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Exploring variation in acute appendectomy in Ireland

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Complete List of Authors:	Ahmed, O; Wexford General Hospital, General Surgery Mealy, Ken; Wexford General Hospital, General and Colorectal Surgery Sorensen, Jan ; Royal College of Surgeons Ireland, Health Outcomes Research Centre
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Exploring geographic variation in acute appendectomy in Ireland

Authors:

Ola Ahmed, Ken Mealy, Jan Sorensen

1. Department of General Surgery, Wexford General Hospital, Wexford, Ireland

   Ms Ola Ahmed

   Trainee Surgeon

2. National Clinical Programme in Surgery, Royal College of Surgeons in Ireland, Dublin 2, Ireland; Department of General Surgery, Wexford General Hospital, Wexford, Ireland

   Mr Ken Mealy

   Consultant Surgeon

3. Healthcare Outcomes Research Centre, Royal College of Surgeons in Ireland, Dublin 2, Ireland

   Professor Jan Sorensen

   Director of the Healthcare Outcomes Research Centre

Correspondence to: Ms Ola Ahmed, Department of General Surgery, Wexford General Hospital, Wexford, Ireland

Email: olasdahmed@gmail.com

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Strengths and limitations of this study

- The study employed a large, well-defined population of the Republic of Ireland.
- All data was age and gender standardised as is seen in other publications analysing geographical variation in healthcare, including the Dartmouth Atlas Project.
- The study does not include data from public institutions, however acute appendicitis is largely managed in public hospitals regardless of medical insurance cover.
- Co-morbidities, procedural complexity and socioeconomic status were also not controlled for when assessing patient characteristics.
- Future studies should expand on this study design and additional examination of regional and local variations perhaps in a risk adjusted setting should be a priority.

Abstract

Objective To explore geographic variations in Irish laparoscopic and open appendectomy procedures.

Design Analysis based on 2014-2017 administrative hospital data from public hospitals.

Setting Counties of the Republic of Ireland.

Participants Irish residents with a hospital admission for an appendectomy as the principle procedure.

Main outcome measures Age and gender standardised laparoscopic and open appendectomy rates for 26 counties. Geographic variation measured with the extremal quotient (EQ), coefficient of variation (CV) and the systematic component of variation (SCV).

Results 24,522 appendectomies were included. 77.9% (n= 19,103) were performed laparoscopically. An 8-fold variation was seen for laparoscopy and an 11-fold variation for the open approach when the area with the highest and lowest rate were compared. An EQ of 1.1 for laparoscopy and 1.2 for open appendectomy was determined. A high CV was demonstrated with a value of 2.9 and 4.0 for laparoscopic and open appendectomy across counties. A SCV of 14.5% and 113.6% for laparoscopic and open appendectomy was observed. A wider variation was determined when children and adults were assessed separately.

Conclusions The geographic distribution in the utility of appendectomy varies considerably across Irish counties. Our data suggests that a patient's likelihood of undergoing a laparoscopic or open appendectomy may be associated with their county of residence.

Introduction

Acute appendicitis continues to be a global disease with escalating incidence rates in rapidly developing and industrialised countries[1]. These epidemiological associations contribute to the growing knowledge on the pathogenesis of acute appendicitis and the influences of environmental triggers[2, 3]. Modern advances in laparoscopic surgery over the past two decades have led to the demonstrable advantage of laparoscopic appendectomy over open techniques across all populations[4-6]. Laparoscopy is associated with shorter hospital length of stay, decreased analgesic requirements, and lower morbidity rates in comparison with open surgery[4, 7, 8]. However, while laparoscopic approaches are preferred in most instances, open appendectomy is still practiced in cases where laparoscopy is difficult or contraindicated.

Reasons for the regional variability of laparoscopic and open appendectomy are still unclear. The observed rates of open appendectomy vary widely in the literature from 6 – 35% with higher variation in the adult population[9-11]. Recent studies of geographic variation appear to demonstrate that a patient's likelihood of undergoing specific surgical procedures depends greatly on where they live[12]. The Dartmouth Atlas Project has shown wide variations of up to 10-fold for a multitude of surgical procedures across geographical areas[13]. Analysing regional variations in the provision of common procedures helps raise questions relating to service provision as well as identify opportunities for improving efficiency and observing best practice. The aim of this study was to investigate the geographic variation in the surgical management of acute appendicitis in the Republic of Ireland using administrative data from public hospitals. We compare the national data of laparoscopic and open appendectomy for children and adults. By analysing and comparing the patterns of utilisation in these two populations, we seek to understand the extent that area of residence may influence the likelihood of treatment with either a laparoscopic or open procedure.

Methods

Data extraction

Anonymised patient data were obtained for a 4-year period from 2014 to 2017 from the National Quality Assurance and Improvement System (NQAIS). NQAIS is an online application based on the Hospital Inpatient Enquiry system (HIPE) operated by the national Health Service Executive in Ireland. Established in 1971, HIPE collects clinical and administrative data on discharges from acute Irish public hospitals. A HIPE record is created following a patient's discharge from hospital and offers demographic and clinical information for the episode of care. We extracted records of all hospital episodes coded with laparoscopic appendectomy or open appendectomy as the primary procedure. From this sample we excluded episodes with primary diagnostic codes different from "Appendicitis", "Suspected appendicitis", or "Rule-out appendicitis" (codes K35-37 in the International Classification of Diseases Version 10 Clinical Modification (ICD-10-CM)), episodes coded as non-emergency admissions, and episodes for patients who are not residents in Ireland. Patients treated in private institutions were also not included in the study.

Patient factors considered in the analysis were age, gender, county of residence, length of stay and readmissions after 7 and 30 days. Children were categorized as patients aged 14 years or younger to correspond with the 5-year age groups in the available census data. National age and gender stratification was derived from the population of 4,761,865 referred to in the 2016-population census[14].

Statistical analysis

Data was analysed using Stata version 15.1 (StataCorp, Texas). Descriptive statistics were recorded for patient characteristics and procedure type. Continuous variables were compared using unpaired t-tests. Association of categorical variables (differences for dichotomous variables between groups) was assessed using the chi-square (X^2) test. Continuous numerical variables were reported as means and standard deviations (SD). Categorical variables were reported as proportions.

To assess relative variability we used methods described by McPhearson and colleagues[15]. The extremal quotient (EQ) is presented as the ratio of the highest and lowest county rate. A value close to 1 indicates low variation in rates across counties. The coefficient of variation (CV) is a measure of relative variability and is calculated as the standard deviation of the county rates divided by the mean of county rates. A large score indicates large variability. The systematic component of variation (SCV) is also a measure of variation. This is the difference between the random component of variation and the total variation and by convention is reported as a percentage. A SCV value greater than 5 indicates large systematic and regional variation[15]. We estimated these variability measures for the whole population and for children and adults separately.

Patient involvement

No patients were involved in setting the research question or the outcome measures, nor were they involved in the developing design or implementation of the study. No patients were asked to advise on interpretation or writing up of results.

Results

National analysis

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; 583 episodes were coded as non-emergency admissions, and 331 episodes related to non-Ireland residents. After exclusion of these episodes, our study sample included 23,684 episodes of care of which 77.6% were laparoscopic appendectomy and 22.4% were open appendectomy. 53.7% of patients were male and the mean age was 25 years (SD 15, range 0-98, median 20).

The proportion of laparoscopic procedures was 59.0% among children and 89.4% among adults (statistically significant difference; chi-squared p<0.01). Figure 1 displays the proportion of appendectomies conducted as laparoscopic procedures for 2014 to 2017 in children and adult patients. Girls were more likely to have laparoscopic procedures than boys (64.6% vs 54.6%, chi-squared p<0.01), and women more likely than men (91.5% vs 87.5%, chi-squared p<0.01). 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). The proportion of laparoscopic procedures increased steadily during the studied years from 2014 to 2017 from 72.7% to 83.3% (trend p<0.01). For children the proportion increased from 51.9% to 66.9%.

Figure 2 displays the number of laparoscopic and open procedures performed on children and adults during the years 2014 to 2017 by county of residency.

The average length of stay for children was 3.0 days, and children with laparoscopic procedures had significantly shorter hospital lengths of stay (0.2 days, t-test p<0.01). The difference for adult patients was larger (3.0 vs 5.0 days, t-test p<0.01) and had a positive age gradient (p<0.01). No

statistical significant difference in average length of stay could be observed over the four years for either children or adults.

The rate of 7 and 30 days readmission was lower for patients treated with laparoscopic procedures compared to open appendectomy (7-day readmissions: 2.9% vs 3.9%, chi-squared p<0.01) (30-day readmissions: 5.4% vs 6.9%, chi-squared p<0.01). However, the difference was statistically insignificant (but with the same direction) for children and significantly larger for adults (2.8% vs 5.2% chi-squared p<0.01; 5.3% vs 7.9% p<0.01). No differences in yearly readmission rates could be observed over the four years.

County analysis

The annual appendectomy rate was estimated at 124.3 procedures per 100,000 persons and 96.5 and 27.8 for laparoscopic and open approaches respectively. Figure 3 demonstrates the gender stratified national annual appendectomy rates per 100,000 persons by 5-year age groups. Online supplementary table 1 shows the proportion of laparoscopic appendectomies per year by county of residence for child and adult population.

Table 1

Rate of laparoscopic procedures								
	Children				Adults			
County	**2014**	**2015**	**2016**	**2017**	**2014**	**2015**	**2016**	**2017**
Carlow	0.74	0.91	0.84	0.90	0.90	0.98	0.96	1.0
Cavan	0.11	0.14	0.08	0.13	0.22	0.51	0.44	0.5
Clare	0.56	0.43	0.59	0.65	0.90	0.94	0.88	0.97
Cork	0.65	0.76	0.8	0.87	0.93	0.96	0.97	0.95
Donegal	0.25	0.46	0.77	0.89	0.54	0.73	0.78	0.86
Dublin	0.44	0.42	0.54	0.64	0.93	0.96	0.96	0.96
Galway	0.39	0.41	0.38	0.47	0.86	0.89	0.89	0.90
Kerry	0.46	0.66	0.71	0.60	0.80	0.85	0.92	0.90
Kildare	0.49	0.62	0.64	0.56	0.97	0.97	0.98	0.98
Kilkenny	0.75	0.84	0.82	0.89	0.89	0.93	0.95	0.99
Laois	0.47	0.45	0.64	0.81	0.80	0.78	0.79	0.96
Leitrim	0.14	0.27	0.11	0.22	0.27	0.15	0.33	0.46
Limerick	0.44	0.50	0.54	0.70	0.89	0.93	0.90	0.95
Longford	0.70	0.97	0.90	0.93	0.90	0.93	0.92	0.92
Louth	0.66	0.61	0.78	0.77	0.96	0.97	0.93	0.96
Mayo	0.73	0.83	0.78	0.79	0.94	0.94	0.98	0.94
Meath	0.59	0.61	0.74	0.75	0.89	0.91	0.94	0.93
Monaghan	0.35	0.30	0.33	0.41	0.59	0.51	0.77	0.51
Offaly	0.65	0.78	0.83	0.78	0.94	0.98	1.00	0.95
Roscommon	0.42	0.39	0.50	0.47	0.69	0.68	0.75	0.865
Sligo	0.12	0.1	0.09	0.19	0.18	0.19	0.20	0.19
Tipperary	0.63	0.68	0.60	0.60	0.94	0.98	0.98	0.98
Waterford	0.75	0.80	0.77	0.74	0.92	0.94	0.98	0.96
Westmeath	0.86	0.84	0.92	0.92	0.89	0.96	0.96	0.97
Wexford	0.25	0.19	0.53	0.52	0.68	0.67	0.82	0.93
Wicklow	0.67	0.61	0.50	0.40	0.98	0.90	0.94	0.97

Figure 4 shows the ratio of observed and expected number of appendectomies in different counties for children and adults. The expected number of procedures was estimated by relating the national age and gender procedure rate to the county population. The ratio takes a value larger than one when the numbers of observed procedures are higher than the expected number of procedures.

