnostic Observation Schedule–2nd Edition
- ADOS CSS = ADOS Calibrated Comparison Score
- BOSCC = Brief Observation of Social Communication Change
- CARS = Childhood Autism Rating Scale
- INDT-ASD = INCLEN Diagnostic Tool for Autism Spectrum Disorder
- M-CHAT-R/F = Modified Checklist for Autism in Toddlers - Revised with Follow-up
- SCQ = Social Communication Questionnaire
- SDQ = Strengths and Difficulties Questionnaire
- SRS = Social Responsiveness Scale

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## Contributors

All authors made contributions towards the scope, structure, and key messages of the Commission. CL and TCh oversaw the drafting of the initial and final report. CL, JMcC, AHa, and ES analysed data presented in the profound autism section. AHa analysed data from the ABC/MoBa for the section on assessment; PC led the subcommittee on medical needs including medications, with contributions from other committee members. AP created Figures 2 and 4. Other authors made contributions to specific sections of the Commission and various tables, figures and panels. All authors reviewed the drafts of the Commission and approved the final version.

## Declaration of Interests