Dear Dr. Volkmar:

Thank you for your email. We have prepared a detailed response to your request, but first we would like to defend our work more broadly.

We believe that "Autism Tsunami" advances the state of the art in modeling the societal costs of autism. A small set of previous studies attempted to measure full-country costs of autism (Jarbrink and Knapp, 2001; Ganz, 2007; Knapp et al., 2009; Buescher et al., 2014; Leigh & Du, 2015; Cakir et al., 2020). We reviewed all of these studies with care, built upon their strengths, corrected many of their weaknesses and improved upon them in a comprehensive fashion.

"Autism Tsunami" was peer reviewed by two reviewers. The first one said, "Simply excellent." The second reviewer stated that "After reading the paper entirely, the abstract understates the true contribution of this study." We were encouraged by this reviewer to reword the abstract and another section of our paper to highlight the unique contributions of our analysis.
Following its publication online and some social media criticism, one of the world's most prominent autism prevalence researchers reached out to tell us that our prevalence models are correct and that forthcoming publications will underscore the accuracy of our model.
We have organized our response here in two parts: 1) to the blog article that appears to have led to your query and 2) to the reviews themselves.

1. Spectrum News

In your August 13 email to us, you wrote, "I am writing to inform you that concerns have been raised about your article 'Autism Tsunami: the Impact of Rising Prevalence on the Societal Cost of Autism in the United States.' These concerns include both potential undisclosed conflicts of interest and potential methodological issues." Forgive us if we are incorrect, but this dual concern mirrors the arguments made against our work in a recent, hostile blog post in *Spectrum News*.

The *Spectrum News* piece was penned by a freelance writer, Sara Luterman, who has an MFA in creative writing. Based on an email query to us it was clear that Sara Luterman had not read any of the relevant cost of autism literature, struggled to understand even the basic facts in our study, and seemed unclear on how to look up and read references. In her outreach to us, she had questions to us about potential undisclosed conflicts of interest and methodological issues, the same issues your email raised.

Undisclosed conflicts of interest. All three authors share a perspective that the rise in autism is real, deeply concerning, and is caused primarily by environmental factors. This is a legitimate scientific viewpoint, shared by many (perhaps most) scientists and supported by an extensive body of scientific literature (Gilbert, 2008; Landrigan et al., 2012; Bennett et al., 2016) as well as government data (IDEA, California DDS, ADDM). Addressing this crisis is the motivation for our work, *as we assume it is for all authors published in JADD*. The idea that this perspective must be disclosed as a "non-financial conflict of interest" is surprising to us (we note that the term "ideological commitments" does not actually appear in the JADD guidelines). A century of research on the history and philosophy of science shows that all authors bring a unique perspective to their work. Yet, after reviewing all 633 Open Access articles published in JADD since 2007, we did not find a single instance in which a JADD author declared any "personal beliefs" as a conflict of interest.

In terms of any alleged financial COIs, the research in connection with "Autism Tsunami" was funded out of our own pockets. Out of an abundance of caution Mark Blaxill listed his work as CFO of an autism treatment center (serving children and, recently, young adults) as a possible conflict. We are concerned about rising autism prevalence and costs, that's why we wrote the article. While *Spectrum News* may want to erase, cancel, and censor anyone who disagrees with their particular viewpoint, suppression of others' views is not good science and such tendencies should be resisted.

Any adverse action against this article would have a chilling effect on scientific discourse in this country. Autism rates and costs will continue to rise. Yet discussion of costs will be inhibited by the fear of being blacklisted. Policy makers will be discouraged from anticipating the increased revenue required to provide services. Productive discussion on causes and prevention will be stifled. Millions of adults with autism will simply be left to fend for themselves in a dystopian future. As the editor of a journal that we have valued for its commitment to fairness, diversity of opinion, and commitment to due process, we hope you will take seriously your scholarly and moral responsibility to defend our article against unfounded and ideologically-motivated attacks.

