PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (see an example) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Unidentified Chronic Fatigue Syndrome (CFS/ME) is a major cause of school absence: surveillance outcomes from school based clinics.
AUTHORS	Esther M Crawley, Alan M Emond, Jonathan A C Sterne

VERSION 1 - REVIEW

REVIEWER	Matthew Hotopf Professor of General Hospital Psychiatry King's College London
REVIEW RETURNED	31/08/2011

THE STUDY	1. METHODS There is insufficient information on the clinical service: please give some information about the nature of the service, catchment, likely barriers to referral, etc. 2. METHODS Which diagnostic criteria for CFS were used? Please reference the definition (p7, lines13-17) 3. ENGLISH The methods are written in a mix of tenses (see p 7 plines 20-32). 4. STATS You provide a headline prevalence estimate of 1% of children with CFS/ME. This does not seem to take account of the fact that one of the 3 schools was girl only? 5. STATS Presumably you did not only use unpaired t tests as some are categorical variables.
REPORTING & ETHICS	The paragraph at the bottom of p7 describes the position with the research ethics committee, who apparently thought that this was not research. If ethics approval was sought and not obtained because the REC made that decision, the authors cannot do much about it. However the wording in the paragraph is a bit ambiguous. My view is that it is understandable that the REC might see use of routine data from the existing clinical service as not being research (which is what the paragraph seems to say), but it is surprising that they did not see the surveillance component as research. Children who are unknown to services were being contacted using information from their schools and it seems to me that there are significant issues of confidentiality and data protection which, in my experience as a researcher and one time REC member, I am surprised the REC did not think amounted to research. Assuming the REC was fully aware of these issues, and still made a decision that the work was not research, then it would be unfair to oppose publication on these grounds, but the authors should make a fuller explanation, and in the interest of openess might wish to make their application to the REC and subsequent correspondence available with the publication. Given these comments, I think that the authors should describe the process of recruitment and consent in more detail than they do. What information was provided to parents? Were parents able to opt out if they did not want data on their child handed to the researcher? What were the consent procedures and information given to children

	and parents identified as eligible for the clinic visit?
GENERAL COMMENTS	I think the paper makes an important point, and gives some intruiging and useful data which might have a significant impact on policy.

REVIEWER	Professor of Neurology & General Practice Academic Neuroscience Centre, PO41 Institute of Psychiatry at King's College London SE5 8AF
REVIEW RETURNED	23/09/2011

RESULTS & CONCLUSIONS	The increase in prevalence is clearly due to the change in definition of CFS. Perhaps this should be made clearer. My knowledge-base is mainly of adults with fatigue. There is trial evidence that CBT and GET may improve outcome. However this has been difficult to reproduce in normal NHS practice (eg Quarmby et al 2007). It may be premature to suggest that screening take place for fatigue (as opposed to migraine for example), until evidence for cost-effective therapies are clearer in practice.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1

1. METHODS. There is insufficient information on the clinical service: please give some information about the nature of the service, catchment, likely barriers to referral etc.
We have added the following to the methods section under diagnosis and management: “The Bath specialist paediatric CFS/ME service covers a region in the south west of England with a population of some 400,000 children aged 5 to 19 years (2001 census) and accepts referrals from schools, general practitioners and paediatricians. Each year, more than 200 children and young people are assessed and treated following NICE guidance1 each year in out patient clinics unless they are too severely affected to attend clinic, in which case they are seen at home. “
We discuss reasons why children with CFS/ME may not be identified in the discussion saying: “There are several possible reasons why children missing significant amounts of school with CFS/ME are not identified. Those with mild or moderate CFS/ME may not see their GP, or may not be recognised as having CFS/ME if they are seen. Alternatively, GPs and paediatricians may not be aware of specialist CFS/ME services or may feel that the child’s CFS/ME is not sufficiently serious to warrant a referral.”
2. METHODS which diagnostic criteria for CFS were used? Please reference the definition (p7 lines 13-17)
We used the diagnostic criteria recommended in the NICE guidelines. We have added: “using diagnostic criteria recommended in the NICE guidelines1” to the second sentence of this paragraph which now reads: “A diagnosis of CFS/ME was given using diagnostic criteria recommended in the NICE guidelines1 to children who had disabling fatigue lasting 3 months or longer with one additional symptom, where no other cause for the fatigue could be established.”
3. ENGLISH The methods are written in a mixture of tenses.
We have changed the sentences in the last paragraph of the methods to the past tense.
4. STATS you provide a headline prevalence estimate of 1% of children with CFS/ME. This does not seem to take account of the fact that one of the 3 schools was girl only.
We agree that if the prevalence of CFS/ME differed between boys and girls then our overall prevalence estimate would be biased. The literature provides little information on this issue, but a paper by Chalder et al2 based on a small number of cases, found little evidence for such differences.
We have added the following to the paragraph describing study limitations in the discussion section: “One of the schools was a girls only school. A cross sectional study of British children found little

