PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	A COHORT STUDY EVALUATING MANAGEMENT OF BURNS IN THE COMMUNITY IN CLINICAL PRACTICE IN THE UK: COSTS AND OUTCOMES
AUTHORS	Guest, Julian F.; Fuller, Graham; Edwards, Jacky

VERSION 1 – REVIEW

REVIEWER	Kamolz Lars-Peter Division of Plastic, Aesthetic and Reconstructive Surgery, Medical University of Graz
REVIEW RETURNED	17-Nov-2019

GENERAL COMMENTS	I think that the Topic is of interest, but there are serious limitations: Burn Details are not mentioned (size, depth,..). Treatment Details are not mentioned. How many of these burn injuries have met the criteria for burn center transfer; this is not mentioned. How is healing time defined? One year is really more than just long? This is not acceptable within Europe!!! The discussion is by far too superficial!

REVIEWER	Jeff Litt University of Missouri USA
REVIEW RETURNED	08-Dec-2019

GENERAL COMMENTS	Overall well written and conceived. I don't personally understand the nature of burn care in the UK, as it seems to me that a wound healing time measured in years is exceptionally long (at least compared to US and my own standards).; more description about the details of this slow healing trajectory would be useful. More specifics about the THIN database, what it is capable of collecting, and why the collected information might be so "spotty" would be useful as an American reader.

REVIEWER	Margriet van Baar ADBC, Rotterdam, the Netherlands
REVIEW RETURNED	13-Dec-2019

GENERAL COMMENTS	General The authors of this paper do fill the paucity of literature on the great volume of burn care in primary and secondary care, in this case in the UK. They use a database and come up with remarkable results on the time to wound healing in these health care settings. The extensive time to wound healing raises concerns on the validity of the results of this project. This is a main issue, which should be addressed before het paper

	can be published. Abstract Please include info on setting and type of patients. Time to wound healing is extreme, please address this already in the conclusion of the abstract Introduction r 57. What negligible evidence is published: which evidence or is it none? Methods Design: please add the specific health care setting in this section. Page 8. R 32 please explain the difference between GP records and community records. R 36-40 necessary?? R 51 Please include reference to earlier work on this cohort What was the final year of patients inclusion? R. 57 How was this criterion checked in the database? Page 9 Does prescription include prescription both in primary and secondary care? Restructure of methods: Data on design of costs analysis and sensitivity analysis should be addressed before the statistical analysis. Are costs of surgery included? Costs data need to be completed with 95%CIs Data are available on both patient and wound level. Which data are used for what analysis. Please clarify in methods and results. The Results Please add flowchart of patient inclusions and exclusion Please present median time to wound healing as well, to delete the influence of outliers. The time to wound healing is extreme. Burn wound are acute wound and wound healing is expected within a few weeks, a few months maximum. So the results are extreme, especially for a database covering primary and secondary care, in which minor burns must be overrepresented. Please check the data. What proportion of wound was healed within 1 month? Also include possible explanations in the discussion. Infection: to analyse the use of antimicrobial agents as a sign of infection is a mistake. These agents are most often applied to prevent any infection, and are not merely in case of any sign of infection. As a result, the labels added to the distinction between antimicrobials used versus are not correct. BMI : The non-significant result is probably the result of a power problem. Please address.

	Discussion: The authors mention burn services (tertiary care) but state that they address primary and secondary care. Is care provided by specialized burn services included or not? Please describe and incorporate this in the manuscript. The main issue is the extreme time to wound healing, which should be discussed. This is not in line with clinical practice and probably related to registration artefacts? The authors do not relate the costs of burn wound with available literature on burn care costs, also outside the UK. Do costs components differ from published cost data? Tables Table 1: please add the number of included patients Please reflect on the findings in t1: data on aetiology is peculiar; categories are not mutually exclusive: small burns versus scalds?? Mean values are normally strongly influenced by outliers. Please present median values as well to gain insight in usual health care patterns in burns in primary and secondary care. T3 This monthly overview is very detailed, If the authors aim to provide a n overview on trends over time, please use a less detailed categorization, for instance per semester. Please add the numbers of patients per time period T 5: suspected infection is an invalid does not reflect the ideas in burn care. These treatments are merely included to prevent infections and not on indication in case of any signs of infection. Figure: Please add the flow chart of inclusion and exclusion of patients.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Kamolz Lars-Peter
Institution and Country: Division of Plastic, Aesthetic and Reconstructive Surgery, Medical University of Graz Please state any competing interests or state 'None declared': No conflict of interest

