

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Exploring geographic variation in acute appendectomy in Ireland: results from a national registry
AUTHORS	Ahmed, O; Mealy, Ken; Sorensen, Jan

VERSION 1 – REVIEW

REVIEWER	Daniel DeUgarte University of California - Los Angeles, United States
REVIEW RETURNED	24-Sep-2018

GENERAL COMMENTS	While the authors provide a well-written manuscript that describes descriptive information about the utilization of laparoscopy for appendicitis in Ireland by county, the content and depth of the study is not of sufficient impact to justify publication in BMJ Open. Perhaps another journal would find it of more interest? In addition, the authors mention in the methods evaluating length of stay and other outcomes. It would be of more interest to confirm that outcomes have improved with adoption of laparoscopy. This might provide more compelling evidence for the need to have surgeons adopt laparoscopy in the county's that have not done so to date.
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REVIEWER	Johanna H. van der Lee Amsterdam UMC the Netherlands
REVIEW RETURNED	08-Oct-2018

GENERAL COMMENTS	<p>In this manuscript a study is presented to evaluate geographical variation in laparoscopic and open appendectomies in Ireland. Considerable variation between counties is observed, which is important information, since it suggests that in some counties the quality of care received by patients may be less than in others. This is an interesting manuscript, but I think that there may be some room for improvement.</p> <p>1. The aim that is reported in the Introduction (to investigate the geographic variation in the surgical management of acute appendicitis in the Republic of Ireland) does not make clear what was the underlying problem why this study was performed, but mainly refers to the methods (... using administrative data from public hospitals). Also the sentences that follow the aim do not show a rationale, but merely state what was done. Could the authors rewrite the aim so that it becomes more clear what is the ultimate goal of this research?</p> <p>2. It would be useful if specific research questions were formulated, from which the information to be retrieved follows</p>
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	<p>logically. Why is information about length of stay and readmissions relevant?</p> <p>3. Counties of residence are used as units for evaluation. I wonder about the rationale for this. To me, it seems more likely that variations exist between hospitals than between counties. What is the ratio of hospitals to counties in Ireland? How much overlap is there between the referral populations of hospitals and counties? Also, it would be interesting to know a little more about the private hospitals, which are excluded. Is the number of private hospitals comparable between counties? Or could part of the variation found between counties be explained by the presence of private hospitals, or their admission policies, in some counties?</p> <p>4. The numbers in this study are large. Therefore, there is sufficient power for detecting even small differences with statistical significance, but the reader does not get a chance to evaluate this when only information such as $p < 0.01$ is given. Most of the results could be presented with 95% confidence intervals, which is much more informative.</p> <p>5. Page 8, line 27. "Online supplementary table 1 shows the proportion of laparoscopic appendectomies per year ...". I suppose this is Table 1 on page 9, where the header is "Rate of laparoscopic procedures". I also suppose the term rate should be replaced by proportion?</p> <p>6. Three different parameters are presented for variability between counties. Why were these three chosen, if no comparison is made between them? It is confusing that in the Methods section it is stated that SCV is "by convention reported as a percentage", whereas in Table 2 CV is described as CV%. How are the random component of the variation and the total variation calculated? Can the authors explain the huge variation in SVC numbers in Table 2, especially in the adult population? Could it be that some calculation error was made?</p> <p>7. In the Discussion variation ratios are presented of 8 and 11 for the laparoscopic and open procedures, respectively, and in children 14 and 6, respectively. It is not clear from what numbers these ratios are calculated. Please explain.</p>
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REVIEWER	esposito ciro University of Naples Federico II
REVIEW RETURNED	16-Jan-2019

GENERAL COMMENTS	very good paper
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REVIEWER	Marco Ceresoli Milano-Bicocca university, Monza, Italy
REVIEW RETURNED	30-Jan-2019

