PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Do omega-3 or other fatty acids influence the development of 'growing pains'? A pre-birth cohort study
AUTHORS	Golding, Jean; Northstone, Kate; Emmett, Pauline; Steer, Colin; Hibbeln, Joseph

VERSION 1 - REVIEW

REVIEWER	Angela Evans AUT university, Auckland, New Zealand AND University of South Australia No competing interests apply
REVIEW RETURNED	03-Jun-2012

THE STUDY	A major potential flaw, unless this can be better reported, is the lack of validity data for the questionnaires which were used to select the participants. Another problem is the reporting of GP at age 8 years, when it has previously been found to be more prevalent in children aged 4-6 years (why age 8 years?). The references and the background are somewhat scant eg one of the three aetiological theories which were long held is mentioned (not fatigue nor anatomical factors). Claim about quality of life, but no supporting reference.
RESULTS & CONCLUSIONS	Very difficult to find results credible when subject selection is questionable. If more information is available regarding questionnaire validity, this should be included (there is a validated questionnaire for identifying GP - was this used - and if not why?).
REPORTING & ETHICS	Ethical approval appears implied rather than clearly specified.
GENERAL COMMENTS	I do hope that you can supply information about the validity of the parental questionnaires please, and also a better reasoning for choosing reports at age 8 years. These aspects are fundamental to the value of the study.

REVIEWER	Dr Angelos Kaspiris MD, MPhil Orthopaedic Surgeon Department of Trauma and Orthopaedics Thriassio General Hospital - NHS Attica Greece I have no competing interests

REVIEW RETURNED	07-Jun-2012

GENERAL COMMENTS	***Comments for Authors*** ***Title:*** *Do omega-3 or other fatty acids influence the development of 'growing pains'? A pre-birth cohort study* This appears to me a very interesting paper with well-presented methods and results. The message is clear with very positive findings, like its originality (as far as I know there is the first research which examines the relationship between omega-3-fatty acids and GP), the large sample of the population and the study of the association between passive smoking and GP, which has not been examined extensively in the international literature. Comments 1. Although, there is a publication showing that GP may be an indicator of an increasing risk of arthritis in adulthood, the authors should have noted the fact that according to the majority of the research articles GP represent rather a lower extremity overuse syndrome than an inflammatory syndrome. 2. The relationship between GP and the lack of Vit D is little controversial (For example: "Paediatric vitamin D deficiency in a southwestern luminous climate" Szalay EA, Tryon EB, Pleacher MD, Whisler SL. J Pediatr Orthop 2011;31(4): 469 – 473) and it could be reported. 3. I would like to be clarified if the questionnaire that was used for the definition of G.P. is based on Petersen's clinical criteria. Furthermore, it would be useful to know precisely not only the inclusion but the exclusion criteria, as well. Additionally, the number of the children with lower limb pains of other aetiologies that have been excluded of the study must be reported. Kind Regards Dr Angelos Kaspiris MD, MPhil

VERSION 1 – AUTHOR RESPONSE

Reviewer: Angela Evans

1.1. A major potential flaw, unless this can be better reported, is the lack of validity data for the questionnaires which were used to select the participants.

At the time of the design of the ALSPAC study, there were no validated questions available. The questions used were developed in association with experts in the field. There was, however concurrent validity within the questions similar to those demonstrated by the reviewer in her later study [The Foot 2004; 14: 42 – 48], as well as by the expected correlations with family history of arthritis. We also demonstrate reliability by comparing results over time. We have included further details of the questions in the Methods section.

1.2. Another problem is the reporting of GP at age 8 years, when it has previously been found to be more prevalent in children aged 4-6 years (why age 8 years?).

Contrary to the reviewer's opinion we have already shown in this cohort that the prevalence of reported growing pains increase with age between ages 5 and 13 [Arch Dis Child 2012;97:52-53]. We chose age 8 as that was the age preceded most closely by measures of plasma fatty acids and measures of the child's diet.

1.3. The references and the background are somewhat scant eg one of the three aetiological theories which were long held is mentioned (not fatigue nor anatomical factors). Claim about quality of life, but no supporting reference.