evidence that female gender was a risk factor for CFS/ME diagnosed using the CDC criteria or parental report2 although adult CFS/ME is more common in women than in men3. If the prevalence of CFS/ME were higher in girls than boys aged 11-16 then we would have overestimated the overall prevalence"

5. STATS Presumably you did not only use unpaired t tests as some are categorical variables.

We have added the following to the statistical methods section: "We compared gender between the two groups using the $\chi 2$ test."

Ethical approval.

We agree that the reasons that ethical committee approval was not required for this clinical evaluation study requires clarification. Our paper reports results from a clinical outreach project from the CFS/ME specialist service working in partnership with local authority attendance officers to improve school attendance. As described in the paper, the specialist service has been advised that ethical approval for routine collection and analysis of service data is not required. The author EC is a community paediatrician and children were seen in school-based clinics. The schools invited children and their parents to attend and a member of the school staff (usually the attendance officer) was present. Information about the children was held by the schools until the child was referred to the specialist CFS/ME service. The project has been of great interest to the Department of Education who included it last year as an exemplar in their training for attendance officers in the UK. Based on the results of this outreach project, school nurses in the local authority now routinely assess children missing school for fatigue. We checked with the co-ordinator for the local REC that recording outcomes on school based clinics run by school nurses is part of service evaluation (and therefore does not require a submission to Ethics) and they have agreed that it is.

Although we regard "surveillance" as part of routine clinical care for community paediatricians, we acknowledge that this term can have other meanings and recognise that this makes the paper read as a research study rather than reporting on a clinical project.

We have made the following changes to clarify these issues:

1. We have changed the last part of the title from: "surveillance study" to "surveillance outcomes from school based clinics".
2. We have changed "surveillance" to "clinics" in the Objectives part of the Abstract which now reads: "To investigate the feasibility of conducting clinics for Chronic Fatigue Syndrome (CFS/ME) in schools"
3. We have changed "surveillance" to "clinical" in the Design part of the Abstract which now reads: "School based clinical project".
4. We have changed "surveillance" to "clinics" in the methods section of the abstract which now reads "We compared children with CFS/ME identified through school based clinics with those referred via health services.
5. We have changed "surveillance meetings" to clinical review at school in the methods section of the abstract. This now reads: "146 children with unexplained absence attended clinical review at school".
6. We have changed "surveillance" to "clinics" in the conclusions in the Abstract "Children diagnosed through school based clinics are less severely affected…."
7. We have changed "surveillance" to "clinics" in the second point in the article focus which now reads: "are school based clinics a feasible way to identify children with CFS/ME and offer treatment?."
8. We have changed "surveillance" to "clinics" in the third point in the Key messages which now reads "Children with CFS/ME who were detected through school based clinics were less severely affected than children referred via health services, and appeared to do well once treated"
9. We have changed "Surveillance was" to "school clinics were" in the strengths and limitations summary of the Article summary which now reads: "School clinics were conducted in 3 schools in the south West which has a well established specialist CFS/ME service. Results may not be generalisable to regions without a CFS/ME service or to regions with different socio-economic factors that impact on school attendance."
10. We have changed "surveillance" to "clinical" and "among" to "assess" and deleted "in CFS/ME" in