GENERAL COMMENTS	<p>Dear authors</p> <p>this is a very interesting analysis of a large administrative database. However is not so clear the aim of the paper. This is a gooda epidemiological analysis and could give interesting ideas for a not clinical point of view.</p> <p>I cannot understand why should i read this paper: which information wuold you like to give us?</p> <p>It could be interesting to analyze the differences in the rate of appendectomy (with the operative technique) among hospitals, based even on that hospital dimesnion (volume of patients treated)</p>
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	<p>and the county dimension (for a not irish reader the dimensions of counties is not known!).</p> <p>Is there a variability among the rate of negative appendectomies (normal appendix at hystological examination)? these data could be interesting in understanding if the volume could improve the diagnostic accuracy of surgeons.</p> <p>Please, improve it</p>
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REVIEWER	<p>Manish M. Tiwari</p> <p>University of Nebraska Medical Center, USA</p>
REVIEW RETURNED	07-Feb-2019

GENERAL COMMENTS	<p>1. This is a very well-written manuscript. It addresses an important question in the field of appendectomy.</p> <p>2. The authors use statistical analysis to demonstrate geographic variation in appendectomy.</p> <p>3. Observations and conclusions are well-drawn.</p> <p>4. Would recommend statistical review prior to publication.</p> <p>5. Although this is a manuscript of significance, reason for rejection is the authors statement regarding ethics board approval. I would like to know why ethics board approval was not obtained or not felt necessary for this study. Although this is a retrospective analysis, ethics board approval may have been necessary for such a study.</p>
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REVIEWER	<p>Peter Hibbert</p> <p>Australian Institute of Health Innovation, Macquarie University, Australia</p>
REVIEW RETURNED	14-Feb-2019

GENERAL COMMENTS	<p>Thanks for the opportunity to review this paper. This paper is topical in that it adds to the knowledge of variation in surgery rates and, as the authors state, this is the first paper in Ireland on emergency appendectomy rates.</p> <p>The introduction outlines the problem nicely but the aims could be explained a little more clearly.</p> <p>The methods are clear except the explanation of systematic component of variation (SCV). I was unclear on how this is calculated.</p> <p>The results were unclear and take a lot of work by the reader to get their head around them. I got lost at times trying to navigate the different figures and I think this is a combination of the flow of the text and some presentation issues. There is a huge amount of data in the paper, which is not a criticism but it makes the author's job challenging to present it and I do not think that this aspect of the paper has been done well. There are also times when % and proportions are mixed up.</p> <p>The statistics presented in the national analysis would really benefit from a summary table. There is a lot of information presented in these paragraphs and a summary table would help the reader refer back to the underlying results.</p> <p>For the information relating to length of stays and readmissions, standard deviations should also be displayed with the means. If the summary table that I mentioned is presented then the standard deviations can be presented in the table. If the aims of the study are to compare regional variations, why are not these figures presented at county level. There may be an argument for</p>
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	<p>removing these LOS and admission data and focussing the paper just on county rates to make the paper simpler.</p> <p>In summary at national and county level I think there are 2 issues that the authors are trying to demonstrate – firstly the rate of appendectomy (see Figure 5) and second the proportion of laps to open appendectomies (the other figures). However the results seem to oscillate between the two. It would be preferable if these 2 result types are more distinctly separated. The results do seem to demonstrate significant variation both in rates of appendectomy and proportion of laps at county level, however this needs to be presented much more clearly.</p> <p>In the Results second paragraph, the statement is made that “the proportion of patients undergoing lap procedures reduced for older patients” has a more complex answer as this is only true for adults not children as Figure 3 seems to illustrate. Figure 3 doesn’t really help the reader understand this statement.</p> <p>The third paragraph of the results relates to county level data not national and is confusing.</p> <p>The results regarding county data mainly just presents the graphs, it doesn’t help the reader highlight the relevant bits. For example Table 1 is massive with 216 data points, too many for a reader to understand without any direction from the author. Similarly, Figure 4 and 6 are referenced but are not given direction from the authors.</p> <p>I did not understand the results of the EQs and SCVs. The EQs were described in the methods as the ratio of the highest and lowest country rates and results were 1.1 or 1.2. But the tables and the figures seem to suggest greater differences between counties. Similarly the SCV in the methods was described as being high if >5 but in the results it is presented as a % in the text and a number in table 2.</p> <p>After wading through the results to understand them and satisfied that variance between counties does exist, the discussion explores the findings in a satisfactory manner. However of note in the discussion is a statement regarding 8 fold and 11 fold variations in the lap and open rates that is unclear from the statement and the results. Is this related to at county level? The limitations of the study are summarised satisfactorily.</p> <p>The paper also needs a conclusion too to be complete.</p> <p>Minor issue:</p> <p>3rd point strengths and limitations: I think you say “public” when you mean “private” – “does not include data from public institutions...”.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer #1

