PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	A cohort study evaluating management of unhealed surgical wounds in the community in clinical practice in the UK: costs and outcomes
AUTHORS	Guest, Julian; Fuller, Graham; Vowden, Peter

VERSION 1 – REVIEW

REVIEWER	Rhiannon Macefield Senior Research Associate University of Bristol, UK
REVIEW RETURNED	29-Mar-2018

GENERAL COMMENTS	This is an interesting and comprehensive piece of work examining the impact of surgical wounds that fail to heal effectively on NHS resource use and cost in the community. The paper is well written and easy to read. The authors clearly present the findings and address the limitations of the study using data collected in the THIN database. I have the following minor comments and suggestions for improvements: 1. Please could the authors include detail on the definition of 'wound healing'. Was this specifically documented in the database or if not how was wound healing confirmed/defined and at what date? This to me is a potentially major limitation of the data in terms of different definitions for what constitutes a 'healed wound' and when/how this was recorded in the database. It may also lead to over/under-estimation of the date that a wound was considered to be healed. Some clarification is warranted in the report. 2. It would be helpful to include some numbers (numerators and denominators) in the results in addition to the percentages. In addition, some indication of the spread of the data for some characteristics/outcomes would be interesting (range, SD). 3. I found the reporting of the percentage of patients with clinically infected wounds and those prescribed systemic anti-infective and/or antimicrobial dressings' in the text (p.15, lines 53-57) confusing in relation to the figures reported in Table 9. Does Table 9 present percentages overall across the time period (rather than just the onset of management in the community)? If so this could be made clearer. 4. Typo in line 32 in the abstract should read 'mean NHS cost'.

REVIEWER	Sathish Thirunavukkarasu Nanyang Technological University, Singapore

REVIEW RETURNED	13-Apr-2018

GENERAL COMMENTS	The paper by Guest at al addresses an important public health issue that is highly relevant for the UK clinical practice with regards to managing unhealed surgical wounds. The paper is very well written, and I have only some minor comments. 1. It would be good to clearly specify what were the clinical outcomes for this analysis. Currently, it is a bit ambiguous. 2. Please present the unit cost figures for various resources in the tables or in supplementary files. Although, references for the unit costs were given on page 10, it would be helpful to see them in the paper itself. 3. Statistical analysis: • Please describe the logistic regression analysis in more detail – what method was used (e.g., enter, stepwise), univariate or multivariate, etc. • Please provide the p value that was set for the level of significance. 4. Please provide 'n' along with percentages and standard deviation for mean values. 5. Table 1 – do you have data for plasma glucose, alcohol intake and intake of drugs like steroids (risk factors for non-healing of wounds)? If available, please provide, and also adjust them in the logistic regression analysis. 6. Please provide 95% CIs for odds ratios, and exact p values (instead of reporting p<0.03). 7. Page 13: I am afraid the odds ratios are reported incorrectly. For example, the odds ratio for suspect infection could be interpreted like this: Compared to no infection, there was a 50% lower risk of non-healing when there was a suspected infection. Please clarify. 8. Please comment on the missing data.

VERSION 1 – AUTHOR RESPONSE

Reviewer(s)' Comments to Author:

Reviewer: 1
Reviewer Name: Rhiannon Macefield
Institution and Country: Senior Research Associate, University of Bristol, UK Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below. This is an interesting and comprehensive piece of work examining the impact of surgical wounds that fail to heal effectively on NHS resource use and cost in the community. The paper is well written and easy to read.

The authors clearly present the findings and address the limitations of the study using data collected in the THIN database.