Figure 5 presents the association between the ratio of observed and expected procedures for children and adults. Counties in the North-East quadrant have higher than expected number of procedures for both children and adults. Counties in the South-West quadrant have lower than expected number of procedures for both children and adults. There appears to be a strong association between the ratio for children and adults indicating that counties with a higher than expected ratio for children also have a higher ratio for adults. Only four counties have a different pattern. Roscommon is the only county where children have more than the expected episodes of care and adults have fewer than the expected episodes of care, while the reverse appears for Kilkenny, Waterford, Donegal and Kildare.

Figure 6 displays the ratio of observed and expected procedures for laparoscopic and open procedures for children and adults separately.

Table 2 reports the measures of variation for the whole population and children and adults separately (available as online supplementary table). The extremal quotient was 1.1 for laparoscopic and 1.2 for open appendectomy. The coefficient of variation was high for both laparoscopic and open appendectomy; 2.9 for laparoscopy and 4 for open procedures, in accordance with the McPhearson calculations. The systematic component of variation was also high for both procedures; 14.5% for laparoscopy and 113.6% for open appendectomy.

Table 2

Whole Population			
	Laparoscopy	**Open**	**Combined**
EQ	1.14	1.19	1.23
CV%	3.29	4.37	3.09
SCV	14.09	119.61	5.40
Children			
	Laparoscopy	**Open**	**Combined**
EQ	1.1	1.06	1.08
CV%	2.17	1.60	1.67
SCV	37.88	36.40	8.39
Adult			
	Laparoscopy	**Open**	**Combined**
EQ	1.19	1.11	1.18
CV%	4.59	2.54	4.35
SCV	9.91	500.49	4.42

Discussion

This study documents a substantial geographic variation in the operative management of acute appendicitis in the Republic of Ireland. To our knowledge, there have been no population-based studies exploring emergency appendectomy variations at a county level in Ireland. While some level of disparity is to be expected, large variations particularly in emergency interventions can indicate potential inequity and inefficiency in the use of sophisticated healthcare and thus illustrate variations in access and use of surgical services. In keeping with the Dartmouth Atlas project, our data demonstrates that a person's likelihood of undergoing a laparoscopic or open appendectomy may be related to their county of residence[13].

Laparoscopic appendectomy is favoured because of its benefits in analgesic requirements post - operatively, shorter length of hospital stay, lower post-operative mortality, and faster return to normal activities[4, 7, 8, 16, 17]. Unsurprisingly, most of the cases in our data were performed laparoscopically. Overall, an 8-fold variation exists for laparoscopic surgery while an 11-fold variation was seen for the open procedure. As with most observational data, causality cannot always be determined. Historical research suggests that the variations in the utility of surgical services may result from clinical uncertainty or heterogeneity in medical literature[18, 19]. One potential hypothetical and important reason for the demonstrated variations is individual surgeon skill and practice. The current study did not control for specific surgeon factors and may reflect a lack of laparoscopic skills in certain areas. Variations in laparoscopic surgery rates are not unheard of. An analyses by Doumouras et al suggested that laparoscopic training may influence the rate of laparoscopic practices in some hospitals[20]. While our study did not evaluate larger teaching hospitals separately, there may be an inherent geographic variation in laparoscopic expertise outside of tertiary referral centres and may also reflect variation in consultant and trainee surgeon performance as the principle operator; a factor not examined in this study.

In this study laparoscopy also appears lower in children and may reflect a deficiency in the paediatric surgery skillset available in the country and an unfamiliarity in operating on children amongst

general surgeons. Multiple reports have stressed the need to provide high quality paediatric surgery services to address the challenges and demands of paediatric patients which may be unavailable in hospitals were adult surgery appears to dominate. This would parallel with the reality that most district or general hospitals in Ireland lack a specialised paediatric surgeon on site and thus cases are performed by adult surgeons. Our study reports a 14-fold variation in paediatric laparoscopic appendectomy and an almost 6-fold variation in open surgery. These findings suggest a potential difference in expertise in relation to paediatric surgery in Ireland.

There are some limitations to this study. As with other studies including data from administrative databases, the reliability of results is based on the accuracy and completeness of systematic coding and data input. We attempt to overcome potential miscoding information by including a large population cohort of patients over a four-year period. We have not accounted for laparoscopic cases that were converted to open due to the potential inclusion of duplicate numbers and inherent miscoding errors. Co-morbidities, procedural complexity and socioeconomic status were also not controlled for when assessing patient characteristics. However, despite these limitations our findings demonstrate concerning conclusions relating to the provision of emergency appendectomy in the Republic of Ireland for the paediatric and adult population. The analysis provides some important implications for health care providers and surgeons in analysing the extent of geographic variation and the disparity in management of a common condition. While we cannot explain the wide variations seen, further analysis at an individual county level with the assessment of more in-depth patient characteristics may uncover opportunities to eliminate variations and ultimately improve delivery of care and patient outcomes. We also await the results of the multi-institutional Right Iliac Fossa Treatment (RIFT audit) study to further analyse the variation in management strategies of patients presenting with RIF pain to centres across the United Kingdom, Ireland, Italy, Portugal and Spain[21].

Contributors: OA conceived and designed the study, analysed the data and drafted and revised the paper. JS designed the study, prepared and analysed the data, drafted and revised the paper. KM interpreted the results and revised the paper. All authors had full access to all the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. OA is the guarantor and affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as originally planned (and, if relevant, registered) have been explained.

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Competing interests: All authors declare no conflicts in interests in the preparation of this study and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Ethical approval: Ethics board approval was not required for the study.

Data sharing: All data has been included either in the main manuscript or as a supplementary file. The authors do not withhold any other data.

References

1. Ferris M, Quan S, Kaplan BS, Molodecky N, Ball CG, Chernoff GW, Bhala N, Ghosh S, Dixon E, Ng S. The Global Incidence of Appendicitis: A Systematic Review of Population-based Studies. *Annals of surgery* 2017;**266**(2): 237-241.
2. Kaplan GG, Dixon E, Panaccione R, Fong A, Chen L, Szyszkowicz M, Wheeler A, MacLean A, Buie WD, Leung T. Effect of ambient air pollution on the incidence of appendicitis. *Canadian Medical Association Journal* 2009;**181**(9): 591-597.
3. Kaplan GG, Tanyingoh D, Dixon E, Johnson M, Wheeler AJ, Myers RP, Bertazzon S, Saini V, Madsen K, Ghosh S. Ambient ozone concentrations and the risk of perforated and nonperforated appendicitis: a multicity case-crossover study. *Environmental health perspectives* 2013;**121**(8): 939.
4. Tate JJT, Dawson JW, Chung SCS, Lau WY, Li AKC. Laparoscopic versus open appendicectomy: prospective randomised trial. *The Lancet* 1993;**342**(8872): 633-637.
5. Southgate E, Vousden N, Karthikesalingam A, Markar SR, Black S, Zaidi A. Laparoscopic vs open appendectomy in older patients. *Archives of Surgery* 2012;**147**(6): 557-562.
6. Adwan H, Weerasuriya CK, Endleman P, Barnes A, Stewart L, Justin T. Laparoscopic versus open appendicectomy in children: A UK District General Hospital experience. *Journal of Pediatric Surgery* 2014;**49**(2): 277-279.
7. Thomson J-E, Kruger D, Jann-Kruger C, Kiss A, Omoshoro-Jones J, Luvhengo T, Brand M. Laparoscopic versus open surgery for complicated appendicitis: a randomized controlled trial to prove safety. *Surgical endoscopy* 2015;**29**(7): 2027-2032.
8. Tiwari MM, Reynoso JF, Tsang AW, Oleynikov D. Comparison of outcomes of laparoscopic and open appendectomy in management of uncomplicated and complicated appendicitis. *Annals of surgery* 2011;**254**(6): 927-932.
9. Katsuno G, Nagakari K, Yoshikawa S, Sugiyama K, Fukunaga M. Laparoscopic Appendectomy for Complicated Appendicitis: A Comparison with Open Appendectomy. *World Journal of Surgery* 2009;**33**(2): 208-214.
10. Masoomi H, Mills S, Dolich MO, Ketana N, Carmichael JC, Nguyen NT, Stamos MJ. Comparison of Outcomes of Laparoscopic Versus Open Appendectomy in Adults: Data from the Nationwide Inpatient Sample (NIS), 2006–2008. *Journal of Gastrointestinal Surgery* 2011;**15**(12): 2226-2231.
11. Litz CN, Ciesla DJ, Danielson PD, Chandler NM. Effect of hospital type on the treatment of acute appendicitis in teenagers. *Journal of Pediatric Surgery* 2018;**53**(3): 446-448.
12. Reames BN, Shubeck SP, Birkmeyer JD. Strategies for reducing regional variation in the use of surgery a systematic review. *Annals of surgery* 2014;**259**(4): 616.
13. Practice TDIoHPaC. The Dartmouth Atlas Project Database. 1996 - 2010.
14. Scoreboard MIP. Central Statistics Office statistical release. In: June; 2015.
15. McPherson K, Wennberg JE, Hovind OB, Clifford P. Small-area variations in the use of common surgical procedures: an international comparison of New England, England, and Norway. *New England journal of medicine* 1982;**307**(21): 1310-1314.
16. Sauerland S, Jaschinski T, Neugebauer EAM. Laparoscopic versus open surgery for suspected appendicitis. *Cochrane Database of Systematic Reviews* 2010(10).
17. Faiz O, Clark J, Brown T, Bottle A, Antoniou A, Farrands P, Darzi A, Aylin P. Traditional and laparoscopic appendectomy in adults: outcomes in English NHS hospitals between 1996 and 2006. *Annals of surgery* 2008;**248**(5): 800-806.
18. Ray-Coquard I, Philip T, Lehmann M, Fervers B, Farsi F, Chauvin F. Impact of a clinical guidelines program for breast and colon cancer in a French cancer center. *Jama* 1997;**278**(19): 1591-1595.
19. Wennberg JE. Dealing with medical practice variations: a proposal for action. *Health Affairs* 1984;**3**(2): 6-33.

20. Doumouras AG, Saleh F, Eskicioglu C, Amin N, Cadeddu M, Hong D. Neighborhood variation in the utilization of laparoscopy for the treatment of colon cancer. *Diseases of the Colon & Rectum* 2016;**59**(8): 781-788.

21. Right Iliac Fossa Pain Treatment (RIFT) Study: protocol for an international, multicentre, prospective observational study. *BMJ open* 2018;**8**(1): e017574.