While the authors provide a well-written manuscript that describes descriptive information about the utilization of laparoscopy for appendicitis in Ireland by county, the content and depth of the study is not of sufficient impact to justify publication in BMJ Open. Perhaps another journal would find it of more interest? In addition, the authors mention in the methods evaluating length of stay and other outcomes. It would be of more interest to confirm that outcomes have improved with adoption of laparoscopy. This might provide more compelling evidence for the need to have surgeons adopt laparoscopy in the county's that have not done so to date.

Thank you kindly for the response. We feel this is an important paper in this era with the growing focus of healthcare access and inequality. This is an area with a large global interest particularly since

the report provided by the Dartmouth Atlas Project. Our paper shows large disparities in access to laparoscopic and open appendectomy rates with county of residence playing a potential role. After considering your comments and those of some of the other reviewers, we have deleted the results of length of stay and readmission to provide a paper focussed solely on geographic variation and access.

Reviewer #2

In this manuscript a study is presented to evaluate geographical variation in laparoscopic and open appendectomies in Ireland. Considerable variation between counties is observed, which is important information, since it suggests that in some counties the quality of care received by patients may be less than in others. This is an interesting manuscript, but I think that there may be some room for improvement.

1. The aim that is reported in the Introduction (to investigate the geographic variation in the surgical management of acute appendicitis in the Republic of Ireland) does not make clear what was the underlying problem why this study was performed, but mainly refers to the methods (... using administrative data from public hospitals). Also the sentences that follow the aim do not show a rationale, but merely state what was done. Could the authors rewrite the aim so that it becomes more clear what is the ultimate goal of this research?
2. It would be useful if specific research questions were formulated, from which the information to be retrieved follows logically. Why is information about length of stay and readmissions relevant?
3. Counties of residence are used as units for evaluation. I wonder about the rationale for this. To me, it seems more likely that variations exist between hospitals than between counties. What is the ratio of hospitals to counties in Ireland? How much overlap is there between the referral populations of hospitals and counties? Also, it would be interesting to know a little more about the private hospitals, which are excluded. Is the number of private hospitals comparable between counties? Or could part of the variation found between counties be explained by the presence of private hospitals, or their admission policies, in some counties?
4. The numbers in this study are large. Therefore, there is sufficient power for detecting even small differences with statistical significance, but the reader does not get a chance to evaluate this when only information such as $p < 0.01$ is given. Most of the results could be presented with 95% confidence intervals, which is much more informative.
5. Page 8, line 27. "Online supplementary table 1 shows the proportion of laparoscopic appendectomies per year ...". I suppose this is Table 1 on page 9, where the header is "Rate of laparoscopic procedures". I also suppose the term rate should be replaced by proportion?
6. Three different parameters are presented for variability between counties. Why were these three chosen, if no comparison is made between them? It is confusing that in the Methods section it is stated that SCV is "by convention reported as a percentage", whereas in Table 2 CV is described as CV%. How are the random component of the variation and the total variation calculated? Can the authors explain the huge variation in SVC numbers in Table 2, especially in the adult population? Could it be that some calculation error was made?
7. In the Discussion variation ratios are presented of 8 and 11 for the laparoscopic and open procedures, respectively, and in children 14 and 6, respectively. It is not clear from what numbers these ratios are calculated. Please explain.

Thank you kindly for your feedback and comments. This critique has been taken into consideration.