Methodological issues. The most prominent named scholar in the *Spectrum News* post was Dr. David Mandell, who according to Luterman, stated "The rise in autism prevalence in recent years can be attributed to better observation and increased diagnosis on the community level." Mandell is at least twenty years out of date in his understanding of autism prevalence. He seems unaware of two multi-million dollar studies on this question funded by the state of California, Byrd et al. (2002) and Hertz-Picciotto and Delwiche (2009) who concluded that better awareness and changes in diagnostic criteria "do not get us close" to explaining the skyrocketing rise in autism prevalence (see also the interview with Hertz-Picciotto in *Scientific American*, Cone, 2009, para. 13). Furthermore, there is now a massive literature that shows that the rise in autism prevalence in the U.S. is real and troubling (see for example, Zablotsky et al. 2017, data from the CA Department of Developmental Services, Nevison, Blaxill and Zahorodny, 2018 and additional work by Walter Zahorodny).

It is possible that Mandell's criticism of our study stems from our critique of his earlier cost of autism study (Buescher et al., 2014). Several years ago, David Mandell and Mark Blaxill had disagreed in a respectful, private exchange on Mandell's extraordinary assumption of only 20% individual productivity loss for both severe and mild autism in the United States in his Buescher et al. (2014) publication. The 2014 paper oddly provided no reference for this critical input to their model. Here is the section of "Autism Tsunami" that references this exchange.

> … Buescher et al. almost certainly underestimated adult ASD costs, primarily due to the exceptionally low value of $10,718/yr assumed for individual productivity loss (both with or without co-occurring ID)... The reason for the low value is that Buescher assumed a high employment rate for all individuals with ASD, regardless of ID status. In contrast, we assume an employment rate of 0% and 30% of those with severe and mild ASD, respectively. Buescher et al. relied on estimates of ASD workforce participation that focused on HFA and Asperger's adults and equated participation in work with productivity (David Mandell, personal communication 2018). By contrast, we define full-time, unsupported employment, which is generally quite low in ASD adults, as a more realistic standard for productivity.

We should note that this personal communication was only necessary because of the absence of any reference in the 2014 paper. In contrast to Mandell's unsupported estimate, here is the literature review that we used to support our estimate as published:

> We surveyed the literature on employment patterns in adults with autism in order to estimate competitive (currently working, full-time, paid) employment rates rather than mere participation in work. Much of this literature focuses on small samples composed largely of High Functioning Autism (HFA)/Asperger's workers (Eaves & Ho, 2008; Jarbrink et al., 2007; Jennes-Cousennes et al., 2006; Larsen & Mauridsen, 1997; Mawhood & Howlin, 1999; Rumsey et al., 1985; Szatmari et al., 1989; Venter et al., 1992) and report rates ranging from 7 to 44%. A few more recent surveys (Farley et al., 2018; Ohl et al., 2017; Roux et al., 2013; Shattuck et al., 2012) that have larger and more diverse samples, report competitive employment rates in a similar range of 7–34%. For our model, we assumed a 100% loss of productivity for severe ASD cases and a 70% loss of productivity for milder ASD cases.

Writing a letter to the editor is the appropriate response to any disagreements Mandell may have and we would gladly respond to such criticism in the customary fashion; by contrast, hinting at (or demanding?) a retraction is a bad faith act that runs counter to scientific norms.

2. The new reviews

Before presenting our detailed response to the three reviews, we note as a general comment that the new reviewers made suggestions and provided good ideas for future investigation. However, no one identified a critical flaw that would lead to erroneous conclusions in our article. Indeed, our overall cost estimates are similar to those from prior literature. The new reviewers may like or prefer other models and assumptions, but authors are allowed discretion to define the scope of their paper and cannot, nor are they required to, do everything in a single paper. A journal is forum for ideas. We encourage people to do their own research, to explore alternative future scenarios, cost estimates, etc. to investigate issues of interest and produce evidence for their ideas. By providing a detailed set of model equations and inputs, we hope that our paper has facilitated this kind of future research.

[The text from the reviewers is in italics and our replies are in plain text below.]

Reviewer #1

There are numerous methodological issues in the article. Below are a few essential ones:

• the literature review presents only studies that back up the authors claims. Many articles that do not support the authors' claims have been omitted (e.g., PROVIDE EXAMPLES).

