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)	Clinical implementation of a new antibiotic prophylaxis regimen for percutaneous endoscopic gastrostomy
AUTHORS	Lagergren, Jesper; Mattson, Fredrik; Lagergren, Pernilla

VERSION 1 - REVIEW

REVIEWER	Dr Allyson Lipp Principal lecturer University of South Wales UK COI statement AL is the first author of a systematic review entitled: Systemic antimicrobial prophylaxis for percutaneous endoscopic gastrostomy Allyson Lipp*, Gail Lusardi Editorial Group: Cochrane Wounds Group Published Online: 21 JAN 2009 Assessed as up-to-date: 15 FEB 2011 DOI: 10.1002/14651858.CD005571.pub2
REVIEW RETURNED	24-Apr-2013

THE STUDY	A reference cited which is central to the article is out of date and secondary to the original Cochrane systematic review. Citing the systematic review would have provided more up to date evidence. (10. Lipp A, Lusardi G. A systematic review of prophylactic antimicrobials in PEG placement. Journal of clinical nursing 2009;18(7):938-48.) Coincidentally the review is currently being updated by the article reviewer (AL) and colleague to include the study cited in this paper (Blomberg J, Lagergren P, Martin L, Mattsson F, Lagergren J. Novel approach to antibiotic prophylaxis in percutaneous endoscopic gastrostomy (PEG): randomised controlled trial. BMJ (Clinical research ed 2010;341:c3115.). Line 51 page 6 reads 'The hospitals was categorised into three groups' and should read 'The hospitals were categorised into three

	groups' Line 32 page 10 well-deigned should read well-designed.
RESULTS & CONCLUSIONS	Having the questionnaire translated into English would have assisted the review process. From deliberation it was established that Question5 related to the comment on p6 about possible bias. Question 5 in the questionnaire is leading and perhaps should have been a more neutral question asking 'on what evidence do you base your PEG prophylaxis?'. If asked about specific evidence the respondent may be tempted to give a socially desirable response of 'yes I have heard of it'.
GENERAL COMMENTS	It is pleasing to review a paper with such a rapid, positive uptake of an innovation. However, any recommendation for uptake of this new practice should be made with caution as it is based on one small clinical trial of 200 patients in contrast to the Cochrane systematic review which incorporates multiple sources of evidence.

REVIEWER	Sanders, David Royal Hallamshire Hospital, Gastroenterology
REVIEW RETURNED	26-Apr-2013

THE STUDY	Am confused but surely the answer to the last question should be no? Ie I have no concerns. Have I misread thsi and I should be saying yes I have no concerns? Please change accordingly. I have no concerns
GENERAL COMMENTS	This research group has provided valuable practice changing research to the field of gastrostomy feeding. I admire and respect the team and their work although I hasten to add I do not know them personally. This is an excellent study and of importance to clinical practice – the idea of implementation and assessing what effect novel data really has is absolutely paramount to changing clinical practice. It is very well written. I have very few comments: 1. I would like a section in methodology explaining what the authors did after publication of their bmj study. How was the information disseminated? For example, how many talks have been given by the group about their data over the last 3 years (to which groups, primary secondary care, nurses, doctors? National meetings local?). What was the size of the audiences? Were there press releases or non-medline articles? Any other medline papers of a related nature? Did Swedish guidelines change? Were there email or app releases? Were there any other forms of active dissemination that I have not thought of that they are aware of? I think this allows us to estimate how hard the data was 'worked' or disseminated and this has bearing perhaps on how successfully the change of practice was as a result of their efforts 2. I would like them to discuss other assessments of this nature from medicine. For example, if you had published work on say taking >4 duodenal biopsies to exclude coeliac disease – what percentage of GI practitioners have adopted this? This allows us to place their intervention effect and subsequent adoption rates (which I think are

impressive) in the context of other changes of practice. Can they supply a few evidence based referenced examples?
See ref below as an example:

Gastrointest Endosc. 2012 Oct;76(4):779-85. doi: 10.1016/j.gie.2012.05.011. Epub 2012 Jun 23.
Sex and racial disparities in duodenal biopsy to evaluate for celiac disease.
Lebwohl B, Tennyson CA, Holub JL, Lieberman DA, Neugut AI, Green PH.
Source
Celiac Disease Center, Department of Medicine, Columbia University Medical Center, New York, New York, USA.
Abstract
BACKGROUND:
Celiac disease (CD) is common but underdiagnosed in the United States. Serological screening studies indicate that, although CD occurs at the same frequency in both sexes, women are diagnosed more frequently than men (2:1). CD is less frequently diagnosed among black patients, though the seroprevalence in this group is not known.
OBJECTIVE:
To measure the rates of duodenal biopsy during EGD for symptoms consistent with CD.
DESIGN:
Retrospective cohort study.
SETTING:
Clinical Outcomes Research Initiative National Endoscopy Database, spanning the years 2004 through 2009.
PATIENTS:
Adults undergoing EGD for the indication of diarrhea, anemia, iron deficiency, or weight loss, in which the endoscopic appearance of the upper GI tract was normal.
MAIN OUTCOME MEASUREMENT:
Performance of duodenal biopsy.
RESULTS:
Of 13,091 individuals (58% female patients, 9% black patients) who met the inclusion criteria, duodenal biopsy was performed in 43%, 45% of female patients and 39% of male patients (P < .0001). Black patients underwent duodenal biopsy in 28% of EGDs performed compared with 44% for white patients (P < .0001). On multivariate analysis, male sex (odds ratio [OR] 0.81; 95% CI, 0.75-0.88), older age (OR for 70 years and older compared with 20-49 years, 0.51; 95% CI, 0.46-0.57), and black patients (OR 0.55; 95% CI, 0.48-0.64) were associated with decreased odds of duodenal biopsy.
LIMITATIONS:
Lack of histopathologic correlation with CD prevalence.
CONCLUSIONS:
In this multiregional endoscopy database spanning the period from 2004 through 2009, rates of duodenal biopsy increased modestly over time, but overall remained low in patients with possible clinical indications for biopsy. Nonperformance of duodenal biopsy during endoscopy may be contributing to the underdiagnosis of CD in the United States

Finally I would congratulate them on their work.

VERSION 1 – AUTHOR RESPONSE

Reviewer: Dr Allyson Lipp
Principal lecturer
University of South Wales
UK

COI statement

AL is the first author of a systematic review entitled:

Systemic antimicrobial prophylaxis for percutaneous endoscopic gastrostomy

Allyson Lipp*,
Gail Lusardi
Editorial Group: Cochrane Wounds Group
Published Online: 21 JAN 2009
Assessed as up-to-date: 15 FEB 2011
DOI: 10.1002/14651858.CD005571.pub2

1. A reference cited which is central to the article is out of date and secondary to the original Cochrane systematic review. Citing the systematic review would have provided more up to date evidence.
(10. Lipp A, Lusardi G. A systematic review of prophylactic antimicrobials in PEG placement. Journal of clinical nursing 2009;18(7):938-48.). Coincidentally the review is currently being updated by the article reviewer (AL) and colleague to include the study cited in this paper (Blomberg J, Lagergren P, Martin L, Mattsson F, Lagergren J. Novel approach to antibiotic prophylaxis in percutaneous endoscopic gastrostomy (PEG): randomised controlled trial. BMJ (Clinical research ed 2010;341:c3115.).
Reply: We have removed the previous reference 7 and replaced it by the new reference suggested in the revised manuscript.

2. Line 51 page 6 reads 'The hospitals was categorised into three groups' and should read 'The hospitals were categorised into three groups'
Reply: Sorry for this grammar error. It has now been corrected.

3. Line 32 page 10 well-deigned should read well-designed.
Reply: Sorry for this miss-spelling. It has now been corrected.

4. Having the questionnaire translated into English would have assisted the review process. From deliberation it was established that Question 5 related to the comment on p6 about possible bias. Question 5 in the questionnaire is leading and perhaps should have been a more neutral question asking 'on what evidence do you base your PEG prophylaxis?'. If asked about specific evidence the respondent may be tempted to give a socially desirable response of 'yes I have heard of it'.
Reply: We agree that question 5 could have been asked in a more open fashion. However, this question was asked only after all other questions regarding use of the new regimen, which counteracts bias.

5. It is pleasing to review a paper with such a rapid, positive uptake of an innovation. However, any recommendation for uptake of this new practice should be made with caution as it is based on one small clinical trial of 200 patients in contrast to the Cochrane systematic review which incorporates multiple sources of evidence.