1. The introduction has been re-written to clarify the underlying problem of geographic variation and offer context. We also make the aim of the study clearer to engage the reader earlier.
2. We have taken these comments into consideration as some of the other reviewers raised the issue of including length of stay and readmission. This information has been removed from the manuscript.
3. The crux of the study is to analyse geographic variations based on county of residence and not hospitals. This is the method used in other papers on geographic variation in the literature which

are cited in the paper. The aim was to determine if county of residence could potentially play a role in determining a patient's likelihood of undergoing an open or laparoscopic appendectomy. Our results would suggest this is possible. Theoretically, all counties in Ireland have a local general hospital which carries out general acute and elective services. However, patients are free to mobilise between counties and hospitals if they choose, with no restrictions. For this reason, we chose to focus on county of residence to describe an unbiased analysis of geographic and regional variations. Our study includes information on public hospitals only which offer this procedure. We have excluded private hospitals as they are outnumbered by public hospitals where appendectomy procedures mostly take place. The focus is again to shed light on geographic variation between counties in a relatively small country.

4. We have now provided more statistical information to allow the readers to interpret our results.

5. Thank you for this comment. We have amended this whereby Table 1 has now become an online supplementary table and reads "proportion".

6. The three parameters used to describe geographic variation are systematic component of variation (SCV), coefficient of variation (CV) and extremal quotient (EQ). These were chosen to allow for international comparison between other studies which use these parameters as a standard measure of statistical dispersion. We have explained the process and measurements in more detail in the methods section and also in table 2.

7. These ratios were obtained by dividing the lowest and highest rates. Because these figures have been a source of confusion, they have been removed from the manuscript as the statistical measures provide solid scientific evidence of dispersion and these measures are relatable internationally.

Reviewer #3

Thank you for your positive feedback.

Reviewer #4

This is a very interesting analysis of a large administrative database. However, it is not so clear the aim of the paper. This is a good epidemiological analysis and could give interesting ideas for a non-clinical point of view.

I cannot understand why should I read this paper: which information would you like to give us?

It could be interesting to analyze the differences in the rate of appendectomy (with the operative technique) among hospitals, based even on that hospital dimension (volume of patients treated) and the county dimension (for a non-Irish reader the dimensions of counties is not known!).

Is there a variability among the rate of negative appendectomies (normal appendix at histological examination)? these data could be interesting in understanding if the volume could improve the diagnostic accuracy of surgeons.

Please, improve it

Thank you for reviewing our study. The aim has been re-written to introduce the rationale behind our study and provide context for global readers who may not be familiar with the important issue of geographic variation and disparity in access to medical services. The focus of our study is geographic variations based on regions to determine if county of residence may influence the likelihood of undergoing an open versus laparoscopic appendectomy. This topic has not been studied before in an Irish context and can allow for global comparisons to be made. The variability in the rate of negative appendectomies is a very interesting topic and we hope to follow up on several factors after we clarify a true rate of general variability in appendectomy rates nationally. We have made some significant changes to the paper to strengthen its impact and relevance and look forward to your opinions.

Reviewer #5

1. This is a very well-written manuscript. It addresses an important question in the field of appendectomy.
 2. The authors use statistical analysis to demonstrate geographic variation in appendectomy.
 3. Observations and conclusions are well-drawn.
 4. Would recommend statistical review prior to publication.
 5. Although this is a manuscript of significance, reason for rejection is the authors statement regarding ethics board approval. I would like to know why ethics board approval was not obtained or not felt necessary for this study. Although this is a retrospective analysis, ethics board approval may have been necessary for such a study
1. Thank you for reviewing our paper and addressing it's relevance to the field of appendectomy.
 2. We have reviewed the statistics and provide clarification in the methods and statistical analysis section.
 3. We wish to acknowledge Healthcare Pricing Office as the source of HIPE (Hospital In-Patient Enquiry) data which is utilised in NQAIS Clinical. Access to NQAIS is widely available to users of the healthcare profession affiliated with the Royal College of Surgeons. The study was discussed with the Clinical Leads of the National Clinical Programme in Surgery, the NQAIS Clinical Steering Group, the HRC-NCP research group, and the Acute Hospital Division (HSE). The data extracted was anonymous, individual patients, hospitals, institutions and surgeons are not identified. As we use widely accessed and anonymised data to formulate our study, the aforementioned leads and the authors felt there was no breach in patient and institutional confidentiality. Only geographic data is presented and this is also widely accessed from the population census which is cited in the paper.