Please leave your comments for the authors below I think that the Topic is of interest, but there are serious limitations:
• Burn Details are not mentioned (size, depth,..). The study is an analysis of actual clinical practice and is based on data documented in patients' medical records extracted from the THIN database. The lack of documentation pertaining to burn details has been reported in the manuscript and is a reflection of actual clinical practice in the UK.
• Treatment Details are not mentioned. This is not accurate. There is a section on Patient Management in the Results and Tables 2 and 3 describe management and treatment.
• How many of these burn injuries have met the criteria for burn center transfer; this is not mentioned. This study is not a clinical trial or prospective observational study. It is an assessment of the health outcomes, resource use and corresponding costs attributable to managing burns in clinical practice, from initial presentation, in the UK. The criteria for transfer to a burn centre was not mentioned in the

patients’ records. Furthermore, in the UK, burn care is stratified into Centres, Units and Facilities. Criteria for referral are provided in the National Burn Care Referral guidance 2012 which recommends that a patient with greater than 3% total body surface area burn, any full thickness burn and any burn not healed at 2 weeks should be referred. Notwithstanding this, 91% of patients in this study were managed in an outpatient referral centre.
• How is healing time defined? One year is really more than just long? This is not acceptable within Europe!!! The THIN database does not define what a wound is nor does it define wound healing. Wound healing was a clinical observation not necessarily confirmed by a specialist and it is unknown if the clinicians who managed these patients used any consistent definition. The Results Section has been amended accordingly and this is now also addressed in the Discussion.
• The discussion is by far too superficial! The Discussion has been amended to include burn chronicity, but without a definition of ‘superficial’ the Authors are unclear what this Reviewer means.

Reviewer: 2
Reviewer Name: Jeff Litt
Institution and Country: University of Missouri USA Please state any competing interests or state ‘None declared’: None declared

Please leave your comments for the authors below
• Overall well written and conceived. I don't personally understand the nature of burn care in the UK, as it seems to me that a wound healing time measured in years is exceptionally long (at least compared to US and my own standards).; more description about the details of this slow healing trajectory would be useful. More specifics about the THIN database, what it is capable of collecting, and why the collected information might be so "spotty" would be useful as an American reader. More information has been provided on healing and the THIN database. The reason why the collected information is “spotty” is a reflection of the manner in which data is reported in patients’ medical records in clinical practice in the UK and is a cause of great concern. This has been discussed in the manuscript as has the need for more education.

Reviewer: 3
Reviewer Name: Margriet van Baar
Institution and Country: ADBC, Rotterdam, the Netherlands Please state any competing interests or state ‘None declared’: None declared

Please leave your comments for the authors below BMJ Open 2019 – 035345

General
• The authors of this paper do fill the paucity of literature on the great volume of burn care in primary and secondary care, in this case in the UK. They use a database and come up with remarkable results on the time to wound healing in these health care settings. The extensive time to wound healing raises concerns on the validity of the results of this project. This is a main issue, which should be addressed before the paper can be published. This study provides a snapshot and we have no other published data to compare it with. Nevertheless, it raises questions about burn wound chronicity which has never been raised before. The cohort of patents in this study, given their significant number of co-morbidities, might not be a representative sample of burn patients in the UK. However, the times to healing are factual and the article is trying to raise awareness of potential problems in terms of managing this cohort of patients. ‘Burn Wound Chronicity’ is not recognised as a phenomena but this data implies that there is a subset of chronic burn wounds in the UK. The Discussion has been amended accordingly.

Abstract
• Please include info on setting and type of patients. This has been amended accordingly.

• Time to wound healing is extreme, please address this already in the conclusion of the abstract. The Conclusion has been amended accordingly.

Introduction
• r 57. What negligible evidence is published: which evidence or is it none? The text has been amended accordingly.

Methods
• Design: please add the specific health care setting in this section. Design has been amended accordingly.

Page 8.
• R 32 please explain the difference between GP records and community records. The text has been clarified.
• R 36-40 necessary?? We are required to include this information in the manuscript.
• R 51 Please include reference to earlier work on this cohort What was the final year of patients inclusion? This has been amended accordingly.
• R. 57 How was this criterion checked in the database? Criteria were based on Read codes. The text has been amended accordingly.

