Comments from the reviewers:

Reviewer: 1

Recommendation:

Comments:
I would like to thank the authors for addressing my initial comments. Following the revision to the article, some of my additional comments relate to some of the amendments made, and the authors may therefore wish to discuss these particular suggestions with the editor. My remaining comments concern only clarity in the numbers presented and interpretation of results.

1) Abstract, last sentence results: “At 32-34 WG, there was a non-statistically significant increase in survival without severe/moderate neuro-motor or sensory disabilities but the proportion of survivors with CP declined (p<0.001).” This sentence in compounded with both a NS and statistically significant result, which on first read came across as confusing - consider revising by splitting the sentence or adding the NS p-value result for survival without severe/moderate disability.

Thank you for this remark. We have added the adjusted p value (0.61) for survival without severe/moderate disability for children born at 32-34 weeks to the abstract.

2) Introduction: A section on the BSID has been added with detail on the preferred use of ASQ. I did not see the value of this paragraph in the Introduction but a sentence could be added on why ASQ was preferred to BSID in the discussion, if it is thought this is of interest to readers.

We added this paragraph in revised version-1, as suggested by Aleid G van Wassenaer-Leemhuis (reviewer 2). However, we agree that the value of it being in the introduction was not sufficiently clear. We really think that introducing the ASQ early is useful for the reader to understand how our results can be used practically. We have tried to rephrase this paragraph to point out how the ASQ could be integrated in a two-step approach for assessing neurodevelopment. In addition, we have added a sentence in “what is already known on the study” and “what this study adds” to emphasise the use of the ASQ for the reader.

3) Data management and statistics: line one, remove '-' before 22 and 24, looks like a negative

Thank you for spotting this. The '-' has now been deleted.

4) SAS MI: define MI to be multiple imputation - can a reference be added for this statistical procedure?

References have been added (Berglund et al, 2004; White et al, 2011). “MI” is in fact the name of the procedure in SAS. We have placed this in quotes to be clear.

5) “Imputation model variables included both those predicting non-response and/or correlated with outcomes” It is unclear to me how it is know which variables predict non-response or what correlations were used - can this be described? The whole section on different imputations models used for different variables seems quite complex and not described in full. It’s difficult to imagine that the analysis as described could hypothetically be reproduced. Can this detail on imputation be added to as an appendix? - the technical details may not be of interest to the general reader. The imputation analysis should also be presented as a sensitivity analysis to the complete case analysis and should be labelled as such - this also follows through in the presentation of the results.

There didn’t appear to be a large difference between CC and MI analyses which is reassuring, accept for perhaps “rates of ASQ scores below threshold increased in all GA groups” which you comment on in the results. Perhaps reassurances of the minor differences between CC vs MI analysis could be made in the discussion (already done) but perhaps some insight on why MI over CC has an increased rate for the ASQ scores could be provided.
We have added a supplemental table (supplemental table 1) with details of the multiple imputation strategy specifying, for each variable, the type of variable included in the model (binary or categorical), the model used to predict missing data and the percentage of each value that was missing.

We have also added a sentence in the discussion -section “limitations”- to explain why multiple imputation over complete case analysis has an increased rate for the ASQ scores.

6) Results: “Cerebral Palsy and sensory outcomes”
The report states that 137 were diagnosed with CP. 128 is reported as the total in Table 1. It’s also unclear where the denominator of 2714 comes from in Table 1. The table footnote suggests that that varying denominators accounts for missing data per variable but it states that CP data were available for 3599 in the manuscript text. Can this be clarified?

In the whole cohort (children born between 24 and 34 weeks), 137 were diagnosed with CP: there were 128 at 24-31 weeks and 9 at 32-34 weeks. The denominator 2714 comes from children born at 24-31 weeks and there are 885 children born at 32-34 weeks. So CP information was available for 3599 children. We agree that the manuscript was difficult to follow with the different GA groupings and, consequently, the different denominators. We have tried to avoid confusion:

1) By specifying in the methods (section “data analysis”) the method of GA grouping: 22-26, 27-31, combined 22-31 and 32-34.
2) By presenting in the results (sections cerebral palsy and sensory outcome and neurodevelopmental outcome) the numbers of children born at 24-31 and 32-34 weeks for both groups with CP data available and ASQ data used for analysis.
3) By shading the columns 22-26, (or 24-26) and 27-31 groups in each table to help the reader to understand that these groups are included in the group of children born at 22-31 weeks or 24-31 weeks, regardless of the outcome.

