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Honorable Chairwoman Bass, Ranking Member Smith and Members of the Subcommittee, thank you for the opportunity to testify before you today. My remarks today will focus on introducing autism spectrum disorder, which is increasingly being recognized as a major public health challenge, its causes and its broad impact here and in Africa. I will first define autism, describe what we have learned about its causes, its impact on diverse populations, and how gaps in understanding and treatment in Africa impact the U.S.

What **is autism?** Autism is a common brain disorder affecting 1/54 children, 4 times more boys than girls[1], and is the leading cause of disability in children under 5[2]. It is a chronic, typically life-long condition[3], with onset in very early infancy, that is characterized by abnormal social development and functioning and the presence of repetitive, restrictive behaviors - the latter often manifest by resistance to change and repetitive movements.

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[1] Maenner MJ, Shaw KA, Baio J*, et al.* Prevalence of Autism Spectrum Disorder Among Children Aged 8 Years - Autism and Developmental Disabilities Monitoring Network, 11 Sites, United States, 2016. MMWR Surveill Summ. 2020;69(4):1-12. Epub 2020/03/28. doi: 10.15585/mmwr.ss6904a1. PubMed PMID: 32214087; PMCID: PMC7119644

[2] Baxter AJ, Brugha TS, Erskine HE*, et al.* The epidemiology and global burden of autism spectrum disorders. Psychol Med. 2015;45(3):601-13. Epub 2014/08/12. doi: 10.1017/S003329171400172X. PubMed PMID: 25108395.

[3] Howlin P. Adults with Autism: Changes in Understanding Since DSM-111. Journal of Autism and Developmental Disorders. 2021. doi: 10.1007/s10803-020-04847-z.

A large proportion of children with autism also have abnormalities in language (about 30% have fewer than 20 words), hypersensitivity to sensory stimuli (light, touch etc.), and gross and fine motor abnormalities, all of which further contribute to disability. Approximately 30% will also have intellectual disability and a smaller proportion will have epilepsy or seizures (10%). The wide variability in severity and allied symptoms has led to the framing of autism as a spectrum, called autism spectrum disorder (ASD)[4].

There is no single test for autism and it represents many different forms, similar to pneumonia, cancer and most other common disorders. Getting an accurate diagnosis is not easy, and is diagnosed by highly trained practitioners, such as psychologists, psychiatrists, neurologists or developmental pediatricians, who observe the child in a structured setting and obtain a medical and developmental history. The need for highly trained professionals can lead to significant delays in diagnosis and treatment.

Outcomes vary widely, but it is clear that early diagnosis and intervention lead to much better outcomes. **Therefore, a major effort in the field has been to diagnose autism as early as possible and initiate behavioral treatments, which have been shown to improve outcomes**[5,6]. There is no pill to fix autism. Medications are limited to those that target symptoms or comorbid conditions (e.g. anxiety, epilepsy). Treatment typically relies on labor-intensive behavioral interventions. Despite this progress, more than half of children with ASD will not live independently[7] and even among those with higher education, long-term employment remains

[4] American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Arlington, VA: American Psychiatric Association; 2013.
[5] Warren Z, McPheeters ML, Sathe N*, et al.* A systematic review of early intensive intervention for autism spectrum disorders. Pediatrics. 2011;127(5):e1303-11. Epub 2011/04/06. doi: 10.1542/peds.2011-0426. PubMed PMID: 21464190.
[6] Lord C, Brugha TS, Charman T*, et al.* Autism spectrum disorder. Nat Rev Dis Primers. 2020;6(1):5. Epub 2020/01/18. doi: 10.1038/s41572-019-0138-4. PubMed PMID: 31949163.
[7] Institution of Education Sciences: National center for special education research. The Post-high school outcomes of young adults with disabilities up to 8 years after high school. 2011.

low[8]. However, modern research is identifying ways to improve this[9] and provides hope for the current generation.