Figure legend:

Figure 1 - Proportion of appendectomies conducted as laparoscopic procedures during 2014-2017 in children and adult patients

Figure 2 – Number of procedures performed during 2014-2017 on county residents

Figure 3 – Crude 4-years rate with laparoscopy and open appendectomy procedures per 100,000 residents

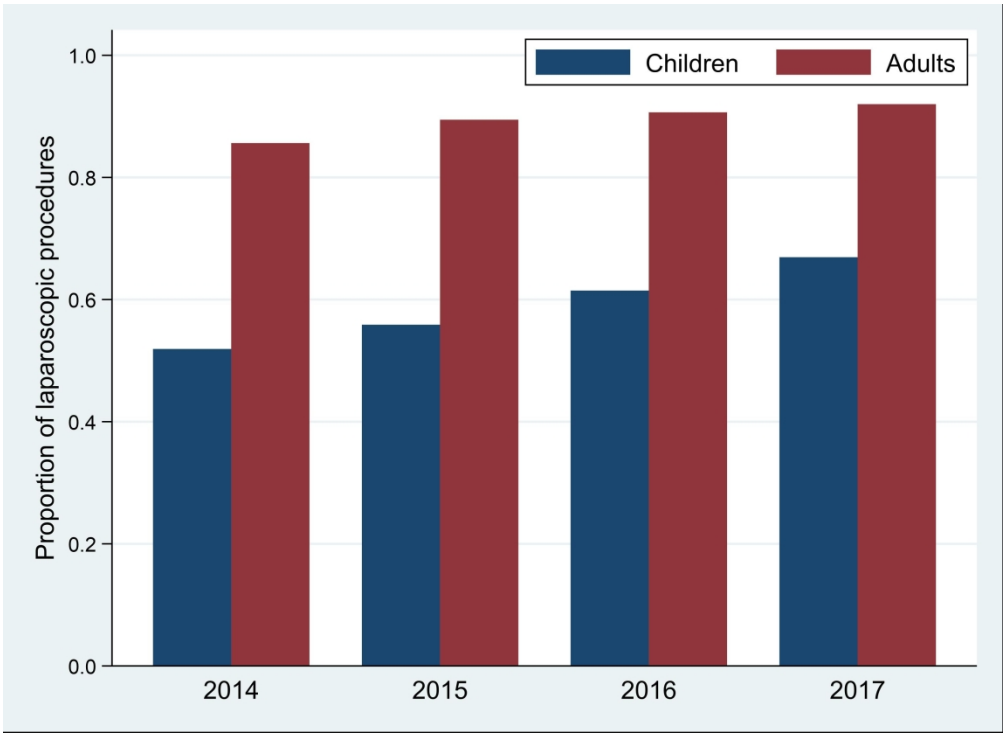
Figure 4 - Ratio of observed/expected number of episodes of appendectomy by county for children and adults

Figure 5 - Association between children and adult's ratio of observed/expected number of episodes of appendectomy by county

Figure 6 - Ratio of observed/expected number of episodes of laparoscopy and open appendectomy by county for children and adults

Table 1 – Proportion of laparoscopic appendectomies per year by county of residence for child and adult population

Table 2 – Variation statistics for the whole population and subpopulations of children and adults



Proportion of appendectomies conducted as laparoscopic procedures during 2014-2017 in children and adult patients

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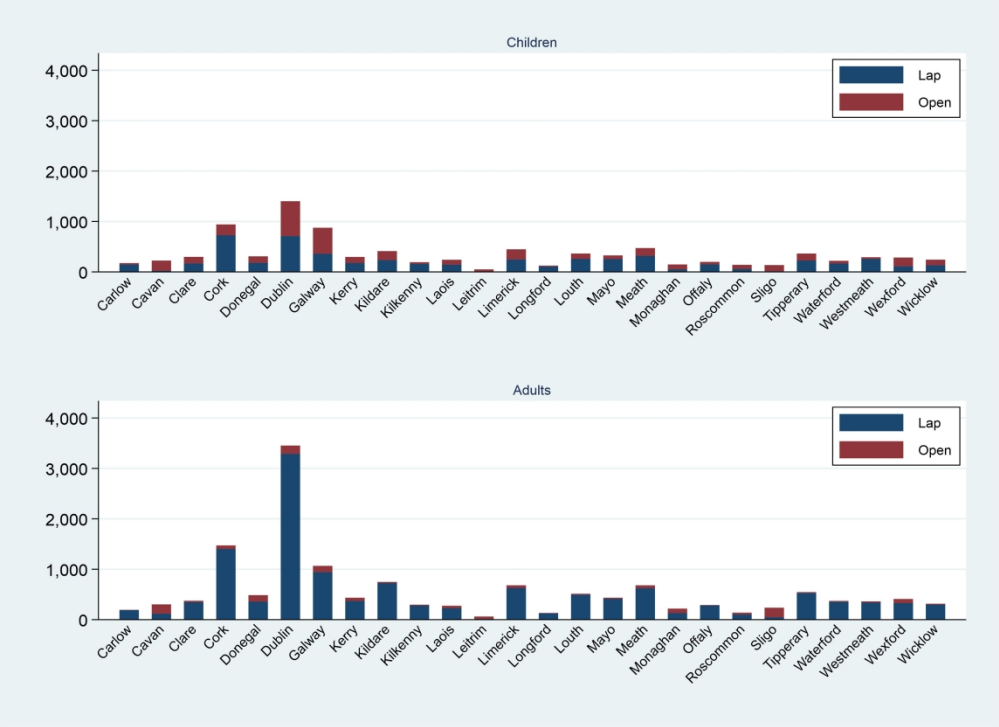

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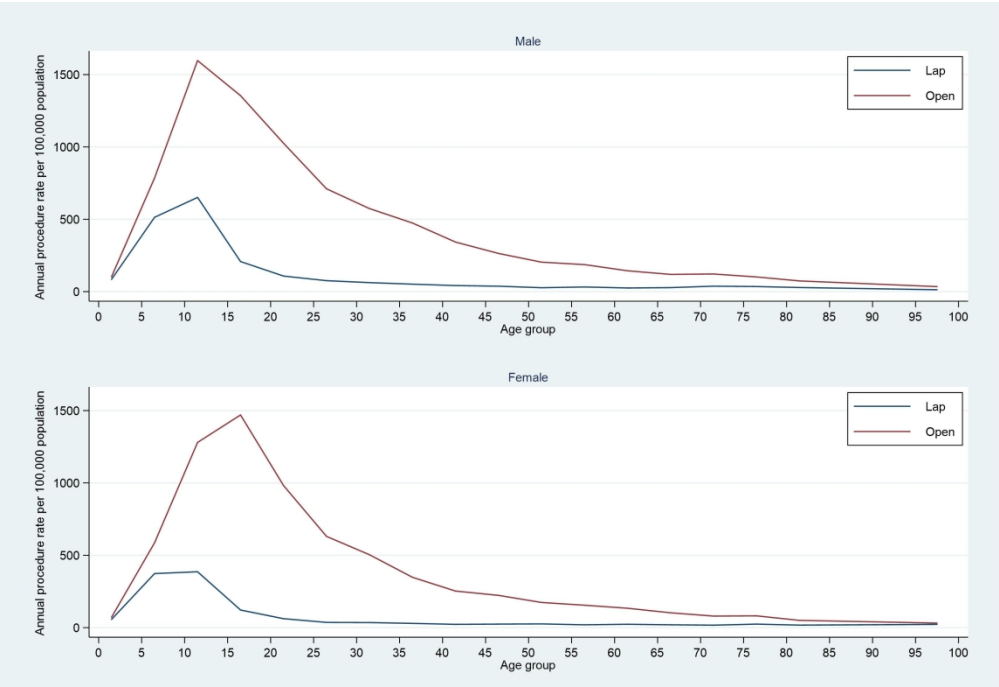

Crude 4-years rate with laparoscopy and open appendectomy procedures per 100,000 residents

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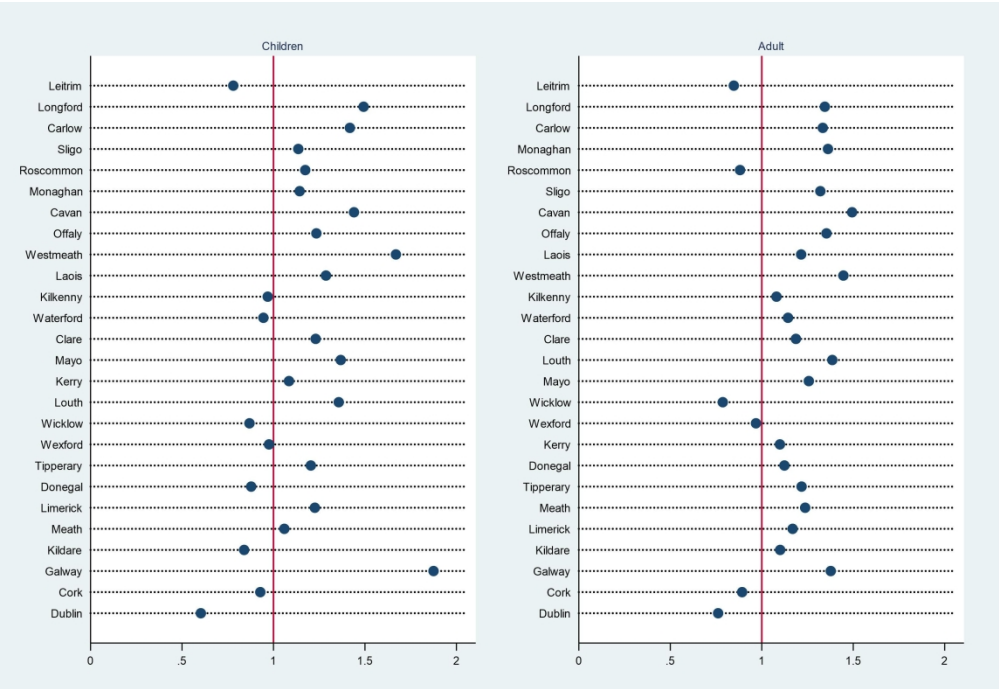

Ratio of observed/expected number of episodes of appendectomy by county for children and adults

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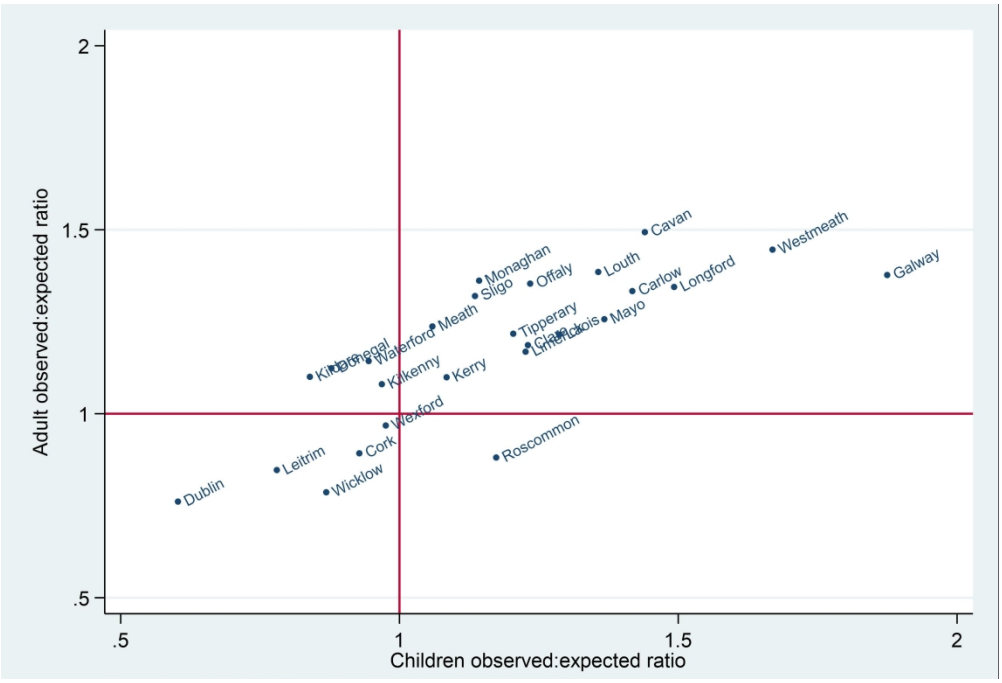

Association between children and adult's ratio of observed/expected number of episodes of appendectomy by county