7) “Among those with CP, 51.6%, 47.4% and 22.0% at 24-26 WG, 27-31 WG, and 32-34 WG, respectively, were a non-ambulatory form of CP.”
I was unclear where these results came from, can they be computed from Table 1? What were the denominators?

These results were added in revised version-1, as suggested by Ravi Mangal Patel(reviewer 4). However, we have not reported the definition and, indeed, this was unclear. In revised version-2, we have defined the ambulatory form of CP in the methods (section CP and sensory deficits). We have also decided to report ambulatory forms of CP rather than non-ambulatory forms, as this is more positive for parents. These results cannot be computed from Table 1 but we have added them to the text.

8) “Severe auditory or visual impairment was reported in less than 1% of children”
Be clear the 1% result refers to overall. Bilateral deafness defined as severe was 1.4% in the 24-26 week group.

We agree with this remark and have specified that bilateral deafness was reported in fewer than 1% of children "included in the cohort”.

9) “Neurodevelopment outcome”
Similarly the report states (and Figure) that for the complete case analysis, 2506 were available for ASQ but the denominator reported in Table 1 is 1884. Can this be clarified?

The misunderstanding is again coming from the distinction between the 2 groups of children: one born at 24-31 weeks (1884) and the other at 32-34 weeks (622) leading to a total of 2506 children. Changes proposed for presentation of CP results have also been applied for the ASQ results and we hope that they will help to avoid confusion.

10) “Other significant disabilities”
Please add in the denominators to the text. Please also now check dominators throughout.
These denominators have been added to the text and all denominators have been checked.

11) Comparison of the 1997 and 2011 EPiPAGE cohorts (9 regions)  
"Changes were not statistically significant for children born at 24 WG, but there were marked improvements at higher GA"  
Be clear which analysis this refers to - the improvement also doesn’t appear to be linear with GA which deserves comment.

We have tried to be clearer in the results section that the improvements occurred between the two study periods; we have referred to Table 3 earlier in that section to help the reader to understand which analysis improvements refer to; we have also commented on the changes seen in each GA group. We have added a supplemental table (supplemental table 5) with the evolution of adjusted differences by week gestation between 24 and 31 weeks. We do not think that additionally stating the change is non-linear further benefits the reader’s comprehension, but we could add this if the editor thinks it is beneficial.

Additional Questions:  
Please enter your name: Jamie Kirkham  
Job Title: Senior Lecturer (Medical Statistics)  
Institution: University of Liverpool  
Reimbursement for attending a symposium?: No  
A fee for speaking?: No  
A fee for organising education?: No  
Funds for research?: No  
Funds for a member of staff?: No  
Fees for consulting?: No  
Have you in the past five years been employed by an organisation that may in any way gain or lose financially from the publication of this paper?: No  
Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this paper?: No  
If you have any competing interests <A HREF= 'http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/declaration-competing-interests' target='_new'>(please see BMJ policy) </a> please declare them here:

Reviewer: 2  
Recommendation:  
Comments:  
The authors have sufficiently improved their paper, in reaction to the comments made. I enjoyed reading it.  
Some points remain.  
They still recommend the ASQ as follow up tool a little too much, where in this paper that describes outcomes on the basis of their ASQ choice, it suffices to explain what the ASQ can and cannot do. Moreover even when using this easy tool it was apparently too problematic to complete for 40% of the parents of the cohort.  
The statement that the Bayley misclassifies is too strong. Isn't it simply so that some children recover and others grow into deficit and that child development is not a fixed fact?  

We fully agree with this remark and have tried to be less strong while still recommending the ASQ as a follow-up tool and also addressing the risk of misclassification with the Bayley. We have also referred to child development, as
suggested by Aleid van Wassenaer-Leemhuis. We have added a comment on the missing data for the ASQ as parents who did not complete the questionnaire or completed the questionnaire outside the expected range were from lower socio-economic status (see Discussion, section "limitations").

Additional Questions:
Please enter your name: Aleid G van Wassenaer-Leemhuis

Job Title: pediatrician

Institution: Emma Children's Hospital AMC

Reimbursement for attending a symposium?: No

A fee for speaking?: No

A fee for organising education?: No

Funds for research?: No

Funds for a member of staff?: No

Fees for consulting?: No

Have you in the past five years been employed by an organisation that may in any way gain or lose financially from the publication of this paper?: No

Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this paper?: No

If you have any competing interests <A HREF='http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/declaration-competing-interests' target='_new'> (please see BMJ policy) </a>please declare them here:

Reviewer: 3

Recommendation:

Comments:
The authors have provided a nicely detailed and thorough response to the comments from the previous review and have addressed my major concerns. However, one response needs additional details and I have one additional comment for the authors to consider:

1. In response to Review 3, comment 10, the authors note adjustment for several variables (also on Page 10, lines 18). The authors should state the rationale for selecting the particular variables to adjust for comparisons of trends over time from 1997 to 2011.