Disparities in diagnosis. It is in this regard that I bring your attention to substantial disparities in the delay of diagnosis in ASD in this country, which indicate that there are substantial problems in access to treatment and services in communities of color, namely for Hispanic and Black children[10]. Rates of ASD prevalence determined by the CDC were initially lower in Black and Hispanic populations in the US, but this was almost certainly due to disparity in recognition and diagnosis, as recent CDC estimates are on par with White children. **However,** there still remain serious delays in diagnosis[11]. On average, Black children with ASD have a 3-year delay in diagnosis relative to White children[12] – this likely has a major negative impact on outcomes[13,14]. This is evidenced by the nearly two-fold higher prevalence of intellectual disability among Black children with ASD at age eight than their White peers[1,*]. Given the enormous cost to society, these disparities likely have an outsized economic and social impact[15]; ASD is estimated to cost $268 to $461 billion US dollars annually for educational and medical services, residential care and productivity loss[16].

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[8] Howlin P. Adults with Autism: Changes in Understanding Since DSM-111. Journal of Autism and Developmental Disorders. 2021. doi: 10.1007/s10803-020-04847-z.

[9] UCLA PEERS Clinic. Available from: https://www.semel.ucla.edu/peers/peers%C2%AE-careers.

[10] Maenner MJ, Shaw KA, Baio J*, et al.* Prevalence of Autism Spectrum Disorder Among Children Aged 8 Years - Autism and Developmental Disabilities Monitoring Network, 11 Sites, United States, 2016. MMWR Surveill Summ. 2020;69(4):1-12. Epub 2020/03/28. doi: 10.15585/mmwr.ss6904a1. PubMed PMID: 32214087; PMCID: PMC7119644

[11] Constantino JN, Abbacchi AM, Saulnier C*, et al.* Timing of the Diagnosis of Autism in African American Children. Pediatrics. 2020;146(3). Epub 2020/08/26. doi: 10.1542/peds.2019-3629. PubMed PMID: 32839243; PMCID: PMC7461218

[12,13] Ibid.

[*] Similar disparities exist in other under-represented groups.

[14] Broder-Fingert S, Mateo CM, Zuckerman KE. Structural Racism and Autismibid. doi: 10.1542/peds.2020-015420. PubMed PMID: 32839244; PMCID: PMC7461217.

[15] Lavelle TA, Weinstein MC, Newhouse JP*, et al.* Economic burden of childhood autism spectrum disordersibid.2014;133:e520-9. Epub 2014/02/12. doi: 10.1542/peds.2013-0763. PubMed PMID: 24515505; PMCID: PMC7034397.

[16] Wright J. Over next decade, cost of autism could escalate sharply: Spectrum; 2015. Available from: https://www.spectrumnews.org/news/over-next-decade-cost-of-autism-could-escalate-sharply/.

This disparity is magnified substantially in the developing world. In West Africa, with an approximate population of about 300 million, there are only about 35 clinicians who work in autism, just a fraction of the number in Washington DC, or any of our major cities. There are about 75 child psychiatrists in Sub-Saharan Africa, which I estimate is fewer than the Upper West Side of Manhattan[17]. Even in the US, there is about 1 child psychiatrist for every 2,000 children or adolescents needing care[18,19], still a shortage, whereas this ratio for autism health providers is approximately 1 per 3.5 million in West Africa!

Causes and prevalence. It is crucial to know the cause of a disease to treat it most effectively. Not knowing what causes a disease leads to all kinds of problematic choices, some serious, such as high-risk therapies with no proven efficacy (e.g., iron chelation therapy[20,21]) and skipping important vaccinations (when there is no real association between childhood vaccinations and ASD[22]), leading to serious illness[23,24], to missing opportunities by providing harmless, but relatively ineffective therapy.

In the last 77 years since its framing as a developmental disorder, concepts of autism within psychiatry have changed significantly in parallel with the development of the concept that

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[17] Healthgrades.com. Child & Adolescent Psychiatry near New York, NY 2021. Available from: https://www.healthgrades.com/adolescent-psychiatry-pediatric-psychiatry-directory/ny-new-york/new-york.

[18] American Academy of Child & Adolescent Psychiatry. Workforce Issues 2019. Available from: https://www.aacap.org/aacap/Resources_for_Primary_Care/Workforce_Issues.aspx.

[19] McBain RK, Kofner A, Stein BD*, et al.* Growth and Distribution of Child Psychiatrists in the United States: 2007–2016. Pediatrics. 2019;144(6):e20191576. doi: 10.1542/peds.2019-1576.

[20] Hoecker M.D. JL. Autism treatment: Can chelation therapy help? : Mayo Clinic; 2016. Available from: https://www.mayoclinic.org/diseases-conditions/autism-spectrum-disorder/expert-answers/autism-treatment/faq-20057933.