Reply: It is difficult to respond to this given that the reviewer did not provide any specific examples. We did include a comprehensive discussion of the previous cost literature (e.g., Jarbrink 2003, 2007; Ganz, 2007; Knapp et al., 2009; Buescher et al., 2014; Leigh and Du, 2015;

Cakir et al., 2020). Our conclusions, in terms of total cost estimates are consistent with prior cost studies, in that most of these studies have estimated future costs on the order of hundreds of billions to trillions of dollars. Furthermore, both Leigh and Du (2015) and Cakir et al. (2020) model future increases in ASD prevalence. The main difference in our work is that we provide a more specific breakdown by age and cost category and how these evolve over time. When our estimates disagree with previous studies, we discuss in detail the reasons why we differ, in many cases referencing new and improved evidence that has emerged in the literature (e.g., on medical costs).

• *in the modeling itself assumptions are made in terms of the prevalence time trends, the cost categories, inflation rates, etc. For example, their use of the birth cohort 1931 as an origin for the time trend paints a false picture (what was the chance of diagnosing those individuals in their childhood years with a diagnosis that only emerged in 1943?); their reliance on California DDS data is highly selective and biased; and they employ scalar multipliers that are speculative. The same applies for assumptions regarding costs (e.g., the loss of productivity for mothers is speculative). However, all these modeling studies do rely on assumptions and therefore, insofar as they explicate these assumptions, that would be acceptable; nevertheless, many reviewers would not be satisfied with these assumptions. The logical request would have been to ask the authors to conduct sensitivity analyses (e.g., show how their results change if one changes assumption 1, 2, 3, etc.) and all assumptions altogether.*

Reply: As the reviewer notes, assumptions are always used in modeling, necessarily so, since models inherently are a simplified representation of the real world. That said, none of our assumptions are "speculative." We provide references for each of our estimates and assumptions, which are organized by cost category in Supplementary Table S1. For prevalence data as a function of birth year, we used the latest data from the CA Department of Developmental Services and included all the years that were available. Our previous JADD paper discusses in detail why the increases in CA DDS prevalence are real (Nevison et al., 2018)

and we felt that it was beyond the scope of the current paper to relitigate that issue. Our scaling estimates are explained clearly and succinctly as follows:

> With respect to the total:severe ASD scaling factors, our lower bound (2.1) is based on comparing ADDM data, which are in some respects the most authoritative, to the comparable California DDS snapshot (on which our severe ASD projections are based), but likely left out many cases of autism that were previously considered Asperger's cases. Our higher bound (3.5) is based on comparing the midpoint NCHS surveys of children to their California DDS equivalents.

The future scenarios and total:severe ASD scalar ranges are a form of sensitivity analysis and are the major uncertainties in our model, as described in our Discussion,

> The uncertainty in our calculations is defined by our range of prevalence scenarios and by the scaling factors we apply to convert severe autism into total ASD. We implicitly assume that the uncertainties in the census projections of overall population and in the individual cost category prices are subsumed in the two larger primary uncertainties. Previous studies have made similar assumptions (e.g., Leigh and Du, 2015).

The sensitivity of our results to the future scenarios and the range of scalars was our focus and was itself so large (see the wide envelopes of uncertainty in figures 2 and 3) that a detailed sensitivity analysis of each individual cost category would not have offered significant additional insight into the likely range of future costs.

• *There are areas of the paper which comprise unexplained allusions to prevention of autism that have simply not been proven.*

Reply: The Prevention scenario is based on empirical data from the California Department of Developmental Services that show that parents with access to education and resources may be succeeding in reducing ASD risk in their children (Nevison and Parker, 2020). This scenario does not favor any particular environmental theory of causation. As discussed in that paper, the specific parental actions that may reduce ASD risk are not well known, but merit detailed and urgent investigation.

Reviewer #2

Costs are real and a result of efforts to relieve real suffering of individuals with ASD—greater costs arise from delayed intervention (e.g. severe injuries from behaviors that have not been proactively addressed), lack of awareness, and other factors. Making sure to incorporate all the right factors into estimates of cost is an important goal of the field and presumably of the authors of this report. There are a few points of concern in this manuscript that I think bear considering. These arise from some assumptions that the authors have made in their modeling that leave the models looking simplistic and seemingly unaware of several factors that have been demonstrated in the study of autism spectrum disorder.

I think it could be argued by the authors that they believe scientifically in looking at the data this way, although I don't think the authors support that very well in the places that they should do so.