I have the following minor comments and suggestions for improvements:

1. Please could the authors include detail on the definition of 'wound healing'. Was this specifically documented in the database or if not how was wound healing confirmed/defined and at what date? This to me is a potentially major limitation of the data in terms of different definitions for what

constitutes a ‘healed wound’ and when/how this was recorded in the database. It may also lead to over/under-estimation of the date that a wound was considered to be healed. Some clarification is warranted in the report. This study was an analysis of unhealed surgical wounds following a documented surgical procedure in the patients’ medical records. The THIN database does not define what a wound is and nor does it define wound healing. Wound healing was a clinical observation not necessarily confirmed by a specialist and it is unknown if the nurses/GPs who managed these patients used any consistent definition. This has now been stated in the Results section.

2. It would be helpful to include some numbers (numerators and denominators) in the results in addition to the percentages. In addition, some indication of the spread of the data for some characteristics/outcomes would be interesting (range, SD). Some numbers and SDs have now been included.

3. I found the reporting of the percentage of patients with clinically infected wounds and those prescribed systemic anti-infective and/or antimicrobial dressings’ in the text (p.15, lines 53-57) confusing in relation to the figures reported in Table 9. Does Table 9 present percentages overall across the time period (rather than just the onset of management in the community)? If so this could be made clearer. The authors have attempted to clarify this.

4. Typo in line 32 in the abstract should read ‘mean NHS cost’. This has been corrected

Reviewer: 2
Reviewer Name: Sathish Thirunavukkarasu
Institution and Country: Nanyang Technological University, Singapore Please state any competing interests or state ‘None declared’: None declared

Please leave your comments for the authors below The paper by Guest at al addresses an important public health issue that is highly relevant for the UK clinical practice with regards to managing unhealed surgical wounds. The paper is very well written, and I have only some minor comments.

1. It would be good to clearly specify what were the clinical outcomes for this analysis. Currently, it is a bit ambiguous. The objective of the Abstract has been amended, but the outcomes were determined by the available data documented in the patients’ records.

2. Please present the unit cost figures for various resources in the tables or in supplementary files. Although, references for the unit costs were given on page 10, it would be helpful to see them in the paper itself. The analysis has utilised >50 different unit costs, for dressings, bandages, prescribed drugs, clinician visits, hospitalisations etc. So such a Table would be very large and unwieldy. So it would be best for the reader to obtain the cost they want by accessing the published source or asking the Authors directly.

3. Statistical analysis:
• Please describe the logistic regression analysis in more detail – what method was used (e.g., enter, stepwise), univariate or multivariate, etc. This has now been included in the Methods.
• Please provide the p value that was set for the level of significance. This has now been included in the Methods.

4. Please provide ‘n’ along with percentages and standard deviation for mean values. This has been provided for the most appropriate values

5. Table 1 – do you have data for plasma glucose, alcohol intake and intake of drugs like steroids (risk factors for non-healing of wounds)? If available, please provide, and also adjust them in the logistic

regression analysis. This data was either not documented in the THIN records or was not extracted. This has now been included in the study limitations.

6. Please provide 95% CIs for odds ratios, and exact p values (instead of reporting p<0.03). This has been amended.

7. Page 13: I am afraid the odds ratios are reported incorrectly. For example, the odds ratio for suspect infection could be interpreted like this: Compared to no infection, there was a 50% lower risk of non-healing when there was a suspected infection. Please clarify. The authors do not agree with this interpretation. The analysis shows that compared to no infection, there was a 50% lower risk of a wound not healing when there was a suspected infection The authors have attempted to clarify this in the text.

8. Please comment on the missing data. This has been included in the Methods.

VERSION 2 – REVIEW

REVIEWER	Rhiannon Macefield University of Bristol, UK
REVIEW RETURNED	10-May-2018

GENERAL COMMENTS	Thank you to the authors for adequately addressing the points raised in the initial review. I'm afraid I still remain confused by the data in Table 9 compared to the text description in the second paragraph of the results reporting 'Infection'. The table shows that 66% + 18% were prescribed an anti-infective and/or an antimicrobial dressing, suggesting as many as 84% may have been at risk or infected at the onset of wound management, rather than 68% as reported in the text? Apologies if this has been misinterpreted - if so perhaps some more clarity could be provided.

