Article details: 2014-0056	
Title	High rates of autism spectrum disorders (ASD) on the Avalon Peninsula, Newfoundland and Labrador, Canada
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Reviewer 1	John C. Duby MD
Institution	Akron Children's Hospital, Akron, Ohio.
Review	I recommend that the manuscript have major revision before acceptance. In general, it will be essential to carefully review the entire paper for grammatical and spelling errors. There are multiple errors throughout the paper. Review of the STROBE checklist indicates that the title and abstract do not explicitly state that this is a cohort study. The word cohort does not appear until p. 9. This should be included in the title, abstract, and early in the methods section. The introduction does not include a hypothesis regarding the rates of autism spectrum disorders in the defined population. Also, it would be valuable to give a more in depth description of the unique population of the area, and the rationale for choosing to specifically consider the possibility of higher rates of ASD beyond a possible association between Type 1 Diabetes and ASD. It is essential to emphasize that the results of this study cannot be generalized, if indeed the population is truly unique. The introduction references the DSM-5 in its description of ASD, but then immediately refers to the DSM-IV terminology. It would be important to clarify this distinction, and acknowledge what the change in terminology may mean in future rates. Since the DSM-IV TR was used to make the diagnosis, how can 27.6% of the sample have a diagnosis of autism spectrum disorder, since this is not a diagnosis that is in DSM-IV TR? Table 2 lists the breakdown of the specific diagnoses with abbreviations. These should be spelled out. While Childhood Disintegrative Disorder is listed in the table, it is never mentioned in the narrative. In addition Table 2 reports rates of neuroimaging, but this is never mentioned in the narrative. I question whether this data is relevant since the aim of the study was to determine prevalence and incidence. Similarly, data on referral to genetics does not seem relevant to the primary aim of the study. Perhaps these should be excluded. I feel that there needs to be a more detailed explanation of how the diagnosis was made. What were the components of the clinical evaluation besides the ADOS. There is reference to the fact that there may be factors that influence the results of the ADOS, but it is unclear whether the ADOS result was the primary finding in determining diagnosis. There is certainly the potential for false positive ADOS results, especially in children with anxiety. The methods section states that only non-syndromic ASD was included, yet the results section lists multiple genetic syndromes as co-morbid conditions. Is this consistent with the described methodology? Shouldn't the cohort prevalence be based on the 2006 population when the cohort was born rather than on the 2011 population? Given the weaknesses described in the introduction regarding administrative data, it seems inappropriate to report this at all for 2011-2013. Although concerns about under-identification with administrative data is outlined, the possibility of over-identification must also be considered. The latest ADDM data is now from 2010, not 2008, and was published in MMWR on 3/28/14. If only 72.4% of cases were referred for services, it raises a concern about whether the other 27.6% exhibited significant enough impairment to actually warrant diagnosis of a disorder. Why weren't all of the cases referred for services? This raises concerns about the possibility of over-diagnosis as opposed to under-diagnosis. This is further supported by the fact that 27.6% of the cases were characterized as "autism spectrum disorder," which is nonspecific. The very wide confidence intervals also imply that the results cannot be generalized due to relatively small sample size. This limitation needs to be made stronger. The introduction expresses confidence that nearly all cases were identified, but in the limitations, it is stated that it cannot be ascertained whether all of the cases were captured. How do you explain this dichotomy?
Reviewer 2	Erin Crouchman
Institution	Children's Hospital of Eastern Ontario, Pediatrics
Review	Thank you for the opportunity to review this piece on the incidence of ASDs in a geographic-specific location in Newfoundland. The authors are commended on their novel data capture that increased accuracy reporting of ASDs in their population. This manuscript is publication ready with the exception of very minor grammar and formatting issues outlined