the last paragraph of the introduction which now reads: “In this paper, we report results from a school based clinical project to assess children missing school,….”
11. We have clarified what we did by deleting “Surveillance was conducted” and adding the following sentence to the first line of the Methods: “This study reports on a pilot clinical service set up with the school attendance service in Bath to try and improve school attendance. The service was offered in three state secondary schools…”.
12. In the methods section, first sentence of the first paragraph we have changed “school surveillance” to “school clinics”. This now reads: “Children identified in school clinics as having fatigue were invited….”
13. We have added the following sentence to the first line of the paragraph in the Ethics section of the methods: “The clinical service in this study was provided as an outreach from the Bath Specialist CFS/ME service.”
14. In the second paragraph of the results we have changed “surveillance meeting” to “clinical review at school” and added “the school clinic” at the end. This sentence now reads: 20% or more school without an identifiable cause and were invited to a clinical review at school. Of these, 112 (76.7%) attended the school clinic.
15. In the results (page 10 paragraph 2) we have changed “surveillance meetings to school clinics”. This now reads: “not attend school clinics were likely to have had CFS/ME”
In the results (page 10) we deleted surveillance from the sub-heading. This now reads: “Comparison of children with CFS/ME identified through school with those referred by health services”
16. In the next heading we have changed “surveillance” to “school”. This now reads: “Outcomes of treated CFS/ME in children identified through school”
17. In the first line of the discussion, we have changed “surveillance project” to “clinics”. This now reads In school based clinics. We have also changed “surveillance” to “clinics” in line 4. We have also changed surveillance to clinics in paragraph 4 of the discussion.
18. In the discussion (page 13, paragraph 2) we have changed “screening” to “assessment”. This now reads: “whereas we assessed children who missed school for any reason”
19. In the implication section, we have left the word surveillance in line 1 as we believe it is an important role for community paediatricians but we have changed surveillance to clinics in line 4 as this refers to our methods.
20. In the first paragraph of the implications section, we have changed “surveillance” to the identification of a potential cause”. This now reads: “the identification of a potential cause is likely to be of benefit in”
21. In the second paragraph (line 8) of the implications section which discussed surveillance, we have changed surveillance to school-clinic. This now reads: “Our finding that more than half (12/23) of children with school-clinic-diagnosed CFS/ME”
22. In the second paragraph of the implications (page 14), we have changed “implement surveillance to “undertake the initial assessments”. This now reads: “can undertake the initial assessments in school clinics”.
23. We have changed the concluding paragraph changing “surveillance” to “clinics” and “for Fatigue” to “identify children with CFS/ME which may” which now reads: “In conclusion, school based clinics are feasible and have the potential to identify children with CFS/ME which may reduce school absence and its harmful effects. Together with referral to specialist services, school based clinics have the potential to improve overall school attendance
24. In authors contributions, we have clarified that EC conducted school clinics by changing “surveillance” to “the school clinics”. This sentence now reads: “EC conceived the idea for this study; conducted the school clinics; analysed the data”.

Reviewer 2

1. The increase in prevalence is clearly due to the change in definition of CFS. Perhaps this should be made clearer.
Our prevalence of diagnosed CFS/ME (3/2855 = 0.11%) is the same as previous school studies so we are not convinced that the change in definition is the entire reason. However we agree it is part of the reason and we have stated (in paragraph 5 of the discussion): “Our prevalence estimate was also higher than estimates of between 0.1% and 0.5% from population based studies[3-5], perhaps because these used the adult definition of CFS/ME, which requires 6 months of fatigue and four additional symptoms.”

2. My knowledge-base is mainly of adults with fatigue. There is trial evidence that CBT and GET may improve outcome. However this has been difficult to reproduce in normal NHS practice (eg Quarmby et al 2007). It may be premature to suggest that screening take place for fatigue (as opposed to migraine for example), until evidence for cost-effective therapies are clearer in practice."

We agree and we have added “Large scale randomised controlled trials are needed in children, however” to the last paragraph in the discussion which now reads: “while the recently reported PACE trial provided strong evidence that these treatments are moderately effective in adults[23]. Large scale randomised controlled trials are needed in children, however our finding that more than half (12/23) of children with school-clinic-diagnosed CFS/ME”

Thank you for your help with this paper.

Yours,

Esther Crawley

Reference List

(1) NICE. Chronic fatigue syndrome/Myalgic encephalomyelitis (or encephalopathy); diagnosis and management. CG53. 2007. National Institute for Health and Clinical Excellence (NICE).

(2) Chalder T, Goodman R, Wessely S, Hotopf M, Meltzer H. Epidemiology of chronic fatigue syndrome and self reported myalgic encephalomyelitis in 5-15 year olds: cross sectional study. BMJ 2003; 327(7416):654-655.
(3) Hempel S, Chambers D, Bagnall AM, Forbes C. Risk factors for chronic fatigue syndrome/myalgic encephalomyelitis: a systematic scoping review of multiple predictor studies. Psychological Medicine 2008; 38(7):915-926.