[21] James S, Stevenson SW, Silove N*, et al.* Chelation for autism spectrum disorder (ASD). Cochrane Database Syst Rev. 2015;5:CD010766. Epub 2015/06/27. doi: 10.1002/14651858.CD010766.pub2. PubMed PMID: 26114777; PMCID: PMC6457964.

[22] Di Pietrantonj C, Rivetti A, Marchione P*, et al.* Vaccines for measles, mumps, rubella, and varicella in childrenibid.2020;4:CD004407. Epub 2020/04/21. doi: 10.1002/14651858.CD004407.pub4. PubMed PMID: 32309885; PMCID: PMC7169657. ibid.

[23] Gahr P, DeVries AS, Wallace G*, et al.* An outbreak of measles in an undervaccinated community. Pediatrics. 2014;134(1):e220-8. Epub 2014/06/11. doi: 10.1542/peds.2013-4260. PubMed PMID: 24913790; PMCID: PMC8167837.

[24] DeStefano F, Shimabukuro TT. The MMR Vaccine and Autism. Annu Rev Virol. 2019;6(1):585-600. Epub 2019/04/16. doi: 10.1146/annurev-virology-092818-015515. PubMed PMID: 30986133; PMCID: PMC6768751.

disorders of cognition and behavior had an organic, brain-based etiology. In the 1960s the prevailing wisdom was that it could largely be attributed to parenting styles, which is not the case[25]. It was not until the early 1980s that autism was classified as a developmental disorder and widely accepted as having a biomedical origin, fueled by the demonstration that autism was heritable and was associated with a variety of genetic syndromes[26]. In fact, heritability for ASD is estimated at about 80%[27,28], and another 15% is caused by non-inherited rare mutations[29] (like Down's Syndrome), indicating that most risk for autism is genetic. But, there is room in some cases for environmental causes, such as certain maternal infections, increasing age of the father, low inter-pregnancy interval, as well as birth complications and preterm birth[30]. Most of the estimates are from developed countries, but given that there is no strong evidence for regional variation in ASD prevalence across the world[31], these estimates likely apply to Africa as well.

Autism has a genetic basis. Over the past two decades, genetic studies have led to a revolution in our understanding of the disorder. This is no exaggeration, as more than 100 ASD risk genes have been identified in the last decade[32,33]. These genes implicate early brain prenatal development as the critical period for ASD risk, and provide a new window onto specific disease

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[25] Geschwind DH. Advances in autism. Annu Rev Med. 2009;60:367-80. Epub 2009/07/28. doi: 10.1146/annurev.med.60.053107.121225. PubMed PMID: 19630577; PMCID: PMC3645857.

[26] Lord C, Brugha TS, Charman T*, et al.* Autism spectrum disorder. Nat Rev Dis Primers. 2020;6(1):5. Epub 2020/01/18. doi: 10.1038/s41572-019-0138-4. PubMed PMID: 31949163.

[27] Tick B, Bolton P, Happé F*, et al.* Heritability of autism spectrum disorders: a meta-analysis of twin studies. Journal of Child Psychology and Psychiatry. 2016;57(5):585-95. doi: https://doi.org/10.1111/jcpp.12499.

[28] Bai D, Yip BHK, Windham GC*, et al.* Association of Genetic and Environmental Factors With Autism in a 5-Country Cohort. JAMA Psychiatry. 2019;76(10):1035-43. doi: 10.1001/jamapsychiatry.2019.1411.

[29] Manoli DS, State MW. Autism Spectrum Disorder Genetics and the Search for Pathological Mechanisms. Am J Psychiatry. 2021;178(1):30-8. Epub 2021/01/02. doi: 10.1176/appi.ajp.2020.20111608. PubMed PMID: 33384012; PMCID: PMC8163016.

[30] Jutla A, Reed H, Veenstra-VanderWeele J. The Architecture of Autism Spectrum Disorder Risk: What Do We Know, and Where Do We Go From Here? JAMA Psychiatry. 2019;76(10):1005-6. doi: 10.1001/jamapsychiatry.2019.1375.

[31] Baxter AJ, Brugha TS, Erskine HE*, et al.* The epidemiology and global burden of autism spectrum disorders. Psychol Med. 2015;45(3):601-13. Epub 2014/08/12. doi: 10.1017/S003329171400172X. PubMed PMID: 25108395.