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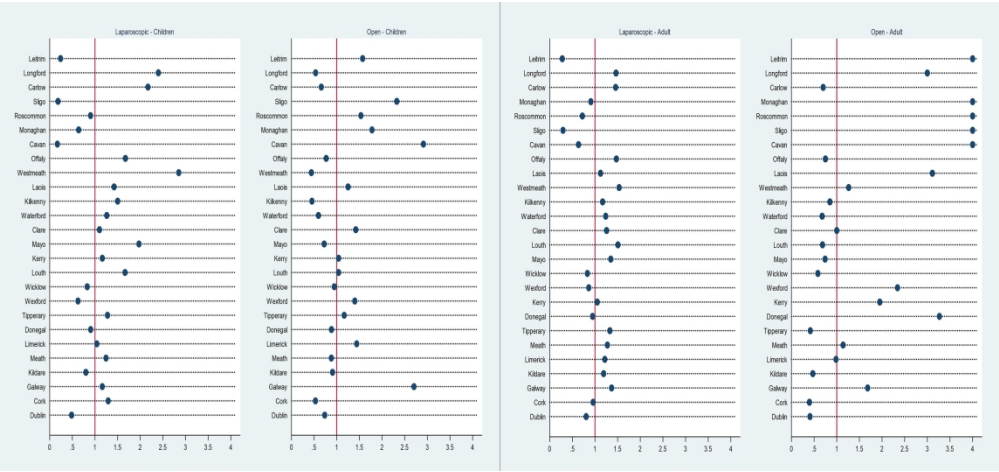

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Authors:

Ola Ahmed, Ken Mealy, Jan Sorensen

1. Department of General Surgery, Wexford General Hospital, Wexford, Ireland

   Ms Ola Ahmed

   Trainee Surgeon

2. National Clinical Programme in Surgery, Royal College of Surgeons in Ireland, Dublin 2, Ireland; Department of General Surgery, Wexford General Hospital, Wexford, Ireland

   Mr Ken Mealy

   Consultant Surgeon

3. Healthcare Outcomes Research Centre, Royal College of Surgeons in Ireland, Dublin 2, Ireland

   Professor Jan Sorensen

   Director of the Healthcare Outcomes Research Centre

Correspondence to: Ms Ola Ahmed, Department of General Surgery, Wexford General Hospital, Wexford, Ireland

Email: olasdahmed@gmail.com

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- Future studies should expand on this study design and additional examination of regional and local variations perhaps in a risk adjusted setting should be a priority.

Abstract

Objective To explore geographic variations in Irish laparoscopic and open appendectomy procedures.

Design Analysis based on 2014-2017 administrative hospital data from public hospitals.

Setting Counties of the Republic of Ireland.

Participants Irish residents with hospital admissions for an appendectomy as the principle procedure.

Main outcome measures Age and gender standardised laparoscopic and open appendectomy rates for 26 counties. Geographic variation measured with the extremal quotient (EQ), coefficient of variation (CV) and the systematic component of variation (SCV).

Results 23,684 appendectomies were included. 77.6% (n= 18,387) were performed laparoscopically. An EQ of 8.3 for laparoscopy and 10.0 for open appendectomy was determined. A high CV was demonstrated with a value of 36.7 and 80.8 for laparoscopic and open appendectomy. A SCV of 14.2 and 124.8 for laparoscopic and open appendectomy was observed. A wider variation was determined when children and adults were assessed separately.

Conclusions The geographic distribution in rates of appendectomy varies considerably across Irish counties. Our data suggests that a patient's likelihood of undergoing a laparoscopic or open appendectomy is associated with their county of residence.

Introduction

Acute appendicitis continues to be a global disease with escalating incidence rates in rapidly developing and industrialised countries[1]. These epidemiological associations contribute to the evolving knowledge on the pathogenesis of acute appendicitis and the influences of environmental triggers[2, 3]. Modern advances in laparoscopic surgery over the past two decades have led to the demonstrable advantage of laparoscopic appendectomy over open techniques across all populations[4-6]. Laparoscopy is associated with shorter hospital length of stay, decreased analgesic requirements, and lower morbidity rates in comparison with open surgery[4, 7, 8]. However, while laparoscopic approaches are preferred in most instances, open appendectomy is still practiced in cases where laparoscopy is difficult or contraindicated.

Analysing regional variations in the provision of common procedures helps raise questions relating to service provision as well as identify opportunities for improving efficiency and observing best practice. The Dartmouth Atlas Project has shown wide variations of up to 10-fold for a multitude of surgical procedures across geographical sites in the United States[9]. This initiative has led to several studies of geographic variation in other countries which appear to demonstrate that a patient's likelihood of undergoing specific surgical procedures depends greatly on where they live[10-13]. Reasons for the regional variability of laparoscopic and open appendectomy are still unclear. The observed rates of open appendectomy vary widely in the literature from 6 – 35% with higher variations in the adult population[14-16]. The aim of this study was to systematically investigate the regional variation of the surgical care of acute appendicitis in the Republic of Ireland. We compare the national data of laparoscopic and open appendectomy rates for children and adults to provide a current view of regional variation rates. By analysing and comparing the patterns of utilisation of

both the adult and paediatric population in Ireland, we seek to understand the extent that area of residence may influence the likelihood of undergoing either a laparoscopic or open procedure.

Methods

Data extraction

Anonymised patient data were obtained for a 4-year period from 2014 to 2017 from the National Quality Assurance and Improvement System (NQAIS). NQAIS is an online application based on the Hospital Inpatient Enquiry system (HIPE) operated by the national Health Service Executive in Ireland. Established in 1971, HIPE collects clinical and administrative data on discharges from acute Irish public hospitals. A HIPE record is created following a patient's discharge from a public hospital and offers demographic and clinical information for the episode of care. The current HIPE system only holds data for public hospitals and no national database is available on the activities in the private hospital sector. This analysis includes only patients treated in public hospitals regardless of their individual insurance status. We obtained records of all hospital episodes coded with laparoscopic appendectomy or open appendectomy as the primary procedure. From this sample we excluded episodes with primary diagnostic codes different from "Appendicitis", "Suspected appendicitis", or "Rule-out appendicitis" (i.e. not coded with K35-37 in the International Classification of Diseases Version 10 Clinical Modification (ICD-10-CM)), episodes coded as non-emergency admissions, and episodes for patients who are not residents in Ireland.

The Republic of Ireland is made up of 26 geographical subdivisions referred to as counties. These counties were used in this study to determine appendectomy rates per geographical area. County of residence is a variable in HIPE which can be utilised to determine residential status of individual cases irrespective of where the actual procedure was performed. We obtained population statistics from the 2016 census from the Central Statistical Office[17].

Patient factors considered in the analysis were age, gender and county of residence**.** Children were categorized as patients aged 14 years or younger to correspond with the 5-year age groups in the available census data. National age and gender stratification was derived from the population of 4,761,865 referred to in the 2016-population census[17].

Statistical analysis

Data was analysed using Stata version 15.1 (StataCorp, Texas). Descriptive statistics were recorded for patient characteristics and procedure type. Continuous variables were compared using unpaired t-tests. Association of categorical variables (differences for dichotomous variables between groups) was assessed using the chi-square (X^2) test. Continuous numerical variables were reported as means and standard deviations (SD). Categorical variables were reported as proportions or percentages.

To assess relative variability we used methods described by McPhearson and colleagues[12]. These established methods of geographic variation are widely used in small-area variation studies and allow for context and comparison across geographical settings and countries[13, 18, 19]. The extremal quotient (EQ) is presented as the ratio of the highest and lowest standardised county rate. A value close to 1 indicates low variation in rates across counties. The coefficient of variation (CV) is a measure of relative variability and is calculated as the standard deviation of the county rates divided by the mean of county rates. A large score indicates large variability. The systematic component of variation (SCV) is also a measure of variation. This is the difference between the random component of variation and the total variation. A large SCV value indicates large systematic and regional variation[12]. We estimated these variability measures for the whole population and for children and adults separately.

Patient involvement

No patients were involved in setting the research question or the outcome measures, nor were they involved in the development of design or implementation of the study. No patients were asked to advise on interpretation or writing up of results.

Results

National analysis

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 of which 77.6% were laparoscopic appendectomies and 22.4% were open appendectomies. 53.7% of patients were male and the mean age was 25 years (SD 15, median 20, range 0-98). These findings are summarized in Table 1.

Table 1 Number of adult and paediatric laparoscopic and open appendectomy

	Laparoscopic (n (%))	Open (n (%))	P value
Children (n=7343)			
Male	2068 (49.1%)	2140 (45.4%)	
Female	1790 (57.1%)	1345 (42.9%)	<0.01
Adult (n=16341)			
Male	7387 (86.8%)	1126 (13.2%)	
Female	7142 (91.2%)	686 (8.8%)	<0.01

The percentage of laparoscopic procedures was 52.5% among children and 88.9% among adults (statistically significant difference; OR 7.2 95% CI 6.8-7.7). Figure 1 displays the proportion of appendectomies conducted as laparoscopic procedures for 2014 to 2017 in children and adult patients. The proportion of laparoscopic procedures increased steadily during the studied years from 2014 to 2017 from 72.7% to 83.3% (trend p<0.01). For children the proportion increased from 43.9% to 61.4% (trend p<0.01).

Girls were more likely to have laparoscopic procedures than boys (57.1% vs 49.1%, OR 1.4 95% CI 1.3-1.5), and women more likely than men (91.2% vs 86.8%, OR 1.6 95% CI 1.4-1.8). 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).

Figure 2 displays the number of laparoscopic and open procedures performed on children and adults during the years 2014 to 2017 by county of residence.

County analysis

The annual appendectomy rate was estimated at 124.4 procedures per 100,000 persons and 96.5 and 27.8 for laparoscopic and open approaches respectively. The online supplementary table 2shows the proportion of laparoscopic appendectomies per year by county of residence for the child and adult population. The data displays a gradual increase in the number of laparoscopic procedures performed in both patient groups during the 4-year study period.

Figure 3 presents the ratio of the observed and expected number of the total appendectomy rates within different counties for both children and adults and displays the geographic dispersions determined. The expected number of procedures was estimated by relating the national age and gender procedure rate to the county population. A value of 1 was determined to be the national average rate to allow for comparison between geographic areas. The ratio takes a value larger than 1 when the numbers of observed procedures are higher than the expected number of procedures. For children, 17/26 counties displayed a higher than average rate of appendectomy procedures. For the adult population, residents from 20/26 counties underwent appendectomy procedures at a higher rate than the national average.

Figure 4 presents the association between the ratio of observed and expected procedures for children and adults. Counties in the north-east quadrant have a higher than expected number of procedures for both children and adults. These counties demonstrate higher rates of appendectomy procedures for their entire populations. There appears to be a strong association between the ratio for children and adults indicating that counties with a higher ratio for children also have a higher ratio for adults. Counties in the south-west quadrant have a lower than expected number of procedures for both children and adults. Using similar reasoning, counties with lower rates of paediatric appendectomy procedures appeared to have low rates for the adult population also. Only

four counties have a different pattern. Roscommon is the only county where children have more than the expected episodes of care and adults have fewer than the expected episodes of care, while the reverse appears for Kilkenny, Waterford, Donegal and Kildare. These remaining four counties display high rates in the adult population but lower than average rates in the paediatric patient group.