Reviewer #6

Thanks for the opportunity to review this paper. This paper is topical in that it adds to the knowledge of variation in surgery rates and, as the authors state, this is the first paper in Ireland on emergency appendectomy rates.

The introduction outlines the problem nicely but the aims could be explained a little more clearly. The introduction has been re-written and the aim of the study has been clarified to engage the reader in the relevance of the study.

The methods are clear except the explanation of systematic component of variation (SCV). I was unclear on how this is calculated.

Thank you for this observation. We acknowledge the manuscript was perhaps confusing in some sections and so the methods and statistical analysis section has been re-written and the methods are explained clearer. We now explain how particular calculations were obtained and provide this in the form of a new table 2 with the breakdown of the equations used.

The results were unclear and take a lot of work by the reader to get their head around them. I got lost at times trying to navigate the different figures and I think this is a combination of the flow of the text and some presentation issues. There is a huge amount of data in the paper, which is not a criticism but it makes the author's job challenging to present it and I do not think that this aspect of the paper has been done well. There are also times when % and proportions are mixed up.

The statistics presented in the national analysis would really benefit from a summary table. There is a lot of information presented in these paragraphs and a summary table would help the reader refer back to the underlying results.

Thank you for this observation. The results have been re-written in a much clearer fashion to allow for easier interpretation and navigation around the paper. We have clarified sections where proportion and percentages are mentioned. We also thank you for suggesting a summary table to present the national analysis and this has now been included as Table 1 in the manuscript. The previous table 3 is now table 2 and also now clearer to display the statistical measures of variation that were used and allow for individual reader interpretation.

For the information relating to length of stays and readmissions, standard deviations should also be displayed with the means. If the summary table that I mentioned is presented then the standard deviations can be presented in the table. If the aims of the study are to compare regional variations, why are not these figures presented at county level. There may be an argument for removing these LOS and admission data and focussing the paper just on county rates to make the paper simpler. We have removed LOS and readmission rates data to focus the paper more on the observational geographical disparity aspect of the paper. Some of the other reviewers also suggested removing this data and we now feel the manuscript is much clearer.

In summary at national and county level I think there are 2 issues that the authors are trying to demonstrate – firstly the rate of appendectomy (see Figure 5) and second the proportion of laps to open appendectomies (the other figures). However the results seem to oscillate between the two. It would be preferable if these 2 result types are more distinctly separated. The results do seem to demonstrate significant variation both in rates of appendectomy and proportion of laps at county level, however this needs to be presented much more clearly.

Figure 2 and Figure 5 have been explained in a clearer fashion in the text.

In the Results second paragraph, the statement is made that “the proportion of patients undergoing lap procedures reduced for older patients” has a more complex answer as this is only true for adults not children as Figure 3 seems to illustrate. Figure 3 doesn't really help the reader understand this statement.

Figure 3 has been removed as it was felt it did not contribute significantly to the study. The previous figure 4 is now figure 3, figure 5 has become figure 4 and figure 6 has become figure 5.

The third paragraph of the results relates to county level data not national and is confusing.

The results regarding county data mainly just presents the graphs, it doesn't help the reader highlight the relevant bits. For example Table 1 is massive with 216 data points, too many for a reader to understand without any direction from the author. Similarly, Figure 4 and 6 are referenced but are not given direction from the authors.

Thank you for this point. We acknowledge that Table 1 is very extensive. It is being provided as an online supplementary material to allow readers to assess the raw data. The aforementioned figures have now been explained and expanded on to guide the reader and provide clarity.