We agree that the rationale for selecting the particular variables to adjust for comparison over time should be stated.

In this study, our aim was to describe outcome at 2 years of a cohort of preterm infants with comparison over time. As usually presented in other cohorts with similar objectives (Moore 2014; Serenius, 2012; Younge, 2017), we have selected the baseline characteristics of the neonates that may influence outcome to adjust for comparisons of trends between 1997 and 2011. This has now been specified in the methods (section “data analysis”).

2. In the response letter, under response #5 to the editors, the authors note: "it has been reported that psychomotor developmental screening measures may over diagnose 15% to 30% of tested children (Kerstjens JM, PloSOne, 2015)." In citing this reference (#39) in the discussion, the authors state: "Despite its limitations, a good predictive value of ASQ for schooling at age 5 has been reported in several populations.38,39″ which seems at odds with the latter statement: “As a screening instrument, ASQ-3 identifies more children at risk of developmental delay than those diagnosed with professionally administered psychometric tests.39″
I would recommend these statements be clarified and that the authors add the estimates of overdiagnoses (15-30%) noted in their response letter to point #5 by the editors to the paper.

We fully agree with this remark, which was very helpful for us to better argue for the utility of the ASQ. After revision-1, we concentrated our arguments on the predictive value of the ASQ which is a real question. However, we think that we did not explain clearly enough how the ASQ can be used as part of a 2 step-approach towards assessing development at 2 years, and we understand the request of Ravi Mangal Patel for this statement to be clarified.

We have therefore referred, in revision-2, to the sensitivity and specificity of the ASQ as good indicators of the ASQ’s value. We have indicated that the correlation of the ASQ with formal assessment increases in children born preterm, and also at 2 years of age when compared with younger children, and that the predictive value of ASQ at 3 years of age for IQ at 5-6 years has recently been described. We have tried to emphasise that a low score on the ASQ needs further evaluation, and that our results may help to define follow-up for each GA group. Thus, we have suggested considering developmental evaluation with the ASQ as a first-step, followed by a standardised evaluation in the event of low ASQ scores.

Additional Questions:
Please enter your name: Ravi Mangal Patel
Job Title: Assistant Professor of Pediatrics
Institution: Emory University & Children's Healthcare of Atlanta
Reimbursement for attending a symposium?: Yes
A fee for speaking?: Yes
A fee for organising education?: No
Funds for research?: No
Funds for a member of staff?: No
Fees for consulting?: No
Have you in the past five years been employed by an organisation that may in any way gain or lose financially from the publication of this paper?: No
Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this paper?: No

If you have any competing interests <A HREF="http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/declaration-competing-interests" target="_new">(please see BMJ policy) </a>please declare them here: Ravi Patel has received honorarium and travel reimbursement from Mednax, Inc, which provides neonatal services through Pediatrix Medical Group.

Reviewer: 4

Recommendation:
Comments:
The authors have done a nice job of revising this manuscript and addressing the reviewer comments and queries. The manuscript now reads with greater focus and clarity. There are still some concerns related to the loss to follow-up rates, the use of community practitioners for neurologic examinations, and the uncertain utility of the ASQ screening test, but the authors have addressed each of these limitations in the discussion. The data are important and will be of interest to a broad audience. I have a few minor comments:
In Supplemental Table 1, data for some of the variables were not presented for the comparisons of infants with and without parental consent – were these data not
available? Also, the footnote on socioeconomic status appears to be misplaced (refers to birth outside France).

Indeed, data for some variables in children without parental consent were unavailable. We have added a sentence in the Methods (section “study design”) explaining that for children without parental consent, status at birth, mortality and limited perinatal data were available. We have also added a footnote to supplemental table 1.

Thank you for spotting the footnote on socio-economic status. It has been corrected.

Is there an error in the confidence interval reported for survival without impairment (page 13 line 26 and in Table 3)?

Thank you for spotting this. There was indeed a typo in the confidence interval and this has now been corrected.