We not only mention the relationship with psychosomatic factors, but also mention anatomical factors by quoting the ultrasound findings in the first paragraph of the Introduction. We do not think that fatigue is a cause of growing pains so much as a condition when they are more apparent to the child. However we have now quoted this reviewer's literature review as new ref [7].

1.4. Very difficult to find results credible when subject selection is questionable. If more information is available regarding questionnaire validity, this should be included (there is a validated questionnaire for identifying GP - was this used - and if not why?).

The questionnaire refered to by the referee was only published in 2004, and our study questions were designed in 1996. There was, consequently no way in which we could have used the former.

We have already stated that a limitation of the study is that the data are collected from the child's mother rather than by direct examination of the child. However we doubt whether this is a serious defect as we have shown in a number of validation studies that the study mothers are reasonably accurate. [see Golding J. Preparation, piloting and validation for a longitudinal birth cohort study. Paediatric and Perinatal Epidemiology 2009; 23 (Supp 1): 201 -212.

1.5. Ethical approval appears implied rather than clearly specified.

As stated in the paper, ethical approval for the study was obtained from the ALSPAC Law and Ethics Committee and the Local Research Ethics Committees. They had specified that analyses of data already collected [and the collection of which they had approved at the time] had the approval of all committees, provided the study complied with the rules already laid down.

1.6. I do hope that you can supply information about the validity of the parental questionnaires please, and also a better reasoning for choosing reports at age 8 years. These aspects are fundamental to the value of the study.

Please see responses above

2. Reviewer: Dr Angelos Kaspiris MD, MPhil

2.1. This appears to me a very interesting paper with well-presented methods and results. The message is clear with very positive findings, like its originality (as far as I know there is the first research which examines the relationship between omega-3-fatty acids and GP), the large sample of the population and the study of the association between passive smoking and GP, which has not been examined extensively in the international literature.

2.2. Although, there is a publication showing that GP may be an indicator of an increasing risk of arthritis in adulthood, the authors should have noted the fact that according to the majority of the research articles GP represent rather a lower extremity overuse syndrome than an inflammatory syndrome.

Thank you; we have added that as quoted in the article by Evans and Scutter

2.3 The relationship between GP and the lack of Vit D is little controversial (For example: “Paediatric vitamin D deficiency in a southwestern luminous climate” Szalay EA, Tryon EB, Pleacher MD, Whisler SL. J Pediatr Orthop 2011;31(4): 469 – 473) and it could be reported.

We have now referred to this paper in the discussion

2.4. I would like to be clarified if the questionnaire that was used for the definition of G.P. is based on Petersen’s clinical criteria. Furthermore, it would be useful to know precisely not only the inclusion but the exclusion criteria, as well. Additionally, the number of the children with lower limb pains of other aetiologies that have been excluded of the study must be reported.

The study did not include Peterson’s criteria, but rather used the details of presence of pain in the limbs of the children which were not ascribed to a pathological cause. We excluded all pathological causes such as cerebral palsy, arthritis, rheumatism, etc [see Supplementary Table 1 of the paper referenced in 1.1]. This resulted in the exclusion of 41 children from the 8-year assessment.

VERSION 2 – REVIEW

REVIEWER	Angela Evans 31 Woodfield Ave Fullarton 31 Woodfield Ave Adelaide South Australia
REVIEW RETURNED	16-Jul-2012

THE STUDY	I'm afraid the questions/questionnaire used to identify GP still requires further clarification: - please provide further information about the reliability test-retest

	process and results - please better describe the concurrent validity and why the inclusion/exclusion criteria from Petersen were not used (as per the other review) If these details are not available, please state this and place greater emphasis on this aspect as a basic limitation of the study, and future recommendations. Thank you for your efforts in clarifying these issues.

VERSION 2 – AUTHOR RESPONSE

- please better describe the concurrent validity (see above)and why the inclusion/exclusion criteria from Petersen were not used (as per the other review)
If these details are not available, please state this and place greater emphasis on this aspect as a basic limitation of the study, and future recommendations.
If these details are not available, please state this and place greater emphasis on this aspect as a basic limitation of the study, and future recommendations.
The major criteria of Peterson concerned omitting cases with known organic cause – and this we did. However we have inserted a statement in regard to failure to collect other pertinent data in the methodology. We have also inserted a statement under the limitations section of the discussion.