Figure 5 displays the ratio of observed and expected procedures for laparoscopic and open procedures for children and adults separately. Wide population dispersions are demonstrated in children for both laparoscopic and open appendectomy. In 16/26 counties children underwent laparoscopic appendectomy at rates higher than the national average, indicating areas with high utilisation. Children from 13/26 counties underwent higher rates of open appendectomy procedures than the rest of the general population. Similarly, adults in 16/26 counties had higher rates of laparoscopic procedures than the rest of the national population, and adults from 12/26 counties underwent higher rates of open appendectomy procedures. Wide dispersions are particularly evident in the adult population with open appendectomy.

Table 2 displays the statistical measures of variation for the combined population and children and adults separately. The extremal quotient was 8.3 for laparoscopic and 10.0 for open appendectomy, demonstrating greater geographic variation for open appendectomy. The coefficient of variation was high for both laparoscopic and open appendectomy; 36.7 for laparoscopic and 80.8 for open procedures, in accordance with the McPhearson interpretations. This demonstrates greater geographic variability in the application of open appendectomy cases. The systematic component of variation was also high for both procedures; 14.2 for laparoscopy and 124.8 for open appendectomy.

Table 2. Variation statistics for laparoscopy, open and combined for children, adult and the whole patient population, 2014-2017.

Population/procedure	Number of episodes 2014-2017	Standardised number of episodes per 100.000 population	Extremal Quotient	Coefficient of Variation	Systematic Component of Variation
Children					
Laparoscopy	3858	383.3	16.9	55.1	41.6
Open	3485	346.2	6.5	55.3	38.2
Combined	7343	729.5	3.2	24.3	9.3
Adult					
Laparoscopy	14529	386.9	7.1	33.3	10.6
Open	1812	48.3	25.7	128.4	502.0
Combined	16341	435.1	2.1	18.9	4.5
Whole population					
Laparoscopy	18387	386.1	8.3	36.7	14.2
Open	5297	111.2	10.0	80.8	124.8
Combined	23684	497.4	2.2	19.6	5.6

Extremal quotient = max(standardised episode rate i)/min(standardised episode rate i).

Coefficient of variation = standard deviation (standardised episode rate i) / mean (standardised episode rate i) *100.

Systematic component of variations = $1/k \left(\sum (O_i - E_i)^2 / E_i^2 - \sum 1/E_i \right) * 100$ where k is number of counties, O_i is observed number of episodes and E_i is expected number of episodes determined by indirect standardisation.

Discussion

This study documents a substantial geographic variation in the operative management of acute appendicitis in the Republic of Ireland. To our knowledge, there have been no population-based studies exploring emergency appendectomy variations at a county level in Ireland. While some level of disparity is to be expected, large variations particularly in emergency interventions can indicate potential inequity and inefficiency in the use of sophisticated healthcare systems, and thus indicate variations in access and use of surgical services. Similar to the Dartmouth Atlas project, our data demonstrates that a person's likelihood of undergoing a laparoscopic or open appendectomy is related to their county of residence[9].

Laparoscopic appendectomy is favoured because of its benefits in analgesic requirements post - operatively, shorter length of hospital stay, lower post-operative mortality, and faster return to normal activities[4, 7, 8, 20, 21]. Unsurprisingly, most of the cases in our data were performed laparoscopically. As with most observational data, causality cannot be determined. Historical research suggests that the variations in the utility of surgical services may result from clinical uncertainty or heterogeneity in medical literature[22, 23]. One potential hypothetical and important reason for the variations could be individual surgeon skill and practice. The current study did not control for specific surgeon factors and may reflect a lack of laparoscopic skills or capacity in certain areas and explain the higher statistical variability for open procedures. Variations in laparoscopic surgery rates are not unheard of. An analyses by Doumouras et al suggested that laparoscopic training may influence the rate of laparoscopic practices in some hospitals[24]. While our study did not evaluate larger teaching hospitals separately, there may be an inherent geographic variation in laparoscopic expertise outside of tertiary referral centres and may also reflect variation in consultant and trainee surgeon performance as the principle operator; a factor not examined in this study.

In this study laparoscopic appendectomy utilisation appears lower in children and may indicate a deficiency in the paediatric surgery skillset available in the country and an unfamiliarity in operating on children amongst general surgeons. Multiple reports have stressed the need to provide high

quality paediatric surgery services to address the challenges and demands of paediatric patients which may be unavailable in hospitals were adult surgery appears to dominate. The findings of this study suggest a potential difference in expertise in relation to paediatric surgery in Ireland. This would parallel with the reality that most district or general hospitals in Ireland lack a specialised paediatric surgeon on site and thus cases are performed by adult surgeons. These findings suggest a potential difference in expertise in relation to paediatric surgery in Ireland.

There are some limitations to this study. As with other studies including data from administrative databases, the reliability of results is based on the accuracy and completeness of systematic coding and data input. We attempt to overcome potential miscoding information by including a large population cohort of patients over a four-year period. We have not accounted for laparoscopic cases that were converted to open due to the potential inclusion of duplicate numbers and inherent miscoding errors. Co-morbidities, procedural complexity and socioeconomic status were also not controlled for when assessing patient characteristics. However, despite these limitations our findings demonstrate concerning conclusions relating to the provision of emergency appendectomy in the Republic of Ireland for both children and adults. The analysis provides some important implications for health care providers and surgeons in analysing the extent of geographic variation and the disparity in management of a common condition. While we cannot explain the wide variations seen, further analysis at an individual county level with the assessment of more in-depth patient characteristics may uncover opportunities to eliminate variations and ultimately improve the delivery of care and patient outcomes. We also await the results of the multi-institutional Right Iliac Fossa Treatment (RIFT audit) study to further analyse the variation in the management strategies of patients presenting with RIF pain to centres across the United Kingdom, Ireland, Italy, Portugal and Spain[25].

Conclusion

Geographic variation analyses can help characterise the overall performance of a health system and determine whether patients receive equal treatment for equal needs. High appendectomy rates with considerable geographical disparity may suggest an imbalance in the provision of a common acute surgical procedure in the Republic of Ireland. Some populations appear more likely to undergo laparoscopic procedures than other populations within a relatively small country. Large statistical variability in the paediatric population may also reflect a discrepancy in surgical paediatric care in areas where these procedures are largely performed by surgeons specialising in adult care. This is the first Irish study to systematically explore the rates and geographical disparity of acute laparoscopic and open appendectomy procedures and help bridge a pre-existing knowledge gap on the topic. Despite the limitations, the study suggests a need for more effective decision-making and planning to ensure consistency and decrease the variability in the management of acute appendicitis.

Contributors: OA conceived and designed the study, analysed the data and drafted and revised the paper. JS designed the study, prepared and analysed the data, drafted and revised the paper. KM interpreted the results and revised the paper. All authors had full access to all the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. OA is the guarantor and affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as originally planned (and, if relevant, registered) have been explained.

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Competing interests: All authors declare no conflicts in interests in the preparation of this study and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Ethical approval: Ethics board approval was not required for the study.

Data sharing: All data has been included either in the main manuscript or as a supplementary file. The authors do not withhold any other data.

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References

1. Ferris M, Quan S, Kaplan BS, Molodecky N, Ball CG, Chernoff GW, et al. The Global Incidence of Appendicitis: A Systematic Review of Population-based Studies. *Annals of surgery* 2017;**266**(2): 237-241.
2. Kaplan GG, Dixon E, Panaccione R, Fong A, Chen L, Szyszkowicz M, et al. Effect of ambient air pollution on the incidence of appendicitis. *Canadian Medical Association Journal* 2009;**181**(9): 591-597.
3. Kaplan GG, Tanyingoh D, Dixon E, Johnson M, Wheeler AJ, Myers RP, et al. Ambient ozone concentrations and the risk of perforated and nonperforated appendicitis: a multicity case-crossover study. *Environmental health perspectives* 2013;**121**(8): 939.
4. Tate JJT, Dawson JW, Chung SCS, Lau WY, Li AKC. Laparoscopic versus open appendicectomy: prospective randomised trial. *The Lancet* 1993;**342**(8872): 633-637.
5. Southgate E, Vousden N, Karthikesalingam A, Markar SR, Black S, Zaidi A. Laparoscopic vs open appendectomy in older patients. *Archives of Surgery* 2012;**147**(6): 557-562.
6. Adwan H, Weerasuriya CK, Endleman P, Barnes A, Stewart L, Justin T. Laparoscopic versus open appendicectomy in children: A UK District General Hospital experience. *Journal of Pediatric Surgery* 2014;**49**(2): 277-279.
7. Thomson J-E, Kruger D, Jann-Kruger C, Kiss A, Omoshoro-Jones J, Luvhengo T, et al. Laparoscopic versus open surgery for complicated appendicitis: a randomized controlled trial to prove safety. *Surgical endoscopy* 2015;**29**(7): 2027-2032.
8. Tiwari MM, Reynoso JF, Tsang AW, Oleynikov D. Comparison of outcomes of laparoscopic and open appendectomy in management of uncomplicated and complicated appendicitis. *Annals of surgery* 2011;**254**(6): 927-932.
9. Practice TDIoHPaC. The Dartmouth Atlas Project Database. 1996 - 2010.
10. Reames BN, Shubeck SP, Birkmeyer JD. Strategies for Reducing Regional Variation in the Use of Surgery A Systematic Review. *Annals of surgery* 2014;**259**(4): 616.
11. Ahmed O, Mealy K, Kelliher G, Keane F, Sorensen J. Exploring geographical variation in access to general surgery in Ireland: Evidence from a national study. *The Surgeon* 2019.
12. McPherson K, Wennberg JE, Hovind OB, Clifford P. Small-area variations in the use of common surgical procedures: an international comparison of New England, England, and Norway. *New England journal of medicine* 1982;**307**(21): 1310-1314.
13. Weeks WB, Paraponaris A, Ventelou B. Geographic variation in rates of common surgical procedures in France in 2008–2010, and comparison to the US and Britain. *Health Policy* 2014;**118**(2): 215-221.
14. Katsuno G, Nagakari K, Yoshikawa S, Sugiyama K, Fukunaga M. Laparoscopic Appendectomy for Complicated Appendicitis: A Comparison with Open Appendectomy. *World Journal of Surgery* 2009;**33**(2): 208-214.
15. Masoomi H, Mills S, Dolich MO, Ketana N, Carmichael JC, Nguyen NT, et al. Comparison of Outcomes of Laparoscopic Versus Open Appendectomy in Adults: Data from the Nationwide Inpatient Sample (NIS), 2006–2008. *Journal of Gastrointestinal Surgery* 2011;**15**(12): 2226-2231.
16. Litz CN, Ciesla DJ, Danielson PD, Chandler NM. Effect of hospital type on the treatment of acute appendicitis in teenagers. *Journal of Pediatric Surgery* 2018;**53**(3): 446-448.
17. Scoreboard MIP. Central Statistics Office statistical release. In: June; 2015.
18. Appleby J, Raleigh V, Frosini F, Bevan G, Gao H, Lyscom T. *Variations in health care: the good, the bad and the inexplicable*. King's Fund, 2011.
19. Birkmeyer JD, Reames BN, McCulloch P, Carr AJ, Campbell WB, Wennberg JE. Understanding of regional variation in the use of surgery. *The Lancet* 2013;**382**(9898): 1121-1129.
20. Sauerland S, Jaschinski T, Neugebauer EAM. Laparoscopic versus open surgery for suspected appendicitis. *Cochrane Database of Systematic Reviews* 2010(10).

21. Faiz O, Clark J, Brown T, Bottle A, Antoniou A, Farrands P, et al. Traditional and laparoscopic appendectomy in adults: outcomes in English NHS hospitals between 1996 and 2006. *Annals of surgery* 2008;**248**(5): 800-806.

22. Ray-Coquard I, Philip T, Lehmann M, Fervers B, Farsi F, Chauvin F. Impact of a clinical guidelines program for breast and colon cancer in a French cancer center. *Jama* 1997;**278**(19): 1591-1595.