My biggest concern about this study is the superficial assumption made that prevalence increases are in fact indicating new individuals with autism in the population instead of a shift in diagnosis of autism and how severely affected those individuals are. Rising prevalence is true, although the science on this topic has demonstrated that a large segment of this increase is because of more ASD diagnoses of individuals who had other diagnoses previously and formal diagnosis of more mildly affected individuals who had no diagnosis before. In the introduction, the authors discuss that attention should be given to the fact that there are individuals with

different levels of impairment which will certainly involve a range of different costs. There no alteration in the ratio of mild to severe ASD cases in the projections in prevalence in the model, and this could easily be addressed with different models with different future ratios. The difference in costs is also not attended to very well even for the consistent ratio that is used. While certainly, to avoid under-estimation, upward prevalence trends should not be ignored, but because a large majority of the increased prevalence occurs in individuals with milder impairment, overestimation may also occur. While it may be true that this is difficult to quantify, it is somewhat biased toward over-estimation and this should be addressed—this is exemplified by the following statements—

Reply: The scientific evidence is overwhelming that the increase in autism prevalence is real. Byrd et al. (2002), Hertz-Picciotto and Delwiche (2009), and Nevison, Blaxill, and Zahorodny (2018) show that better awareness, diagnostic expansion, and diagnostic substitution are insufficient explanations for the rise in autism over the last 50 years. Government data and reports also show sharply rising prevalence including the CA Department of Developmental Services and the Autism and Developmental Disabilities Monitoring Network (see for example, Zablotsky et al. 2017 and numerous publications by Walter Zahorodny). All of our cost estimates are in line with previous societal cost of autism studies. Our study is the first to show that costs shift over time, from costs focused mostly on children such as education to adult residential and support services as the first large wave of the autism epidemic ages out of the school system and their parents eventually die.

"We assumed that the same miscellaneous non-medical costs applied to those severely and more mildly affected." (at the very least, as a clinician, I know this to be an untrue assumption—families with severely affected individuals have to spend a great deal more on safety devices, supports for ADLs, etc than those with less severely affected individuals. This is likely supported with data in the literature also).

And "We made no assumption about a differential EIBI usage in severe and mild cases." This again, seems like an odd approach given the clear much greater usage of EIBI for severely affected individuals in my experience and demonstrated in the literature.

And "We made no assumptions about differences in medical costs across severe and mild cases." Again, individuals severely affected use medical care at much higher rates in my experience and by data in the literature.

Reply: The intuition is that 'surely there must be differences in costs between severe and more moderate autism cases when it comes to non-medical costs, EIBI utilization, and medical costs.' At first that was our intuition as well. But we searched high and low in the literature and did not find concrete evidence to support this for most of our cost categories. Take for example Zerbo et al. (2019) and Zuvekas et al. (2020). These are arguably two of the best studies on health care utilization and costs among people on the autism spectrum (Zerbo et al. focuses on the adult population using data from Kaiser Permanent and Zuvekas et al. focuses on the pediatric population using two large government data sets). One would think that these studies would observe a difference in utilization and cost between severe and more mild cases of autism but they do not. If the underlying data did not draw a distinction between severe and mild neither did we (and we are skeptical of other models, most notably Buescher et a. 2014, who arbitrarily and without references assumed that mild costs were half of severe costs). However, we have set up our model to distinguish mild and severe costs, such that distinct values can be used in the future if/when better information becomes available.

In addition, if individuals were previously diagnosed with non-ASD disorders, they were likely receiving services of some kind… then the "costs of ASD" may rise while costs of other disorders fall which is not discussed at all and should be, particularly when thinking about the costs of ASD as a percent of total GDP. And if individuals had a non-diagnosed impairment previously and then was diagnosed with ASD, with the same amount of disability previously that is now more likely to be diagnosed, their disability was actually already impacting their families' finances in

many of the same ways, but now has a name. By not acknowledging this, the authors data has several distortions of the costs-- there are these many individuals in our communities who have autism and weren't previously diagnosed. That clearly would then mean that society has already absorbed a great deal of the costs needed to help adults with ASD because those individuals do already exist; per these models, these costs are only going to happen in the future, so in the model, the base already contains these costs so there is more of an upswing in costs than should be. The authors should find some way to address this complexity, perhaps with additional variants of their model, or a discussion of how some increased financial costs for families to support individuals with ASD will co-occur with decreased financial cost of other disorders. Additional models could be laid out to reflect different scenarios of the costs already existing to address this.