I did not understand the results of the EQs and SCVs. The EQs were described in the methods as the ratio of the highest and lowest country rates and results were 1.1 or 1.2. But the tables and the figures seem to suggest greater differences between counties. Similarly the SCV in the methods was described as being high if >5 but in the results it is presented as a % in the text and a number in table

2.

The statistical analysis section has been expanded on and the measures are explained in more detail. This section in the results is explained clearer now and we have provided an amended Table 2 further describing the ratios and statistics used.

After wading through the results to understand them and satisfied that variance between counties does exist, the discussion explores the findings in a satisfactory manner. However of note in the discussion is a statement regarding 8 fold and 11 fold variations in the lap and open rates that is unclear from the statement and the results. Is this related to at county level? The limitations of the study are summarised satisfactorily.

The statement regarding 8 and 11 fold variations has been removed as it was deemed confusing and problematic by a number of reviewers.

The paper also needs a conclusion too to be complete.

A conclusion has now been provided.

Minor issue:

3rd point strengths and limitations: I think you say “public” when you mean “private” – “does not include data from public institutions...”.

This has been corrected.

We wish to thank the editors and reviewers extensively for allowing the manuscript to be re-submitted for further review. We hope that all the reviewers' concerns have now been addressed and look forward to hearing from you.

VERSION 2 – REVIEW

REVIEWER	Johanna H. van der Lee Amsterdam UMC the Netherlands
REVIEW RETURNED	09-Apr-2019

GENERAL COMMENTS	<ol style="list-style-type: none"> 1. Why has the title been changed? The study design is not that of a cohort study, so I disagree with the addition “a cohort study”. 2. Page 5. I would prefer ‘persons’ instead of ‘cases’. 3. Why have numbers changed in the abstract? New version “23,684 appendectomies were included. 77.6% (n= 18,387)” versus old version “24,522 appendectomies were included. 77.9% (n= 19,103)” 4. Numbers are confusing. “A total of 26,760 episodes of care discharged through January 1st 2014 to December 31st 2017 were extracted. In this sample 2,260 episodes were coded with diagnoses other than K35-K37; 1047 episodes were coded as non-emergency admissions; 341 episodes related to non-Ireland residents. After exclusion of these episodes, our study sample included 23,684 episodes of care” If I subtract 2,260, 1047 and 341 from 26,760, the result is 23,112, not 23,684. Please explain. 5. Percentages in Table 1 need to be recalculated. They do not add up to 100%. 6. Not highlighted, but changed numbers are also “percentage of laparoscopic procedures was 52.5% among children and 88.9% among adults” (new version) versus “proportion of laparoscopic procedures was 59.0% among children and 89.4% among adults”. Please explain. 7. “A clear age gradient was observed for the whole population and for men and women separately (trend $p < 0.01$). The proportion of patients undergoing laparoscopic procedures reduced for older patients (logistic regression $p < 0.01$) and appears statistically lower for patients older than 45 years ($p < 0.01$).” It is not clear on what data this information is based nor what statistical methods were used. 8. The text below “Conclusion” is not a conclusion based on the results, but some general statements 9. Although the authors did take many of the reviewers' comments seriously, the fact that numbers have changed without explanation between the first version and this first revision do not enhance my confidence in the results of this study. Actually, I stopped reading because not all changes were highlighted, in particular changes in numbers, even after a specific request to the authors to do so. I am not happy with the amount of time the reviewers need to invest when the authors are so sloppy.
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REVIEWER	Peter Hibbert Australian Institute of Health Innovation Macquarie University Australia
REVIEW RETURNED	24-Mar-2019

GENERAL COMMENTS	<p>Thanks for making the changes to the manuscript, it is much simpler, clearer and improved.</p> <p>Some minor points: in the methods, when describing the CV and SCV, you say what a "large" score indicates ie increased variability. If it is possible, can you tell the reader what is a "large" or a "small" score? I understand this may not be possible.</p> <p>In table 1, the % for male children open appendectomy should be 50.8% not as stated 45.4%</p> <p>The sentence before the heading "County Analysis" should come after the heading. Also, can you add in the the mean and medians for these numbers please?</p> <p>Abstract: "principle" should be "principal".</p> <p>In the results, you have correctly displayed the results for the measures of variation. However, given the readership are unlikely to understand what they mean, consider re-wording such that some interpretation is shown.</p> <p>Finally, a request: the figures did not have figures numbers on them, could these be included for these manuscript reviews please?</p>
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VERSION 2 – AUTHOR RESPONSE

Reviewer #1

Thanks for making the changes to the manuscript, it is much simpler, clearer and improved.