23. Wennberg JE. Dealing with medical practice variations: a proposal for action. *Health Affairs* 1984;**3**(2): 6-33.

24. Doumouras AG, Saleh F, Eskicioglu C, Amin N, Cadeddu M, Hong D. Neighborhood variation in the utilization of laparoscopy for the treatment of colon cancer. *Diseases of the Colon & Rectum* 2016;**59**(8): 781-788.

25. Right Iliac Fossa Pain Treatment (RIFT) Study: protocol for an international, multicentre, prospective observational study. *BMJ open* 2018;**8**(1): e017574.

Figure legend:

Figure 1 - Proportion of appendectomies conducted as laparoscopic procedures during 2014-2017 in children and adult patients

Figure 2 – Number of procedures performed during 2014-2017 on county residents

Figure 3 - Ratio of observed/expected number of episodes of appendectomy by county for children and adults.

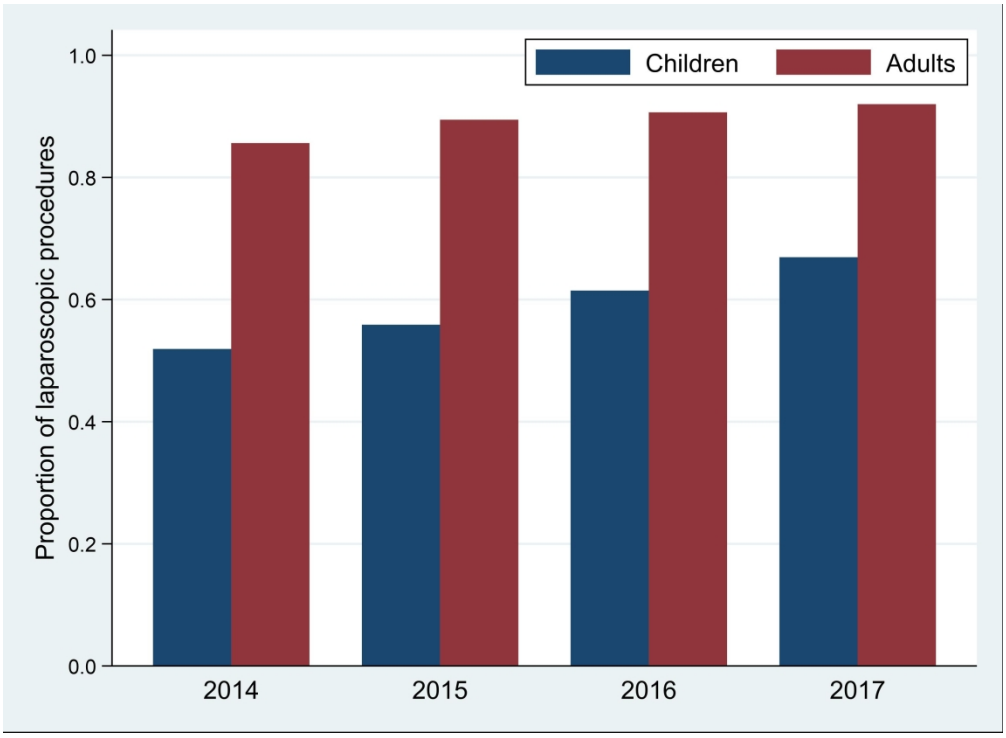
Figure 4 - Association between children and adult's ratio of observed/expected number of episodes of appendectomy by county**.**

Figure 5 - Ratio of observed/expected number of episodes of laparoscopy and open appendectomy by county for children and adults.

Table 1 – Adult and paediatric laparoscopic and open appendectomy percentage rates.

Table 2 – Variation statistics for laparoscopy, open and combined for children, adult and the whole patient population, 2014-2017.

Online supplementary table – Proportion of laparoscopic appendectomies per year by county of residence for child and adult population.



Proportion of appendectomies conducted as laparoscopic procedures during 2014-2017 in children and adult patients

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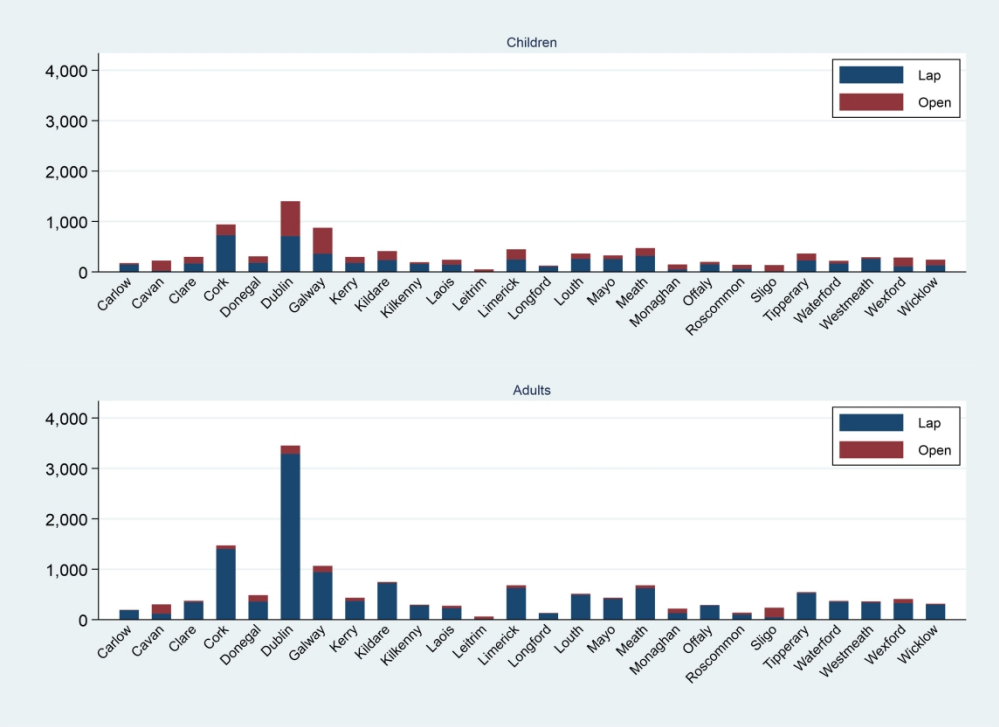

Number of procedures performed during 2014-2017 on county residents

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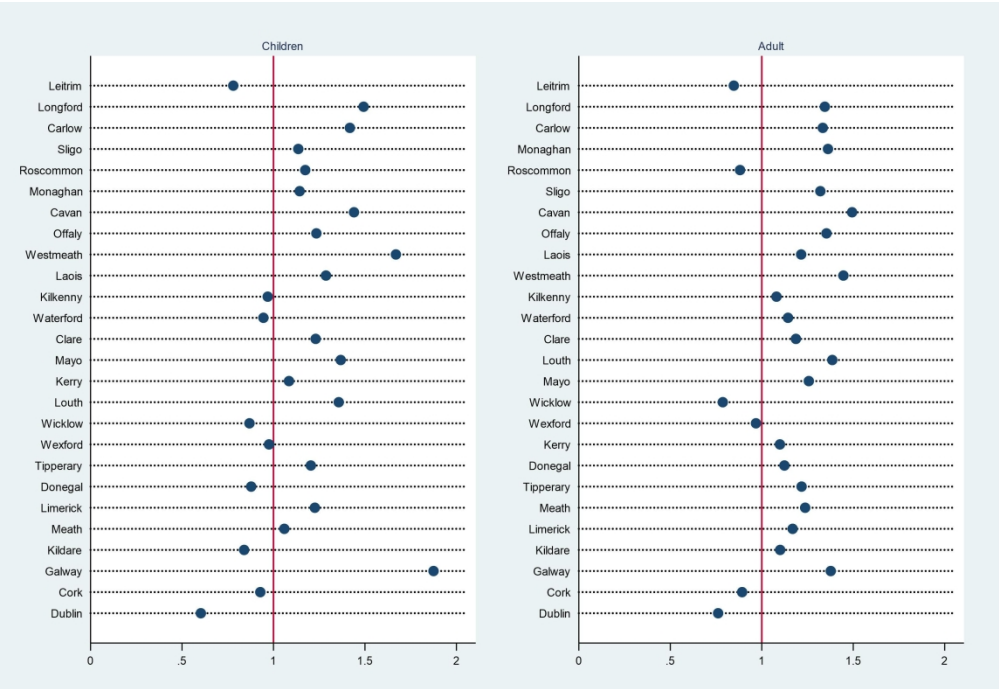

Ratio of observed/expected number of episodes of appendectomy by county for children and adults.

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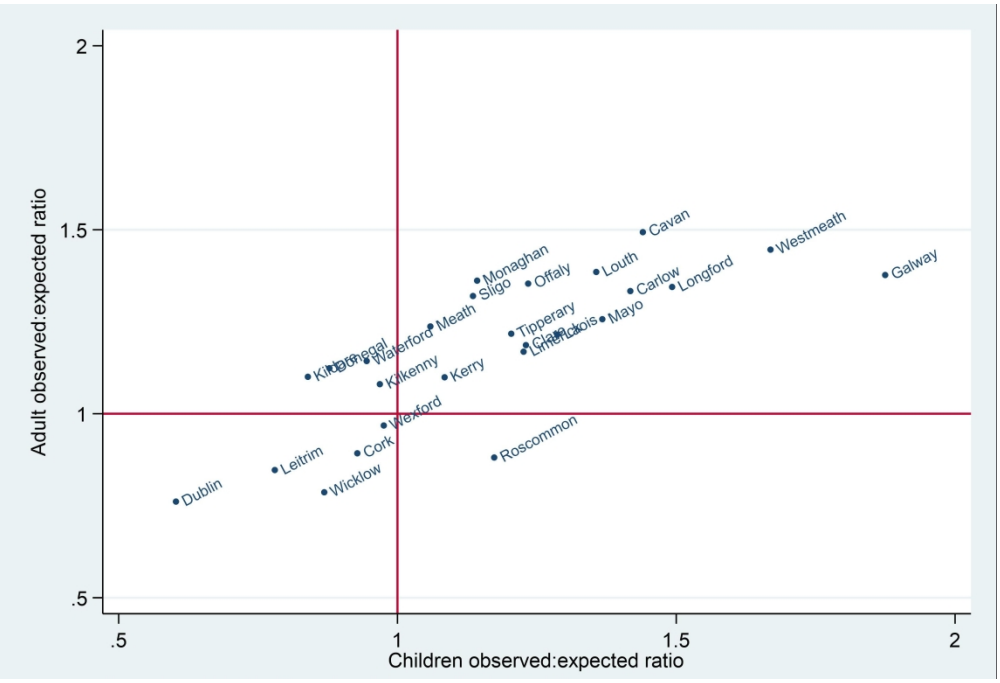
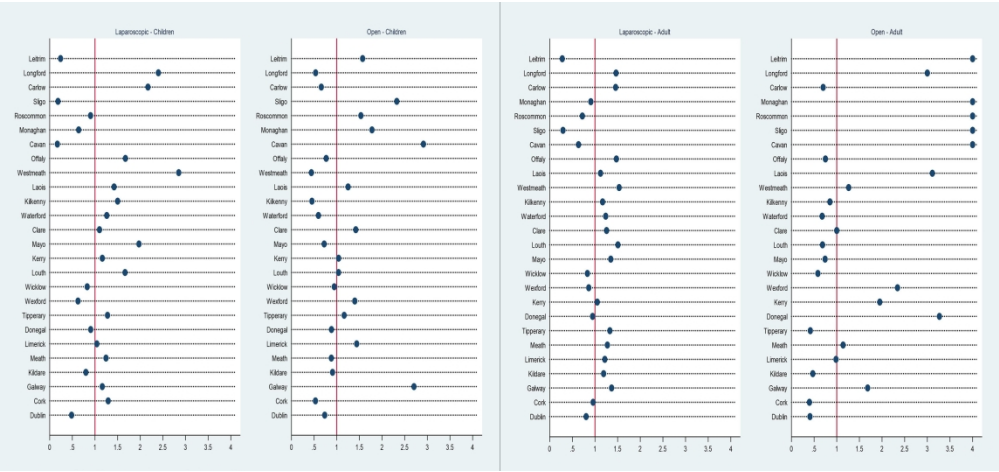


Association between children and adult's ratio of observed/expected number of episodes of appendectomy by county

279x188mm (300 x 300 DPI)



Ratio of observed/expected number of episodes of laparoscopy and open appendectomy by county for children and adults.