Reply: We respectfully and fundamentally disagree with the reviewer on this point, for all the reasons described in detail in our Introduction. Our cost paper is based on the latest ASD prevalence data as a function of birth year from the CA Department of Developmental Services. Our previous JADD paper (*Nevison et al.*, 2018) discusses in detail why the increases in CA DDS prevalence are real and we felt that it was beyond the scope of the current paper to relitigate that issue. Furthermore, previous cost papers (e.g., Leigh and Du (2015) have made the assumption of constant prevalence over time, so our calculations offer a unique comparison to that viewpoint.

My second biggest concern is as follows. I can understand why the authors wanted to demonstrate with their prevention model how any decrease in costs of addressing care of individuals with ASD will lag behind any prevention efforts substantially because of its life-long nature. However, the prevention scenario is used in strange ways—first, it is only implemented on the high prevalence curve.

Reply: The high prevalence curve is our best guess "Base Case" scenario, since it is based on the most recent available CA DDS prevalence data from early 2021. Thus, we felt it was most appropriate to apply the Prevention scenario to the Base Case trajectory.

This is despite the fact that the study they base the potential decrease in rate demonstrated that the decrease occurred years ago, prior to this recent upswing.

Reply: As shown in Nevison and Parker (2020), the decrease in ASD prevalence among certain privileged subgroups of children occurred starting around birth year 2000, but the increase in prevalence among other groups is still ongoing through at least birth year 2016.

Second, even as a proponent myself for considering early preventive measures to support healthy brain development with interventions in pregnancy that maximize nutrition and maternal psychosocial support, I have a hard time wrapping my head around what the authors are basing their potential prevention-induced change in prevalence on. They seem to be taking one possible explanation from the Nevisen and Parker study without attention to the fact that the first explanation offered in that study for the drop in rate was that wealthy families were no longer using DDS-based but rather private services. This is the most likely explanation, but the authors choose a second idea from this paper, much less well supported, that some kind of consideration of healthier maternal diet could account for this decrease. First, even well documented examples of how early diet can reduce the prevalence of neurodevelopmental disorders does not support the change in prevalence incorporated by the authors into their model—for example, with folic acid supplementation and neural tube defect prevention, for example, where a clear mechanism of action was known for at least 10 years prior to the fortification of wheat flour in the US, drops in NTD rates after fortification only accounted for about a new prevalence 25-30% below the total case rate during the pre-fortification period. Of course, this matters and I am not trying to argue it doesn't, but it's a far cry from the drop in prevalence from "prevention" suggested by the authors. And the authors don't even discuss what might be involved in these prevention efforts leaving that component of the model very

poorly justified. In addition, the drop in prevalence from prevention is reportedly based on the drop seen in the Nevison and Parker study. In actual fact, the initial rate in that study was 0.8 and it dropped to 0.6, representing a much lower impact of the "prevention" than is represented here.

Reply: This is not an accurate description of the data presented in Nevison and Parker (2020). In Figure 2 of that paper, ASD prevalence rose as high as 1.2% in birth year 2000 among white children in wealthy counties before dropping to 0.6% by birth year 2013. In other counties, ASD prevalence rose as high as 1.9% by birth year 2013. Thus the drop to 0.6% in wealthy counties by birth year 2013 is significant both with respect to the wealthy counties themselves and to the ongoing upward trajectory of prevalence in other counties.

This is a very strange part of this study and there is little discussion of what the authors believe this represents other than unknown preventive measures that wealthy people are using.

Reply: As discussed in Nevison and Parker (2020), the specific actions by California parents that may be reducing ASD risk are not well known, but merit detailed investigation. The reviewer, for example, provides some useful suggestions involving nutrition and psychological and social support of expectant mothers. Alternatively, if there is no true reduction of risk but simply a withdrawal of wealthy parents from CA DDS (which seems inconsistent with the chronology of the private insurance laws in California) that needs to be investigated and clarified too.