I would recommend including the information provided in appendix 2 of the author response document as supplementary material with the manuscript to provide the reader with a greater understanding of how CP was determined.

This information has been added as supplemental file 1.

In the discussion regarding the hypothesis that rates of active treatment at 22-23 weeks are associated with improved outcomes for infants born at later gestational ages, I do not think the Rysavy NEJM paper (ref 53) can be used to refute the hypothesis (“there was no evidence that hospital rates of active treatment at 22-23 weeks had a positive influence..”) since that analysis focused on associations between active treatment rates and outcomes of infants within gestational age strata. A more appropriate reference may be Smith PB, et al. Approach to Infants Born at 22 to 24 Weeks’ Gestation: Relationship to Outcomes of More-Mature Infants, Pediatrics, 2012.

Thank you for this remark. We fully agree that the paper of Rysavy cannot be used to refute the proposal that active treatment at 22-23 weeks is associated with improved outcomes for infants born at later gestational ages. However, we referred to this paper as it was suggested by Prakash Shah (reviewer 1) in the first revision. In this second revised version, we have clarified the Rysavy results and added the paper of Smith, as suggested by Noelle Younge, which is more relevant to this point.

Additional Questions:
Please enter your name: Noelle Younge
Job Title: Assistant Professor of Pediatrics
Institution: Duke University Medical Center
Reimbursement for attending a symposium?: No
A fee for speaking?: No
A fee for organising education?: No
Funds for research?: No
Funds for a member of staff?: No
Fees for consulting?: No
Have you in the past five years been employed by an organisation that may in any way gain or lose financially from the publication of this paper?: No
Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this paper?: No
If you have any competing interests <A HREF="http://www.bmj.com/about-
**Information for submitting a revision**

Deadline: Your revised manuscript should be returned within one month.

How to submit your revised article: Log into [http://mc.manuscriptcentral.com/bmj](http://mc.manuscriptcentral.com/bmj) and enter your Author Center, where you will find your manuscript title listed under "Manuscripts with Decisions." Under "Actions," click on "Create a Revision." Your manuscript number has been appended to denote a revision.

You will be unable to make your revisions on the originally submitted version of the manuscript. Instead, revise your manuscript using a word processing program and save it on your computer. Once the revised manuscript is prepared, you can upload it and submit it through your Author Center. When submitting your revised manuscript, you will be able to respond to the comments made by the reviewer(s) and Committee in the space provided. You can use this space to document any changes you make to the original manuscript and to explain your responses. In order to expedite the processing of the revised manuscript, please be as specific as possible in your response to the reviewer(s). As well as submitting your revised manuscript, we also require a copy of the manuscript with changes highlighted. Please upload this as a supplemental file with file designation 'Revised Manuscript Marked copy'. Your original files are available to you when you upload your revised manuscript. Please delete any redundant files before completing the submission.

When you revise and return your manuscript, please take note of all the following points about revising your article. Even if an item, such as a competing interests statement, was present and correct in the original draft of your paper, please check that it has not slipped out during revision. Please include these items in the revised manuscript to comply with BMJ style (see: [http://www.bmj.com/about-bmj/resources-authors/article-submission/article-requirements](http://www.bmj.com/about-bmj/resources-authors/article-submission/article-requirements) and [http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists](http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists)).

Items to include with your revision (see [http://www.bmj.com/about-bmj/resources-authors/article-types/research](http://www.bmj.com/about-bmj/resources-authors/article-types/research)):

1. What this paper adds/what is already known box (as described at [http://resources.bmj.com/bmj/authors/types-of-article/research](http://resources.bmj.com/bmj/authors/types-of-article/research))

2. Name of the ethics committee or IRB, ID# of the approval, and a statement that participants gave informed consent before taking part. If ethics committee approval was not required, please state so clearly and explain the reasons why (see [http://resources.bmj.com/bmj/authors/editorial-policies/guidelines](http://resources.bmj.com/bmj/authors/editorial-policies/guidelines)).

3. Patient confidentiality forms when appropriate (see [http://resources.bmj.com/bmj/authors/editorial-policies/copy_of_patient-confidentiality](http://resources.bmj.com/bmj/authors/editorial-policies/copy_of_patient-confidentiality)).