REVIEWER	Sathish Thirunavukkarasu Nanyang Technological University, Singapore
REVIEW RETURNED	20-May-2018

GENERAL COMMENTS	Thank you for addressing my earlier comments. The paper reads well. I only have a few queries requiring explanation. 1. The authors say that they previously identified a random sample of 6000 patients with a wound from the THIN database. Could you please explain how this sample size was determined and for what purpose this random sampling was done? Also, please comment on how far the sample of 707 patients identified from within this cohort is representative of all patients (that would satisfy the eligibility criteria for this study) in the THIN database? 2. Logistic regression analysis results can be provided in tables for better readability.

VERSION 2 – AUTHOR RESPONSE

AUTHORS' REPLIES TO THE REVIEWERS' COMMENTS

Reviewer: 1

Reviewer Name: Rhiannon Macefield

Institution and Country: University of Bristol, UK Please state any competing interests or state ‘None declared’: None declared

Please leave your comments for the authors below Thank you to the authors for adequately addressing the points raised in the initial review. I'm afraid I still remain confused by the data in Table 9 compared to the text description in the second paragraph of the results reporting 'Infection'. The table shows that 66% + 18% were prescribed an anti-infective and/or an antimicrobial dressing, suggesting as many as 84% may have been at risk or infected at the onset of wound management, rather than 68% as reported in the text? Apologies if this has been misinterpreted - if so perhaps some more clarity could be provided.

The numbers are correct but the syntax is currently misleading. It should read:

13% of the patients’ records documented their wound as being clinically infected at the onset of their management in the community. Another 55% of patients were prescribed a systemic anti-infective and/or antimicrobial dressing at this time, suggesting that as many as 68% of all the wounds in our study population may have been considered to be at risk of infection or infected at the time of initial presentation in the community (Table 9). Additionally, 31% of patients with a putative infection had diabetes compared to 18% of patients who did not have an infection; $p<0.005$.

Over the 12 months follow-up period, 18% of patients received only an antimicrobial dressing, indicative of concern about the local bioburden or a possible localised wound infection, and 66% were prescribed a systemic anti-infective. The duration of continuous prescribing of an antimicrobial dressing in the patients’ records was a mean of 4.2 months per patient. However, 28% of patients received continuous prescribing of topical antimicrobials for >6 months, according to documentation in their case record.

The title of Tables 9 and 10 should read

Incidence of putative infection with associated healing and costs over the 12-months follow-up period

Incidence of putative infection with associated healing and costs stratified by planned/emergency procedures over the 12-months follow-up period

Reviewer: 2

Reviewer Name: Sathish Thirunavukkarasu

Institution and Country: Nanyang Technological University, Singapore Please state any competing interests or state ‘None declared’: Non declared

Please leave your comments for the authors below Thank you for addressing my earlier comments. The paper reads well. I only have a few queries requiring explanation.

1. The authors say that they previously identified a random sample of 6000 patients with a wound from the THIN database. Could you please explain how this sample size was determined and for what purpose this random sampling was done? Also, please comment on how far the sample of 707 patients identified from within this cohort is representative of all patients (that would satisfy the eligibility criteria for this study) in the THIN database? The authors had previously obtained a random sample of records of 6000 adult patients with a documented history of a wound for whatever reason from the THIN database, for previous wound studies. The study population of 707 patients was identified within this cohort of 6,000 patients according to the following criteria:

• Were 18 years of age or over.

• Had undergone a surgical procedure either during or after 2012.

• Had a surgical wound which had remained unhealed for 4 weeks after the surgical procedure

• Had at least 12 months continuous medical history in their case record from the first mention of their surgical wound unless it healed.

2. Logistic regression analysis results can be provided in tables for better readability. The authors consider that 10 Tables was sufficient and that the readers would be able to assimilate the information they needed From the text. Editor please advise.