The idea that early intervention can reduce impairment to very low levels and therefore reduce costs is a compelling one which would require more complex modeling than simply a reduction in rate… it would be about altering severity and impairments of those who have ASD which seems a much more reasonable scientific concept (in, for example, the Peters-Scheffer et al 2012 article below). Intervening early is a potential component of reducing preventable aspects of ASD impairments. I think the discussion could benefit from consideration of how the economics of investing in early intervention could prevent later impairments and health effects for

individuals with ASD and therefore reduce the costs. The authors cite three studies suggesting that early intervention does not change adult cost of ASD, but I don't understand how the Fein et al study demonstrates this (I was not able to access the Camarata article or the dissertation cited the latter of which will admittedly not have gone through the normal peer review process so is not a very useful justification for this idea). If they wish to present multiple models related to positive versus absent cost savings from early intervention, that seems like it would be an important contribution to the literature.

> *Peters-Scheffer N, Didden R, Korzilius H, Matson J. Cost comparison of early intensive behavioral intervention and treatment as usual for children with autism spectrum disorder in The Netherlands. Res Dev Disabil. 2012 Nov-Dec;33(6):1763-72. doi: 10.1016/j.ridd.2012.04.006. Epub 2012 Jun 14. PMID: 22705454.*

Reply: We are one of the few cost of autism studies to directly estimate the cost of EIBI: Ganz (2007) included EIBI costs by age but did not attempt to model future benefits; Leigh and Du (2015) included a scenario with a crude estimate of adult benefits from EIBI; Cakir et al. (2020) did not include EIBI at all; Buescher et al. (2014) subsumed EIBI in their education cost and did not model future benefits, although they made one brief reference to Peters-Scheffer as a possible idea for further investigation. In fact, modeling EIBI's current costs let alone future benefits is difficult due to lack of data (e.g., the Fein and Camarata articles do not provide a quantitative assessment of EIBI benefits that could be used in a cost model). Furthermore, new research suggests many studies that have claimed future cost savings from early intervention were conducted by providers with financial conflicts of interest (Crowley et al., 2021). Lead author Mark Blaxill is the CFO of a clinic that provides such behavioral intervention, so we are well aware of the literature and its limitations. As detailed in the Methods section, our EIBI cost estimates are based on eight prior studies (Jacobsen et al., 1998; Butter et al., 2003; Sallows & Graupner, 2005; Ganz, 2007; Chasson et al., 2007; Amendah et al., 2011; Cidav et al., 2017; and Yingling & Bell, 2019). At present (and especially in view of the Crowley et al. 2021 study) there are little or no quantitative data to guide implementation of a scenario in which EIBI leads to

later cost savings in our model, which requires detailed cost estimates broken down by age and category (see Table 1).

If the point of the prevention scenario is simply to show that there are persistent costs even with a dramatic change in frequency of ASD, perhaps simply showing what would happen if ASD rates plateaued right now would be sufficient. The fact that the prevention scenario isn't based on anything specifically spelled out undermines the point that the prevention model is trying to make.

Reply: We note in the Methods that, "The Prevention scenario is included as an illustrative example of what might be possible if strategies for reducing ASD risk are identified and addressed in the near future. While many of the parameter choices are open for debate, we used the following assumptions and values…" Thus, it is not intended as a definitive scenario but as an illustrative example that is based in real data described in Nevison and Parker (2020).

In addition, even in "number-crunching" scientific papers, the people in question are real and the language should try to do justice to this. Particularly in more clinically-oriented journals, efforts should be made to demonstrate how the economics reflect the importance of the patients and their care. The authors should add to and clarify the language used to ensure readers understand that while this research tries to pinpoint the economic impact of ASD, that this economic impact reflects the need/desire of families, schools, healthcare agencies, and others to address individual impairment, suffering, and health problems of those living with ASD. This is particularly important in the places in the manuscript where the ideas and work are distilled, such as in the abstract, in the beginning of the introduction, in the end of the introduction and in the discussion.

For example, the first sentence of the abstract:

"The cost of ASD in the U.S. is estimated using a forecast model that for the first time accounts for the true historical increase in ASD."

This sentence could be re-written to help readers understand what costs arise from:

"The cost of interventions to reduce impairment and address health problems of individuals with ASD in the U.S. is estimated using a forecast model that for the first time accounts for the true historical increase in ASD."