4. Competing interests statement (see [http://resources.bmj.com/bmj/authors/editorial-policies/competing-interests](http://resources.bmj.com/bmj/authors/editorial-policies/competing-interests))

5. Contributorship statement + guarantor (see [http://resources.bmj.com/bmj/authors/article-submission/authorship-contributorship](http://resources.bmj.com/bmj/authors/article-submission/authorship-contributorship))

6. Transparency statement: (see [http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/transparency-policy](http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/transparency-policy))

7. Copyright statement/licence for publication (see [http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/copyright-open-access-and-permission-reuse](http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/copyright-open-access-and-permission-reuse))
8. Data sharing statement (see http://www.bmj.com/about-bmj/resources-authors/article-types/research)

9. Funding statement and statement of the independence of researchers from funders (see http://resources.bmj.com/bmj/authors/article-submission/article-requirements).

10. Patient involvement statement (see http://www.bmj.com/about-bmj/resources-authors/article-types/research).

11. Please ensure the paper complies with The BMJ’s style, as detailed below:

a. Title: this should include the study design eg "systematic review and meta-analysis."

b. Abstract: Please include a structured abstract with key summary statistics, as explained below (also see http://resources.bmj.com/bmj/authors/types-of-article/research). For every clinical trial - and for any other registered study - the last line of the abstract must list the study registration number and the name of the register.

c. Introduction: This should cover no more than three paragraphs, focusing on the research question and your reasons for asking it now.

d. Methods: For an intervention study the manuscript should include enough information about the intervention(s) and comparator(s) (even if this was usual care) for reviewers and readers to understand fully what happened in the study. To enable readers to replicate your work or implement the interventions in their own practice please also provide (uploaded as one or more supplemental files, including video and audio files where appropriate) any relevant detailed descriptions and materials. Alternatively, please provide in the manuscript urls to openly accessible websites where these materials can be found.

e. Results: Please report statistical aspects of the study in line with the Statistical Analyses and Methods in the Published Literature (SAMPL) guidelines http://www.equator-network.org/reporting-guidelines/sampl/. Please include in the results section of your structured abstract (and, of course, in the article's results section) the following terms, as appropriate:

i. For a clinical trial: Absolute event rates among experimental and control groups; RRR (relative risk reduction); NNT or NNH (number needed to treat or harm) and its 95% confidence interval (or, if the trial is of a public health intervention, number helped per 1000 or 100,000.)

ii. For a cohort study: Absolute event rates over time (eg 10 years) among exposed and non-exposed groups; RRR (relative risk reduction.)

iii. For a case control study: OR (odds ratio) for strength of association between exposure and outcome.

iv. For a study of a diagnostic test: Sensitivity and specificity; PPV and NPV (positive and negative predictive values.)

v. For a systematic review and/or meta-analysis: Point estimates and confidence intervals for the main results; one or more references for the statistical package(s) used to analyse the data, eg RevMan for a systematic review. There is no need to provide a formal reference for a very widely used package that will be very familiar to general readers eg STATA, but please say in the text which version you used. For articles that include explicit statements of the quality of evidence and strength of recommendations, we prefer reporting using the GRADE system.

f. Discussion: To minimise the risk of careful explanation giving way to polemic, please write the discussion section of your paper in a structured way. Please follow this structure: i) statement of principal findings of the study; ii) strengths and weaknesses of the study; iii) strengths and weaknesses in relation to other studies, discussing important differences in results; iv) what your study adds (whenever possible please discuss your study in the light of relevant systematic reviews and meta-analyses); v) meaning of the study, including possible explanations and implications for clinicians and policymakers and other researchers; vi) how your study could promote better decisions; vi) unanswered questions and future research.
g. Footnotes and statements

Online and print publication: All original research in The BMJ is published with open access. Our open access policy is detailed here: http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/copyright-open-access-and-permission-reuse. The full text online version of your article, if accepted after revision, will be the indexed citable version (full details are at http://resources.bmj.com/bmj/about-bmj/the-bmjs-publishing-model). The print and iPad BMJ will carry an abridged version of your article. This abridged version of the article is essentially an evidence abstract called BMJ pico, which we would like you to write using the template downloadable at http://resources.bmj.com/bmj/authors/bmj-pico. Publication of research on bmj.com is definitive and is not simply interim "epublication ahead of print", so if you do not wish to abridge your article using BMJ pico, you will be able to opt for online only publication. Please let us know if you would prefer this option. If your article is accepted we will invite you to submit a video abstract, lasting no longer than 4 minutes, and based on the information in your paper’s BMJ pico evidence abstract. The content and focus of the video must relate directly to the study that has been accepted for publication by The BMJ, and should not stray beyond the data.