Some minor points: in the methods, when describing the CV and SCV, you say what a "large" score indicates ie increased variability. If it is possible, can you tell the reader what is a "large" or a "small" score? I understand this may not be possible.

This has been developed further in the methods section and the relevant references (McPhearson et al 1982; Chassin et al 1986 have been added).

In table 1, the % for male children open appendectomy should be 50.8% not as stated 45.4%

The table figures have been changed as they were deemed confusing. The original percentages reflected the procedure type within a gender eg: $2068 / 2068 + 2140 \times 100$ etc . This calculation has been changed to display the results in a better format which is readable and easily understood by the reader i.e $2068 / 7343 \times 100$ etc.

The sentence before the heading "County Analysis" should come after the heading. Also, can you add in the the mean and medians for these numbers please?

The sentence in question was part of the previous paragraph. However due to formatting of the manuscript appeared on a separate page above the "County analysis" discussion. It has now been included in that section of the manuscript. The mean and median values were purposely excluded from the manuscript to focus the study on the rates of variations and the statistical measures of dispersion. Our methods and illustration of the results are in line with the methods of several studies on geographic variations.

Abstract: "principle" should be "principal".

This has been changed.

In the results, you have correctly displayed the results for the measures of variation. However, given the readership are unlikely to understand what they mean, consider re-wording such that some interpretation is shown.

We have expanded on this in the methods and results section.

Finally, a request: the figures did not have figures numbers on them, could these be included for these manuscript reviews please?

The numbers were included in the file name. Apologies for this. This is now done on the figures themselves.

Reviewer #2

Why has the title been changed? The study design is not that of a cohort study, so I disagree with the addition "a cohort study".

A study design was added as per the recommendations of the previous reviewers in keeping with BMJ Open guidelines "The article title should include the research question and the study design". Our methods reflect those of an observational study and it was felt that a cohort study was best suited as the study design. A cohort study perhaps does not describe the manuscript effectively as per your review. This can be changed to "an observational study" at the pre publication stage.

2. Page 5. I would prefer 'persons' instead of 'cases'.

This has been done.

3. Why have numbers changed in the abstract? New version "23,684 appendectomies were included. 77.6% (n= 18,387)" versus old version "24,522 appendectomies were included. 77.9% (n= 19,103)"

The data was revised again the same calculations were applied. The calculations were separately repeated by each individual author to ensure accuracy. Supplementary material and calculations are included to allow the reader to also revise these.

4. Numbers are confusing. "A total of 26,760 episodes of care discharged through January 1st 2014 to December 31st 2017 were extracted. In this sample 2,260 episodes were coded with diagnoses other than K35-K37; 1047 episodes were coded as non-emergency admissions; 341 episodes related to non-Ireland residents. After exclusion of these episodes, our study sample included 23,684 episodes of care" If I subtract 2,260, 1047 and 341 from 26,760, the result is 23,112, not 23,684. Please explain.

We apologise for this error. The calculations were repeated, and the numbers were corrected. This has been revised multiple times by each author to ensure reliability of the results. The degree of variations is unchanged and the statistically significant findings also remain the same.

5. Percentages in Table 1 need to be recalculated. They do not add up to 100%.

The original percentages reflected the procedure type within a gender eg: $2068 / (2068 + 2140) \times 100$ etc. This calculation has been changed to display the results in a better format which is readable and easily understood by the reader i.e. $2068 / 7343 \times 100$ etc.