A sentence could be added to the abstract to put "costs" in a context, to prevent readers from misunderstanding that money is not the end goal. For example: "Considering costs is a way to ensure that enough resources are available long term to help any individual with ASD who needs interventions."

And saying "preventing impairments and health concerns of ASD" may be a more clear statement than "preventing ASD."

Reply: These are minor points about style. All authors make discursive choices. There are no universally agreed upon rules as to what those discursive choices should be. All of the authors of this paper are aware first-hand of the real-world impacts of autism via family and friends on the spectrum. We are also aware, in ways that perhaps this reviewer misses, of the serious problems that await them if we overlook rising prevalence and cost with no plan in place for how to respond.

Some other specific points in the methods:

Why are the losses of maternal income extended to parents of individuals up to age 52? Wouldn't some of the other costs incorporated in the model actually take over some of the household income losses after individuals with ASD shift to other sources of support? Should

productivity estimates be reflective of a population with a similar range of IQ as those with ASD?

Reply: While income loss to mothers is included for children up to age 51, these costs become very small at that point, given our assumption of an average maternal age of 28 and the fact that mean female earnings drop precipitously after about age 60. We felt it would have been inappropriate to assume that parent productivity loss drops abruptly to zero once a child ages out of the school system, given the lack of societal support for adults with ASD that leaves many parents responsible for their adult children's care.

Reviewer #3

1. The authors make some assumptions that are questionable and others that are incorrect. For example:

Reply: Assumptions are a part of economic modeling. Our assumptions are based on the best available information, which was gathered over the two years we spent researching and developing our model. We provide justifications for every assumption and list detailed references in Supplementary Table S1.

a. Assuming growing prevalence ending up at 3%. They do this by using epidemiologic studies from the 70s as a baseline, ignoring changing definitions of ASD and changing surveillance methods. If your baseline point is super low (2 per 10,000), then your projected prevalence, comparing that very low estimate to current estimates, is by definition going to be super high.

Reply: Our cost paper is based on the latest ASD prevalence data as a function of birth year from the CA Department of Developmental Services. Our previous JADD paper (Nevison et al., 2018) discusses in detail why the increases in CA DDS prevalence are real and we felt that it was beyond the scope of the current paper to relitigate that issue.

b. They assume that new cases on average will have the same support needs as previously identified cases. But we know that a lot of the "excess" prevalence identified is among cases with much lower support needs

Reply: It is not clear what the reviewer means by "excess" prevalence as that term is not commonly used in the literature. We set up our model to allow for lower costs among those more mildly affected. Indeed, we included those lower costs whenever we had some justification for doing so (for parental productivity and individual productivity loss). For the other 4 cost categories, the supporting literature did not distinguish between severe and milder costs (and it seemed likely that the reported costs reflected an average of severe and milder costs). An alternative approach (e.g., the one adopted by Buescher et al., 2014) would have been to assume that milder costs were half those of severe costs (but there is no anchor in the literature to support that assumption). We have listed the details of our equations in the Appendix and our inputs in Table 1 to allow others to perform their own updated calculations.

c. They use the Cidav et al. study to examine costs associated with reduced household income. As far as I can tell, they double the loss of income. It had estimated a 28% loss of household income, and they seem to use 56% as the number.

Reply: The reviewer is misrepresenting our model. Cidav et al. (2012) estimated 56% productivity loss for mothers of children with autism and no productivity loss for fathers which averages out to 28% productivity loss across the household when both parents are included. Since mothers with severely affected children are more likely to experience lost productivity than those with more mildly affected children, we assumed 75% loss for severe and 25% for milder, which averages to nearly 50% across mild and severe mothers (i.e., is slightly conservative with respect to the Cidav et al. 56% value) and 25% productivity loss across the average autism household when both parents are included (again, in line with Cidav et al.). We

assumed no productivity loss for fathers of mild or severely affected children, in accord with Cidav et al.

d. That same study examined families of children up to age 18. They extend that household income loss up to families of children up to age 42. There are no data to support that.

Reply: Given the lack of available support services for adults on the spectrum, as the first large wave of the autism epidemic ages out of the school system it is likely that parents will continue to provide some level of care and experience some productivity loss. The lack of data stems from the fact that historically there were not many adults on the spectrum; our model is the first to capture the fact that a large cohort of people on the spectrum are aging out of the school system and need adult services (particularly housing but also residential day programs and other supportive services) immediately.