[32] Satterstrom FK, Kosmicki JA, Wang J*, et al.* Large-Scale Exome Sequencing Study Implicates Both Developmental and Functional Changes in the Neurobiology of Autism. Cell. 2020;180(3):568-84 e23. Epub 2020/01/26. doi: 10.1016/j.cell.2019.12.036. PubMed PMID: 31981491; PMCID: PMC7250485.

[33] Ruzzo EK, Perez-Cano L, Jung JY*, et al.* Inherited and De Novo Genetic Risk for Autism Impacts Shared Networksibid.2019;178(4):850-66 e26. Epub 2019/08/10. doi: 10.1016/j.cell.2019.07.015. PubMed PMID: 31398340; PMCID: PMC7102900.

mechanisms. These genes are now serving as targets for the development of new therapies by the biotech and pharmaceutical industries by providing specific causes (similar to the idea of knowing what bacteria to treat in pneumonia). In this way, genetic findings are providing a "hope for a new neurology of autism," and a bridge towards Precision Medicine in ASD: "the right treatment, for the right patient, at the right time."

Disparities. However, very little work has been done to elucidate the genetic causes of ASD in African American or African populations. This is important because ancestry plays a big role in genetic risk, such that different ancestries may have different genetic contributions to disorders such as autism. Therefore, we can't necessarily use the information gathered in White European populations in African or African American populations. Further, having a diverse group of ancestries studied can substantially reduce the rate of genetic misdiagnosis in every group, including European ancestries. Studying diverse ancestries is also crucial help in pinpointing the actual causal genetic changes in patients, enabling one to sift through the huge amounts of data to find the real cause. So, understanding the basis of ASD in Africa will have large beneficial impacts on ASD in the United States and the world.

Summary and Recommendations.

1) Our understanding of autism has changed markedly in the last two decades due to growth and advances in research and clinical treatment. Continuing that trajectory is essential to decreasing societal burden. In most cases, research is tightly coupled to the groups offering state-of-the art clinical care, forming a virtuous circle where the research findings can be more rapidly put into practice.
2) The vast majority of research has been done in White European populations, and there is a need to increase inclusion of diverse populations, especially Black Americans, who represent 11% of the US population, but are severely under-represented in autism and brain disease research in general. The same holds true for Hispanic Americans.

3) Further, we must lower structural barriers that limit access to diagnostic services and treatment in under-resourced communities[34], which will have a long-term impact by permitting earlier and more effective intervention. Innovative "ehealth" approaches need to be studied validated, so as to expand provider reach (e.g. telehealth), without reducing effectiveness.
4) Access to qualified providers in communities of color is a major problem and this work force needs urgent expansion.
5) Insurance programs supporting under-resourced communities, such as Medicaid, need to provide equitable rates for mental health services required by autistic individuals[35].

Why Africa? Expanding research and clinical care in Africa has the advantage that advances in understanding and clinical care can be accomplished at far lower cost than in the developed world. To be effective and sustainable, this effort must work via supporting local clinicians and researchers, who can be trained to the state-of-the-art via exchange programs and interactions with colleagues in the US.

My own experience mentoring and working closely with one of the few neurologists in Mali has demonstrated that remote mentoring can be effective[36]. Through this effort, my Malian colleague is building a world-class research program and has translated two widely-used instruments for autism screening to be culturally appropriate.

Workforce expansion and training in Africa is sorely needed and is feasible and cost effective. This will have a direct impact on local populations, lowering the overall economic and societal burden of disease, by intervening earlier, and will also have direct impact for the US, via its economic impact, and the knowledge gained, which can be directly applied to our population.

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[34] Broder-Fingert S, Mateo CM, Zuckerman KE. Structural Racism and Autism. Pediatrics. 2020;146(3). Epub 2020/08/26. doi: 10.1542/peds.2020-015420. PubMed PMID: 32839244; PMCID: PMC7461217.
[35] Ibid.
[36] Sangare M, Toure HB, Toure A*, et al.* Validation of two parent-reported autism spectrum disorders screening tools M-CHAT-R and SCQ in Bamako, Mali. eNeurologicalSci. 2019;15:100188. Epub 2019/03/30. doi: 10.1016/j.ensci.2019.100188. PubMed PMID: 30923752; PMCID: PMC6423411.