6. Not highlighted, but changed numbers are also "percentage of laparoscopic procedures was 52.5% among children and 88.9% among adults" (new version) versus "proportion of laparoscopic procedures was 59.0% among children and 89.4% among adults". Please explain.

Apologies for not highlighting this in the resubmission. Percentages had been changed to proportion on the advice of a reviewer from the previous submission. This has now been highlighted.

7. "A clear age gradient was observed for the whole population and for men and women separately (trend $p < 0.01$). The proportion of patients undergoing laparoscopic procedures reduced for older patients (logistic regression $p < 0.01$) and appears statistically lower for patients older than 45 years ($p < 0.01$). It is not clear on what data this information is based nor what statistical methods were used.

This result was based on the open and laparoscopic appendectomy rates. The sentences has been reformatted and reads much clearer now. This has been highlighted.

8. The text below “Conclusion” is not a conclusion based on the results, but some general statements

The conclusion has been reformatted and amended to reflect the implications of the results if the study and the focus of future studies on this topic.

9. Although the authors did take many of the reviewers’ comments seriously, the fact that numbers have changed without explanation between the first version and this first revision do not enhance my confidence in the results of this study. Actually, I stopped reading because not all changes were highlighted, in particular changes in numbers, even after a specific request to the authors to do so. I am not happy with the amount of time the reviewers need to invest when the authors are so sloppy.

Thank you for your critique of our paper and for allowing us to strengthen the manuscript in order to engage more readers and effectively communicate our message. We feel this is an important paper in this era with the growing focus of healthcare access and inequality. This is an area with a large global interest particularly since the report provided by the Dartmouth Atlas Project. Our paper shows large disparities in access to laparoscopic and open appendectomy rates with county of residence playing a potential role.

We wish to thank the editors and reviewers extensively for allowing the manuscript to be re-submitted once more for further review. We hope that all the reviewers’ concerns have now been addressed and look forward to hearing from you.

VERSION 3 – REVIEW

REVIEWER	J.H. van der Lee Amsterdam UMC, the Netherlands
REVIEW RETURNED	04-Jul-2019
GENERAL COMMENTS	<p>Thank you for the changes made in response to my grumpy comments. There are still some minor issues I would like to mention (again).</p> <p>1. This is definitely NOT a cohort study. Please change the title to observational study, study of administrative files or something like that.</p> <p>2. The precentages in Table 1 are now almost more confusing than they were before. It turns out there was only one wrong percentage in the former table (the 45.4% open appendectomies in boys). Please return to the former version and give percentages that add up to 100 per row.</p> <p>3. Could you please give data, either in a table or a figure, underlying the conclusion about the age gradiënt? I don't see any information about age per group. I would expect this in Table 1.</p> <p>Thank you!</p>

VERSION 3 – AUTHOR RESPONSE

Reviewer #2

Thank you for the changes made in response to my grumpy comments. There are still some minor issues I would like to mention (again).

1. This is definitely NOT a cohort study. Please change the title to observational study, study of administrative files or something like that.
2. The percentages in Table 1 are now almost more confusing than they were before. It turns out there was only one wrong percentage in the former table (the 45.4% open appendectomies in boys). Please return to the former version and give percentages that add up to 100 per row.
3. Could you please give data, either in a table or a figure, underlying the conclusion about the age gradient? I don't see any information about age per group. I would expect this in Table 1.

Thank you!

1. The title has been changed to "Exploring geographic variation in acute appendectomy in Ireland: results from a national registry"
2. The percentages in table 1 have been changed back to the original submission. However, an extra column "total" has been added to "add up" the total percentage to 100% on each horizontal row. In the previous submission, the total percentage was representing the total of all the rows. We hope this is now clearer.
3. A new "Figure 2" has been added to explain the age and gender distributions and the odds ratio calculated to further define the analysis. All other figures have been updated i.e the original figure 2 is now figure 3, figure 3 is now figure 4 etc.

Thank you for reviewing our paper and for allowing us to strengthen the manuscript in order to engage more readers and effectively communicate our message. We hope that all the reviewers' concerns have now been addressed and look forward to hearing from you.