279x131mm (300 x 300 DPI)

Online Supplementary Table Proportion of laparoscopic appendectomies per year by county of residence for child and adult population

Proportion of laparoscopic procedures								
	Children				Adults			
County	**2014**	**2015**	**2016**	**2017**	**2014**	**2015**	**2016**	**2017**
Carlow	0.74	0.91	0.84	0.90	0.90	0.98	0.96	1.0
Cavan	0.11	0.14	0.08	0.13	0.22	0.51	0.44	0.5
Clare	0.56	0.43	0.59	0.65	0.90	0.94	0.88	0.97
Cork	0.65	0.76	0.8	0.87	0.93	0.96	0.97	0.95
Donegal	0.25	0.46	0.77	0.89	0.54	0.73	0.78	0.86
Dublin	0.44	0.42	0.54	0.64	0.93	0.96	0.96	0.96
Galway	0.39	0.41	0.38	0.47	0.86	0.89	0.89	0.90
Kerry	0.46	0.66	0.71	0.60	0.80	0.85	0.92	0.90
Kildare	0.49	0.62	0.64	0.56	0.97	0.97	0.98	0.98
Kilkenny	0.75	0.84	0.82	0.89	0.89	0.93	0.95	0.99
Laois	0.47	0.45	0.64	0.81	0.80	0.78	0.79	0.96
Leitrim	0.14	0.27	0.11	0.22	0.27	0.15	0.33	0.46
Limerick	0.44	0.50	0.54	0.70	0.89	0.93	0.90	0.95
Longford	0.70	0.97	0.90	0.93	0.90	0.93	0.92	0.92
Louth	0.66	0.61	0.78	0.77	0.96	0.97	0.93	0.96
Mayo	0.73	0.83	0.78	0.79	0.94	0.94	0.98	0.94
Meath	0.59	0.61	0.74	0.75	0.89	0.91	0.94	0.93
Monaghan	0.35	0.30	0.33	0.41	0.59	0.51	0.77	0.51
Offaly	0.65	0.78	0.83	0.78	0.94	0.98	1.00	0.95
Roscommon	0.42	0.39	0.50	0.47	0.69	0.68	0.75	0.865
Sligo	0.12	0.1	0.09	0.19	0.18	0.19	0.20	0.19
Tipperary	0.63	0.68	0.60	0.60	0.94	0.98	0.98	0.98
Waterford	0.75	0.80	0.77	0.74	0.92	0.94	0.98	0.96
Westmeath	0.86	0.84	0.92	0.92	0.89	0.96	0.96	0.97
Wexford	0.25	0.19	0.53	0.52	0.68	0.67	0.82	0.93
Wicklow	0.67	0.61	0.50	0.40	0.98	0.90	0.94	0.97

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*5*
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	n/a
		(*d*) If applicable, explain how loss to follow-up was addressed	n/a
		(*e*) Describe any sensitivity analyses	n/a
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7
		(b) Indicate number of participants with missing data for each variable of interest	n/a
		(c) Summarise follow-up time (eg, average and total amount)	n/a
Outcome data	15*	Report numbers of outcome events or summary measures over time	7,8,9,10,
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8,9, 10
		(*b*) Report category boundaries when continuous variables were categorized	8, 9
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8,9,10,
Discussion			
Key results	18	Summarise key results with reference to study objectives	11, 12,13,
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12
Generalisability	21	Discuss the generalisability (external validity) of the study results	12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Exploring geographic variation in acute appendectomy in Ireland: a cohort study

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Exploring geographic variation in acute appendectomy in Ireland: a cohort study

Authors:

Ola Ahmed, Ken Mealy, Jan Sorensen

1. Department of General Surgery, Wexford General Hospital, Wexford, Ireland

   Ms Ola Ahmed

   Trainee Surgeon

2. National Clinical Programme in Surgery, Royal College of Surgeons in Ireland, Dublin 2, Ireland; Department of General Surgery, Wexford General Hospital, Wexford, Ireland

   Mr Ken Mealy

   Consultant Surgeon

3. Healthcare Outcomes Research Centre, Royal College of Surgeons in Ireland, Dublin 2, Ireland

   Professor Jan Sorensen

   Director of the Healthcare Outcomes Research Centre

Correspondence to: Ms Ola Ahmed, Department of General Surgery, Wexford General Hospital, Wexford, Ireland

Email: olasdahmed@gmail.com

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Strengths and limitations of this study

- The study employed a large, well-defined patient population of the Republic of Ireland.
- All data was age and gender standardised as is standard when analysing geographical variation in healthcare, including the Dartmouth Atlas Project.
- The study does not include data from private hospitals, however acute appendicitis is largely managed in public hospitals regardless of medical insurance cover.
- Co-morbidities, procedural complexity and socioeconomic status were not controlled for when assessing patient characteristics.
- Future studies should expand on this study design and additional examination of regional and local variations perhaps in a risk adjusted setting should be a priority.

Abstract

Objective To explore geographic variations in Irish laparoscopic and open appendectomy procedures.

Design Analysis based on 2014-2017 administrative hospital data from public hospitals.

Setting Counties of the Republic of Ireland.

Participants Irish residents with hospital admissions for an appendectomy as the principal procedure.

Main outcome measures Age and gender standardised laparoscopic and open appendectomy rates for 26 counties. Geographic variation measured with the extremal quotient (EQ), coefficient of variation (CV) and the systematic component of variation (SCV).

Results 23,684 appendectomies were included. 77.6% (n= 18,387) were performed laparoscopically. An EQ of 8.3 for laparoscopy and 10.0 for open appendectomy was determined. A high CV was demonstrated with a value of 36.7 and 80.8 for laparoscopic and open appendectomy. A SCV of 14.2 and 124.8 for laparoscopic and open appendectomy was observed. A wider variation was determined when children and adults were assessed separately.

Conclusions The geographic distribution in rates of appendectomy varies considerably across Irish counties. Our data suggests that a patient's likelihood of undergoing a laparoscopic or open appendectomy is associated with their county of residence.

Introduction

Acute appendicitis continues to be a global disease with escalating incidence rates in rapidly developing and industrialised countries[1]. These epidemiological associations contribute to the evolving knowledge on the pathogenesis of acute appendicitis and the influences of environmental triggers[2, 3]. Modern advances in laparoscopic surgery over the past two decades have led to the demonstrable advantage of laparoscopic appendectomy over open techniques across all populations[4-6]. Laparoscopy is associated with shorter hospital length of stay, decreased analgesic requirements, and lower morbidity rates in comparison with open surgery[4, 7, 8]. However, while laparoscopic approaches are preferred in most instances, open appendectomy is still practiced in cases where laparoscopy is difficult or contraindicated.

Analysing regional variations in the provision of common procedures helps raise questions relating to service provision as well as identify opportunities for improving efficiency and observing best practice. The Dartmouth Atlas Project has shown wide variations of up to 10-fold for a multitude of surgical procedures across geographical sites in the United States[9]. This initiative has led to several studies of geographic variation in other countries which appear to demonstrate that a patient's likelihood of undergoing specific surgical procedures depends greatly on where they live[10-13]. Reasons for the regional variability of laparoscopic and open appendectomy are still unclear. The observed rates of open appendectomy vary widely in the literature from 6 – 35% with higher variations in the adult population[14-16]. The aim of this study was to systematically investigate the regional variation of the surgical care of acute appendicitis in the Republic of Ireland. We compare the national data of laparoscopic and open appendectomy rates for children and adults to provide a current view of regional variation rates. By analysing and comparing the patterns of utilisation of both the adult and paediatric population in Ireland, we seek to understand the extent that area of residence may influence the likelihood of undergoing either a laparoscopic or open procedure.

Methods

Data extraction

Anonymised patient data were obtained for a 4-year period from 2014 to 2017 from the National Quality Assurance and Improvement System (NQAIS). NQAIS is an online application based on the Hospital Inpatient Enquiry system (HIPE) operated by the national Health Service Executive in Ireland. Established in 1971, HIPE collects clinical and administrative data on discharges from acute Irish public hospitals. A HIPE record is created following a patient's discharge from a public hospital and offers demographic and clinical information for the episode of care. The current HIPE system only holds data for public hospitals and no national database is available on the activities in the private hospital sector. This analysis includes only patients treated in public hospitals regardless of their individual insurance status. We obtained records of all hospital episodes coded with laparoscopic appendectomy or open appendectomy as the primary procedure. From this sample we excluded episodes with primary diagnostic codes different from "Appendicitis", "Suspected appendicitis", or "Rule-out appendicitis" (i.e. not coded with K35-37 in the International Classification of Diseases Version 10 Clinical Modification (ICD-10-CM)), episodes coded as non-emergency admissions, and episodes for patients who are not residents in Ireland.

The Republic of Ireland is made up of 26 geographical subdivisions referred to as counties. These counties were used in this study to determine appendectomy rates per geographical area. County of residence is a variable in HIPE which can be utilised to determine residential status of individual persons irrespective of where the actual procedure was performed. We obtained population statistics from the 2016 census from the Central Statistical Office[17].

Patient factors considered in the analysis were age, gender and county of residence**.** Children were categorized as patients aged 14 years or younger to correspond with the 5-year age groups in the

available census data. National age and gender stratification was derived from the population of 4,761,865 referred to in the 2016-population census[17].

Statistical analysis

Data was analysed using Stata version 15.1 (StataCorp, Texas). Descriptive statistics were recorded for patient characteristics and procedure type. Continuous variables were compared using unpaired t-tests. Association of categorical variables (differences for dichotomous variables between groups) was assessed using the chi-square (X^2) test. Continuous numerical variables were reported as means and standard deviations (SD). Categorical variables were reported as proportions or percentages.

To assess relative variability we used methods described by McPhearson and colleagues[12]. These established methods of geographic variation are widely used in small-area variation studies and allow for context and comparison across geographical settings and countries[13, 18, 19]. The extremal quotient (EQ) is presented as the ratio of the highest and lowest standardised county rate. A value close to 1 indicates low variation in rates across counties. The coefficient of variation (CV) is a measure of relative variability and is calculated as the standard deviation of the county rates divided by the mean of county rates. A value greater than 0.3 is considered "highly variable" in accordance to studies by McPhearson et al with higher scores indicating greater variability[12, 20]. The systematic component of variation (SCV) is also a measure of variation. This is the difference between the random component of variation and the total variation. Homogeneity in rates between areas would result in a value of zero. A large SCV value indicates large systematic and regional variation[12]. We estimated these variability measures for the whole population and for children and adults separately.

Patient involvement

No patients were involved in setting the research question or the outcome measures, nor were they involved in the development of design or implementation of the study. No patients were asked to advise on interpretation or writing up of results.