	below. From an epidemiological perspective, the design was adequate and novel resulting in an increased case capture rate, and the statistics were properly applied including the use of accurate denominators in calculations. Minor notes: Authors are encouraged to move the strengths of their study to the Discussion section as opposed to the Introduction. Authors report that 1:45 is higher than in other populations, but this has been reported previously - authors encouraged to cite those studies. Minor grammatical and formatting issues: pg4, line39 - subject/verb agreement pg6, line29 - format in text citation Text refers to Table 2 then Table 4. Table 3 reported after these - ordering needs to be fixed Given the size of the sample, it's safe to report results to the tenths position. Currently, both the tenths and hundredths are used. Consistency. pg9, line44 - subject/verb agreement pg10, line 23 - spell out "Seven" at the beginning of a sentence pg12, line11 - format in text citation pg12, line27 - currently "reference", should be "referenced" or "referred" - tense agreement pg12, line30 - format in text citation pg13, line44 - subject/verb agreement References list at the end requires editing for correct formatting, as well as font size. Congratulations on a well-designed, well reported study.
Author response to reviewers	1. Please clarify your primary and secondary objectives and the rationale for conducting this study. We have revised the text to state: “The primary aim of our study is to review the incidence rate of children diagnosed with ASD living on NL’s Avalon Peninsula at the time of diagnosis over a five year period (2006-2010). We also use the available data to determine the prevalence of ASD for the cohort of children born between January 1st, 2006 and December 31st, 2006, up to December 31st, 2013. Our other secondary objectives included examining the characteristics of the children who have been diagnosed on the Avalon Peninsula and examining some of the diagnostic tests and referral pattern of these patients.” 2. You have measured the incidence and prevalence of physician-diagnosed ASD. The validity of these diagnoses is uncertain. Please consider the use of 'diagnosis of ASD' in place of ‘ASD’. We are not sure if your concern is specifically about the validity of ASD diagnoses, or if the concern is about any type of diagnosis that is based on physician / professional interpretative diagnostics more generally. In any case, we have changed the text accordingly where it is appropriate. 3. Please elaborate as to how a child would be identified for inclusion in your cohort. We have revised the text to state: “We also examined the cohort prevalence for all children born on the Avalon Peninsula in the year 2006. We used as the denominator of the cohort the average number of children age 4 and 5 reported in the 2011 Canadian Census, as children born in 2006 would have been either 4 or 5 years old at the time of the 2011 census. As illustrated in Appendix 1, the population between 4 and 5 years on the Avalon was quite stable for the two years, so that the impact of the rounding on either year was no more than +/- 0.11%. Positive cases included were those with a diagnosis of non-syndromic ASD confirmed by a multidisciplinary team and who fit the DSM-IV-TR definition of ASD, age <15 years and living on the Avalon Peninsula, NL at the time of diagnosis and born in 2006.” 4. You report a male: female ratio of 6:1. This is higher than what has been reported elsewhere. Please discuss in the interpretation section. As we state in the introduction, others have actually reported male to female ratios as high as 6.5:1. But we do discuss the sex breakdown further in the discussion section. 5. Please include a completed STROBE checklist. A strong argument in favour of the cohort approach should be discussed in the interpretation section. We do include a completed STROBE checklist as requested, but would disagree with the characterization of the study as a cohort study, rather than a prevalence study. It is true that we are looking at a cohort of people, in our case a birth cohort of people born on the Avalon Peninsula in 2006 as one of our secondary objectives. Yet the study only looks at one feature of this population, the number who have been diagnosed with ASD. Unlike true cohort studies, there is no control group(s), and factorial associations or disease progress are not being investigated. Similarly, our intention was not to follow this cohort, but rather estimate the disease prevalence for the population. In the title of the article, we now refer to the “cohort prevalence” as perhaps the most accurate

	description. In this way, much of the STROBE statement is not applicable to our work, but we believe that we in keeping with the spirit of the STROBE initiative, that our research is "reported transparently so that readers can follow what was planned, what was done, what was found, and what conclusions were drawn." 6. The approach used to determine the denominators used in the calculation of incidence and prevalence rates is quite rudimentary. More sophisticated and standard approaches should be considered. We choose to use this approach to calculate denominators in the original article based in part on the advice of a professional health statistician, who felt it was the most appropriate choice given the available data. The second reviewer of the article also says that "the statistics were properly applied, including the use of accurate denominators in calculations." We have asked a second colleague with a background in statistics for advice further, who also felt that the approach we have used is likely the most appropriate given the limited population data available. While agreeing that there are other approaches available, to the best our knowledge these other approaches, given the limited data would present similar potential for error (e.g. inability to account for children who died or moved from the region during the subsequent four years). Unless further evidence is given for why another approach would be superior, we have decided to maintain the current method of analysis. 7. Please ensure your final word count is below 2500 words and the abstract is about 250 words. / For only the most standard abbreviations (i.e., 95% CI, SD, OR, RR, HR), please spell out at first mention and include the abbreviation in parentheses. The abbreviations may be used throughout the remainder of the manuscript. Please remove all other abbreviations (i.e., ASD, ADOS, PDD-NOS). As with the previous version of the article, we have keep word count below 2500 words and the abstract is about 250 words. We have removed the abbreviations ADOS and PDD-NOS from the text. It should be noted however that the Autism Diagnostic Observational Schedule is widely referred to as the ADOS in practice. We have chosen to keep the abbreviation ASD. Next to be fairly comment abbreviation, even for patients and families affected by autism, not using the abbreviation, plus the request to add the term the "diagnosis of" (see point 2 above), would add about 150 words to the article, without imparting any further information, making it difficult to remain within the word count and, we feel, hampering the readability of the article. 8. Please use plain numbers in brackets for your references. Done. 9. The title should reflect the objectives of your study: We revised the title of the study to: "The Incidence and Cohort Prevalence of autism spectrum disorders on the Avalon Peninsula, Newfoundland and Labrador, Canada" 10. Restructure the article, shorten the introduction to no more than two paragraphs, include subheadings. Done 11. Move Table 1 an Appendix, Combine Tables 2 and 3, remove separate frequency column, add a column showing the denominator used in the calculation of incidence, renumber tables accordingly. Done 12. Review paper grammatical and spelling errors. Done. 13. Emphasize that the results of this study cannot be generalized, if indeed the population is truly unique. We do this in the limitations section. 14. Clarify the distinction between DSM-iv and DSM-V terminology, and acknowledge what the change in terminology may mean in future rates. Since the DSM-IV TR was used to make the diagnosis, how can 27.6% of the sample have a diagnosis of autism spectrum disorder. We discuss this now in the discussion section. 15. Table 2 reports rates of neuroimaging, but this is never mentioned in the narrative. We now discuss the referral rates in the text. 16. There needs to be a more detailed explanation of how the diagnosis was made. We now say in the text: "Cases were confirmed through multiple observations, consultation with a development pediatrician, a detailed patient history, and in most cases, the use of at least one module of the Autism Diagnostic Observational Schedule."

	17. The methods section states that only non-syndromic ASD was included, yet the results section lists multiple genetic syndromes as co-morbid conditions. We thank the reviewers for identify this issue. We have removed the cases with genetic syndromes as a co-morbid conditions, and reanalyzed all of the data. 18. Use the latest ADDM data. Done.