2. Their focus is on preventing autism and their numbers about "preventable autism" seem pulled out of a hat. There is no discussion of improving the service system. Cost estimates from Buescher et al. show is that you can pay now by providing high quality services and supports, or you will pay later by paying for residential care and adult services. Honestly that's where the emphasis should be.

Reply: As explained above, Buescher et al. (2014) does *not* model cost savings from early intervention. Leigh and Du (2015) *do* include a possible cost mitigation scenario (reducing costs by a factor of 2) based on the purported benefits of EIBI. However, the initial optimism associated with EIBI has faded somewhat. EIBI clearly helps some people on the spectrum. The provision of EIBI has vastly expanded over the last thirty years. But the projected (extraordinary) cost savings have yet to show up in the macroeconomic data (as autism costs, particularly amongst the growing population of adults with autism, continue to rise). We state in the text,

> We opted for a prevention scenario to explore the possibility of future mitigation, rather than an intervention scenario, due to the lack of empirical evidence that early intervention actually reduces adult costs by a factor of 2 (Rogers et al., 2012; Fein et al., 2013; Camarata, 2014).

A further complication is that recent research, presented at INSAR 2021, suggests that many studies that have claimed future cost savings from early intervention were conducted by providers with financial conflicts of interest (Crowley et al., 2021). Those authors concluded that methodological issues have plagued studies on the effectiveness of early autism interventions for nearly three decades. These problems include multiple types of bias and an overreliance on caregivers to report outcomes.

The prevention scenario numbers are based on data from CA Dept of Developmental Services as explained in Nevison and Parker (2020) which is the reference in the text. There appears to be a signal in the data and that signal should be explored. The prevention scenario is based on real world data out of wealthy counties in California where autism rates have declined in white and Asian families while they have continued to increase in Latino and African American populations throughout the state.

****

We believe that the spirited and yes, sometimes uncomfortable, debate elicited by this article is the essence of the scientific process. We have responded to the reviewers in extensive detail and shown that our methodological approach was sound, well referenced, and based on the best available information; in many cases we advanced the state of the art compared to previous cost studies. Based on the foregoing we kindly ask you to remove the Editor's Note and take no further action so that our research can continue to be a catalyst for new insights and perspectives.

Kind regards,
Mark Blaxill, Toby Rogers, & Cynthia Nevison

Additional references in this letter:

Bennett, D. et al. (2016). Project TENDR: Targeting environmental neurodevelopmental risks the TENDR consensus statement. *Environmental Health Perspectives, 124*(7), A118–A122. https://doi.org/10.1289/EHP358

Byrd, R., et. al. (2002). Report to the legislature on the principal findings from The Epidemiology of Autism in California: A comprehensive pilot study. M.I.N.D. Institute, University of California, Davis.
https://www.dds.ca.gov/wp-content/uploads/2019/06/Autism_FinalStudy_20021017.pdf

Cone, M. (2009). New study: Autism linked to environment. *Scientific American*, *44*.
https://www.scientificamerican.com/article/autism-rise-driven-by-environment/

Crowley, S. M., M. P. Sandbank, K. Bottema-Beutel, T. G. Woynaroski, The quality of studies in autism early intervention research International Society for Autism Research (INSAR), 2021 annual meeting, Poster 216.003, Virtual Meeting, May 5, 2021.

Gilbert, S. G. (2008). Scientific consensus statement on environmental agents associated with neurodevelopmental disorders. Collaborative on Health and the Environment, Learning and Developmental Disabilities Initiative. https://www.healthandenvironment.org/docs/xaruploads/LDDIStatement.pdf.

Hertz-Picciotto, I., & Delwiche, L., (2009, January). The rise in autism and the role of age at diagnosis. *Epidemiology, 20*(1), 84–90. https://doi.org/10.1097/EDE.0b013e3181902d15

Landrigan, P. J., Lambertini, L., & Birnbaum, L. S. (2012). A research strategy to discover the environmental causes of autism and neurodevelopmental disabilities. *Environmental Health Perspectives*, 120(7), A258–A260. https://doi.org/10.1289/ehp.1104285.