Page 9
• Does prescription include prescription both in primary and secondary care? GP prescriptions only. The text has been amended accordingly.
• Restructure of methods: Data on design of costs analysis and sensitivity analysis should be addressed before the statistical analysis. With due respect to the Reviewer, the Authors are of the opinion that since the statistical analyses are applied to the clinical outcomes and resource use and not to costs or sensitivity analysis, the current structure should remain.
• Are costs of surgery included? Costs data need to be completed with 95%CIs. The cost of surgical admissions are incorporated in the total cost of patient management as shown in Table 4. The Authors are unclear why CIs would be required for the costs in Table 4?
• Data are available on both patient and wound level. Which data are used for what analysis. Please clarify in methods and results. The Authors are unclear what the Reviewer is referring to. The analysis describes the management of a burn and the text has been clarified in places of ambiguity.

Results
• Please add flowchart of patient inclusions and exclusion Please present median time to wound healing as well, to delete the influence of outliers. This study is not a clinical trial or prospective observational study. It is an assessment of the health outcomes, resource use and corresponding costs attributable to managing a cohort of burns in clinical practice, from initial presentation, in the UK. Hence, all wounds in the cohort were included in the analysis and therefore a flowchart is not appropriate.
• The time to wound healing is extreme. Burn wound are acute wound and wound healing is expected within a few weeks, a few months maximum. So the results are extreme, especially for a database covering primary and secondary care, in which minor burns must be overrepresented. The Manuscript has been amended to address this.
• Please check the data. What proportion of wound was healed within 1 month? 30% healed within 1 month. This has now been included in the text. Also include possible explanations in the discussion. The Discussion has been amended accordingly.
• Infection: to analyse the use of antimicrobial agents as a sign of infection is a mistake. These agents are most often applied to prevent any infection, and are not merely in case of any sign of infection. As a result, the labels added to the distinction between antimicrobials used versus are not correct. The labelling has been amended. However, in the majority of burn units in the UK, antibiotics are not

routinely prophylactically administered to burn patients because of concerns regarding antibiotic resistance, high cost, and the risk of adverse drug effects. However, they are routinely given to patients with burn injuries by either emergency departments or GPs as there is a lack of understanding of the normal inflammatory process of a burn. In this study's cohort, only 21% of all the burns were treated with an antimicrobial dressing at some point during the study's follow-up period. Consequently, the antimicrobial use may have been appropriate, but without adequate assessment of depth, a judgement cannot be made. This has been discussed in the Discussion.
• BMI :The non-significant result is probably the result of a power problem. Please address. This has now been addressed.

Discussion:
• The authors mention burn services (tertiary care) but state that they address primary and secondary care. Is care provided by specialized burn services included or not? Please describe and incorporate this in the manuscript. The patients' records do not distinguish in all cases whether patients were managed by burns or plastics services. Table 2 demonstrates that 91% of all patients were seen in hospital outpatient departments by one or other of these services. However, there is significant variation in the way burns are managed and followed-up by burns services in the UK. Some services will regularly review the patient in their own clinics until the wound is healed, whereas other services will either teach patients to undertake self-care or utilise a shared-care model with either the community nursing team or practice nurses. The Authors were unable to verify from the documented data in the patients' records what model of care was used for each patient and whether they were followed up by specialist services to full healing. The Results and Discussion have been amended accordingly.
• The main issue is the extreme time to wound healing, which should be discussed. This is not in line with clinical practice and probably related to registration artefacts? This is not in line with clinical trial results but is a reflection of actual clinical practice in the UK. The Discussion has been amended accordingly.
• The authors do not relate the costs of burn wound with available literature on burn care costs, also outside the UK. Do costs components differ from published cost data? The Discussion has now been expanded to include this. However, the Authors are unsure of the value or relevance in doing so, since there are no recent publications and comparison with older studies may not be appropriate because of changes in patient management, hospital admission pathways and healthcare resource use over the intervening period coupled with differences in methodological approaches and unit costs. Additionally, it would be inappropriate to compare the total healthcare costs of managing burns across the primary and secondary care sectors in the UK with costs of managing burns in a tertiary burn centre in another country.