Reply: We agree that this is an important issue. We have therefore added a discussion about this in the revised manuscript (page 10).

Reviewer: David S Sanders
Royal Hallamshire Hospital, Gastroenterology

This research group has provided valuable practice changing research to the field of gastrostomy feeding. I admire and respect the team and their work although I hasten to add I do not know them personally.
Reply: Thank you very much for these positive remarks.

This is an excellent study and of importance to clinical practice – the idea of implementation and assessing what effect novel data really has is absolutely paramount to changing clinical practice. It is very well written.
Reply: Thank you for this positive evaluation.

I have very few comments:

1. I would like a section in methodology explaining what the authors did after publication of their bmj study. How was the information disseminated?
For example, how many talks have been given by the group about their data over the last 3 years (to which groups, primary secondary care, nurses, doctors? National meetings local?). What was the size of the audiences?
Were there press releases or non-medline articles? Any other medline papers of a related nature? Did Swedish guidelines change? Were there email or app releases?
Were there any other forms of active dissemination that I have not thought of that they are aware of?
I think this allows us to estimate how hard the data was 'worked' or disseminated and this has bearing perhaps on how successfully the change of practice was as a result of their efforts.
Reply: This is a good suggestion. The text presenting the dissemination of the study in the introduction section has been moved to the methods section and been made more clear.

2. I would like them to discuss other assessments of this nature from medicine. For example, if you had published work on say taking >4 duodenal biopsies to exclude coeliac disease – what percentage of GI practitioners have adopted this? This allows us to place their intervention effect and subsequent adoption rates (which I think are impressive) in the context of other changes of practice. Can they supply a few evidence based referenced examples?
See ref below as an example:
Gastrointest Endosc. 2012 Oct;76(4):779-85. doi: 10.1016/j.gie.2012.05.011. Epub 2012 Jun 23.
Sex and racial disparities in duodenal biopsy to evaluate for celiac disease.
Lebwohl B, Tennyson CA, Holub JL, Lieberman DA, Neugut AI, Green PH.
Source
Celiac Disease Center, Department of Medicine, Columbia University Medical Center, New York, New York, USA.
Abstract
BACKGROUND:
Celiac disease (CD) is common but underdiagnosed in the United States. Serological screening studies indicate that, although CD occurs at the same frequency in both sexes, women are diagnosed more frequently than men (2:1). CD is less frequently diagnosed among black patients, though the seroprevalence in this group is not known.
OBJECTIVE:
To measure the rates of duodenal biopsy during EGD for symptoms consistent with CD.

DESIGN:
Retrospective cohort study.
SETTING:
Clinical Outcomes Research Initiative National Endoscopy Database, spanning the years 2004 through 2009.
PATIENTS:
Adults undergoing EGD for the indication of diarrhea, anemia, iron deficiency, or weight loss, in which the endoscopic appearance of the upper GI tract was normal.
MAIN OUTCOME MEASUREMENT:
Performance of duodenal biopsy.
RESULTS:
Of 13,091 individuals (58% female patients, 9% black patients) who met the inclusion criteria, duodenal biopsy was performed in 43%, 45% of female patients and 39% of male patients (P < .0001). Black patients underwent duodenal biopsy in 28% of EGDs performed compared with 44% for white patients (P < .0001). On multivariate analysis, male sex (odds ratio [OR] 0.81; 95% CI, 0.75-0.88), older age (OR for 70 years and older compared with 20-49 years, 0.51; 95% CI, 0.46-0.57), and black patients (OR 0.55; 95% CI, 0.48-0.64) were associated with decreased odds of duodenal biopsy.
LIMITATIONS:
Lack of histopathologic correlation with CD prevalence.
CONCLUSIONS:
In this multiregional endoscopy database spanning the period from 2004 through 2009, rates of duodenal biopsy increased modestly over time, but overall remained low in patients with possible clinical indications for biopsy. Nonperformance of duodenal biopsy during endoscopy may be contributing to the underdiagnosis of CD in the United States

Reply: This is a good suggestion. We have added a discussion about this example (page 10).

Finally I would congratulate them on their work.
Reply: Many thanks.