Table 1
• Please add the number of included patients This has been added.
• Please reflect on the findings in t1: data on aetiology is peculiar; categories are not mutually exclusive: small burns versus scalds?? This is how the burns are described/documented in the patients' records.
• Mean values are normally strongly influenced by outliers. Please present median values as well to gain insight in usual health care patterns in burns in primary and secondary care. This has been added.

Table 3
• This monthly overview is very detailed, If the authors aim to provide an overview on trends over time, please use a less detailed categorization, for instance per semester. Providing a less detailed categorisation would potentially mislead the reader about the inconsistencies and lack of continuity in dressing use at each change of wound dressing, which occurs every 3-4 days.
• Please add the numbers of patients per time period This would be potentially misleading to the

reader. There are 294 burns in the cohort. In each month a proportion of burns weren't treated with a dressing because their wound had healed. Additionally, other burns were not managed with a dressing(s) at different times, reflecting clinical practice.

Table 5
• Suspected infection is an invalid does not reflect the ideas in burn care. These treatments are merely included to prevent infections and not on indication in case of any signs of infection. The syntax has been amended. However, in the majority of burn units in the UK, antibiotics are not routinely prophylactically administered to burn patients because of concerns regarding antibiotic resistance, high cost, and the risk of adverse drug effects. However, they are routinely given to patients with burn injuries by either emergency departments or GPs as there is a lack of understanding of the normal inflammatory process of a burn. In this study's cohort, only 21% of all the burns were treated with an antimicrobial dressing at some point during the study's follow-up period. Consequently, the antimicrobial use may have been appropriate, but without adequate assessment of depth, a judgement cannot be made. This has been discussed in the Discussion.

Figure:
• Please add the flow chart of inclusion and exclusion of patients. This study is not a clinical trial or prospective observational study. It is an assessment of the health outcomes, resource use and corresponding costs attributable to managing a cohort of burns in clinical practice, from initial presentation, in the UK. Hence, none of the wounds were excluded from the analysis and therefore a flowchart is not appropriate.

VERSION 2 – REVIEW

REVIEWER	Lars Kamolz Medical University Graz, Austria
REVIEW RETURNED	11-Jan-2020

GENERAL COMMENTS	I think that the paper is of interest; for some results the authors have used Mean and Median; Why? I think that the statistician should review the data.

REVIEWER	Margriet van Baar ADBC Netherlands
REVIEW RETURNED	21-Jan-2020

GENERAL COMMENTS	The major limitation is the operationalization of time to wound healing. The idea that the episode of care reflects the time to wound healing is a misconception. Time to wound healing studies in burns, although done in specialized burn care provide a clear description of the actual time to wound healing. The authors present the episodes of care as a proxy for time to wound healing, resulting in extreme time to wound healing. This is a fatal flaw. I suggest to consult an expert in the field of burn care to discuss the issues in this paper.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

I think that the paper is of interest; for some results the authors have used Mean and Median; Why? Another Reviewer suggested we provide median values. We have now removed them as they served no apparent purpose.

Reviewer: 3

The major limitation is the operationalization of time to wound healing. The idea that the episode of care reflects the time to wound healing is a misconception. Time to wound healing studies in burns, although done in specialized burn care provide a clear description of the actual time to wound healing. The authors present the episodes of care as a proxy for time to wound healing, resulting in extreme time to wound healing. This is a fatal flaw. I suggest to consult an expert in the field of burn care to discuss the issues in this paper.

This Reviewer's comments are inaccurate. A wound was only considered healed at the time the managing clinician documented in the patient's record that the wound had actually healed. This had been stated in the Results section, but we have changed the wording to remove any ambiguity. We did not consider an episode of care as a proxy for time to healing. Furthermore, the inverse of what Reviewer 3 is suggesting is that patients continued to receive wound management after their wound had healed and that would not have occurred.

Our study is a reflection of what happened in clinical practice in the real world in the UK and we have addressed the long time to healing in the Discussion. It may be that Reviewer 3 does not have experience of, or appreciate, UK-based largely community delivered burn care services and is looking at our results in isolation from the perspective of time-to-healing studies at specialised burns centres. The healing times in this study are consistent with healing times across a range of different wound types, as referred to in the Discussion.

The notion that our study is 'fatally flawed' is unjustifiable as one of the authors is a leading global health economic expert in the field of wound care for over 20 years and published an extensive list of >200 peer reviewed articles. Another author is a leading global clinical expert in the field of burn care.