Results

National analysis

A total of 26,760 episodes of care discharged through January 1st 2014 to December 31st 2017 were extracted. In this sample 1902 episodes were coded with diagnoses other than K35-K37; 885 episodes were coded as non-emergency admissions; 289 episodes related to non-Ireland residents. After exclusion of these episodes, our study sample included 23,684 episodes of care of which 77.6% were laparoscopic appendectomies and 22.4% were open appendectomies. 53.7% of patients were male and the mean age was 25 years (SD 15, median 20, range 0-98). These findings are summarized in Table 1.

Table 1 Number of adult and paediatric laparoscopic and open appendectomy

	Laparoscopic (n (%))	Open (n (%))	P value
Children (n=7343)			
Male	2068 (28.2%)	2140 (29.1%)	
Female	1790 (24.4%)	1345 (18.3%)	<0.01
Adult (n=16341)			
Male	7387 (45.2%)	1126 (6.9%)	
Female	7142 (43.7%)	686 (4.2%)	<0.01

The percentage of laparoscopic procedures was 52.6% among children and 88.9% among adults (statistically significant difference; OR 7.2 95% CI 6.8-7.7). Figure 1 displays the proportion of appendectomies conducted as laparoscopic procedures for 2014 to 2017 in children and adult patients. The proportion of laparoscopic procedures increased steadily during the studied years from 2014 to 2017 from 72.7% to 83.3% (trend p<0.01). For children the proportion increased from 43.9% to 61.4% (trend p<0.01).

Girls were more likely to have laparoscopic procedures than boys (57.1% vs 49.1%, OR 1.4 95% CI 1.3-1.5), and women more likely than men (91.2% vs 86.8%, OR 1.6 95% CI 1.4-1.8). A clear age gradient was observed when comparing laparoscopic and open appendectomy procedures for the whole population and for both men and women separately (trend p<0.01). The proportion of

patients undergoing laparoscopic procedures reduced for older patients in both genders (logistic regression $p<0.01$) and appears statistically lower for patients older than 45 years ($p<0.01$).

County analysis

Figure 2 displays the number of laparoscopic and open procedures performed on children and adults during the years 2014 to 2017 by county of residence. The annual appendectomy rate was estimated at 124.4 procedures per 100,000 persons and 96.5 and 27.8 for laparoscopic and open approaches respectively. The online supplementary table shows the proportion of laparoscopic appendectomies per year by county of residence for the child and adult population. The data displays a gradual increase in the number of laparoscopic procedures performed in both patient groups during the 4-year study period.

Figure 3 presents the ratio of the observed and expected number of the total appendectomy rates within different counties for both children and adults and displays the geographic dispersions determined. The expected number of procedures was estimated by relating the national age and gender procedure rate to the county population and demonstrates the inter-county discrepancies in a risk adjusted setting. A value of 1 was determined to be the national average rate to allow for comparison between geographic areas. The ratio takes a value larger than 1 when the numbers of observed procedures are higher than the expected number of procedures. This would indicate a high volume county when compared with the national average value. For children, 17/26 counties displayed a higher than average rate of appendectomy procedures. For the adult population, residents from 20/26 counties underwent appendectomy procedures at a higher rate than the national average.

Figure 4 presents the association between the ratio of observed and expected procedures for children and adults. Counties in the north-east quadrant have a higher than expected number of procedures for both children and adults. These counties demonstrate higher rates of appendectomy procedures for their entire populations. There appears to be a strong association between the ratio

for children and adults indicating that counties with a higher ratio for children also have a higher ratio for adults. Counties in the south-west quadrant have a lower than expected number of procedures for both children and adults. Using similar reasoning, counties with lower rates of paediatric appendectomy procedures appeared to have low rates for the adult population also. Only four counties have a different pattern. Roscommon is the only county where children have more than the expected episodes of care and adults have fewer than the expected episodes of care, while the reverse appears for Kilkenny, Waterford, Donegal and Kildare. These remaining four counties display high rates in the adult population but lower than average rates in the paediatric patient group.

Figure 5 displays the ratio of observed and expected procedures for laparoscopic and open procedures for children and adults separately. Wide population dispersions are demonstrated in children for both laparoscopic and open appendectomy. In 16/26 counties children underwent laparoscopic appendectomy at rates higher than the national average, indicating areas with high utilisation. Children from 13/26 counties underwent higher rates of open appendectomy procedures than the rest of the general population. Similarly, adults in 16/26 counties had higher rates of laparoscopic procedures than the rest of the national population, and adults from 12/26 counties underwent higher rates of open appendectomy procedures. Wide dispersions are particularly evident in the adult population with open appendectomy.

Table 2 displays the statistical measures of variation for the combined population and children and adults separately. The extremal quotient was 8.3 for laparoscopic and 10.0 for open appendectomy, demonstrating greater geographic variation for open appendectomy. The coefficient of variation was high for both laparoscopic and open appendectomy; 36.7 for laparoscopic and 80.8 for open procedures, in accordance with the McPhearson interpretations[12]. This demonstrates greater geographic variability in the application of open appendectomy cases. The systematic component of variation was also high for both procedures; 14.2 for laparoscopy and 124.8 for open appendectomy.

Table 2. Variation statistics for laparoscopy, open and combined for children, adult and the whole patient population, 2014-2017.

Population/procedure	Number of episodes 2014-2017	Standardised number of episodes per 100.000 population	Extremal Quotient	Coefficient of Variation	Systematic Component of Variation
Children					
Laparoscopy	3858	383.3	16.9	55.1	41.6
Open	3485	346.2	6.5	55.3	38.2
Combined	7343	729.5	3.2	24.3	9.3
Adult					
Laparoscopy	14529	386.9	7.1	33.3	10.6
Open	1812	48.3	25.7	128.4	502.0
Combined	16341	435.1	2.1	18.9	4.5
Whole population					
Laparoscopy	18387	386.1	8.3	36.7	14.2
Open	5297	111.2	10.0	80.8	124.8
Combined	23684	497.4	2.2	19.6	5.6

Extremal quotient = max(standardised episode rate i)/min(standardised episode rate i).

Coefficient of variation = standard deviation (standardised episode rate i) / mean (standardised episode rate i) *100.

Systematic component of variations = $1/k \left(\sum (O_i - E_i)^2 / E_i^2 - \sum 1/E_i \right) * 100$ where k is number of counties, O_i is observed number of episodes and E_i is expected number of episodes determined by indirect standardisation.

Discussion

This study documents a substantial geographic variation in the operative management of acute appendicitis in the Republic of Ireland. To our knowledge, there have been no population-based studies exploring emergency appendectomy variations at a county level in Ireland. While some level of disparity is to be expected, large variations particularly in emergency interventions can indicate potential inequity and inefficiency in the use of sophisticated healthcare systems, and thus indicate variations in access and use of surgical services. Similar to the Dartmouth Atlas project, our data demonstrates that a person's likelihood of undergoing a laparoscopic or open appendectomy is related to their county of residence[9].

Laparoscopic appendectomy is favoured because of its benefits in analgesic requirements post - operatively, shorter length of hospital stay, lower post-operative mortality, and faster return to normal activities[4, 7, 8, 21, 22]. Unsurprisingly, most of the cases in our data were performed laparoscopically. As with most observational data, causality cannot be determined. Historical research suggests that the variations in the utility of surgical services may result from clinical uncertainty or heterogeneity in medical literature[23, 24]. One potential hypothetical and important reason for the variations could be individual surgeon skill and practice. The current study did not control for specific surgeon factors and may reflect a lack of laparoscopic skills or capacity in certain areas and explain the higher statistical variability for open procedures. Variations in laparoscopic surgery rates are not unheard of. An analyses by Doumouras et al suggested that laparoscopic training may influence the rate of laparoscopic practices in some hospitals[25]. While our study did not evaluate larger teaching hospitals separately, there may be an inherent geographic variation in laparoscopic expertise outside of tertiary referral centres and may also reflect variation in consultant and trainee surgeon performance as the principle operator; a factor not examined in this study.

In this study laparoscopic appendectomy utilisation appears lower in children and may indicate a deficiency in the paediatric surgery skillset available in the country and an unfamiliarity in operating on children amongst general surgeons. Multiple reports have stressed the need to provide high

quality paediatric surgery services to address the challenges and demands of paediatric patients which may be unavailable in hospitals were adult surgery appears to dominate. The findings of this study suggest a potential difference in expertise in relation to paediatric surgery in Ireland. This would parallel with the reality that most district or general hospitals in Ireland lack a specialised paediatric surgeon on site and thus cases are performed by adult surgeons. These findings suggest a potential difference in expertise in relation to paediatric surgery in Ireland.

There are some limitations to this study. As with other studies including data from administrative databases, the reliability of results is based on the accuracy and completeness of systematic coding and data input. We attempt to overcome potential miscoding information by including a large population cohort of patients over a four-year period. We have not accounted for laparoscopic cases that were converted to open due to the potential inclusion of duplicate numbers and inherent miscoding errors. Co-morbidities, procedural complexity and socioeconomic status were also not controlled for when assessing patient characteristics. However, despite these limitations our findings demonstrate concerning conclusions relating to the provision of emergency appendectomy in the Republic of Ireland for both children and adults. The analysis provides some important implications for health care providers and surgeons in analysing the extent of geographic variation and the disparity in management of a common condition. While we cannot explain the wide variations seen, further analysis at an individual county level with the assessment of more in-depth patient characteristics may uncover opportunities to eliminate variations and ultimately improve the delivery of care and patient outcomes. We also await the results of the multi-institutional Right Iliac Fossa Treatment (RIFT audit) study to further analyse the variation in the management strategies of patients presenting with RIF pain to centres across the United Kingdom, Ireland, Italy, Portugal and Spain[26].

Conclusion

Geographic variation analyses can help characterise the overall performance of a health system and determine whether patients receive equal treatment for equal needs. This is the first Irish study to systematically explore the rates and geographical disparity of acute laparoscopic and open appendectomy procedures and help bridge a pre-existing knowledge gap on the topic. The high appendectomy rates seen in several counties in this study may suggest an imbalance in the provision of a common acute surgical procedure in the Republic of Ireland. Some populations appear more likely to undergo laparoscopic procedures than other populations with considerable geographical disparity observed within a relatively small country. Large statistical variability in the paediatric population may also reflect a discrepancy in surgical paediatric care in areas where these procedures are largely performed by surgeons specialising in adult care. Based on these results, we recommend future studies to focus on the practicality of this and further analysis into the structure of emergency paediatric surgery particularly in district hospitals. Despite the limitations, our study suggests a need for more effective decision-making and planning to ensure consistency and decrease the variability in the management of acute appendicitis.

Contributors: OA conceived and designed the study, analysed the data and drafted and revised the paper. JS designed the study, prepared and analysed the data, drafted and revised the paper. KM interpreted the results and revised the paper. All authors had full access to all the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. OA is the guarantor and affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as originally planned (and, if relevant, registered) have been explained.

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Ethical approval: Ethics board approval was not required for the study.

Data sharing: All data has been included either in the main manuscript or as a supplementary file. The authors do not withhold any other data.

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References

1. Ferris M, Quan S, Kaplan BS, Molodecky N, Ball CG, Chernoff GW, et al. The Global Incidence of Appendicitis: A Systematic Review of Population-based Studies. *Annals of surgery* 2017;**266**(2): 237-241.
2. Kaplan GG, Dixon E, Panaccione R, Fong A, Chen L, Szyszkowicz M, et al. Effect of ambient air pollution on the incidence of appendicitis. *Canadian Medical Association Journal* 2009;**181**(9): 591-597.
3. Kaplan GG, Tanyingoh D, Dixon E, Johnson M, Wheeler AJ, Myers RP, et al. Ambient ozone concentrations and the risk of perforated and nonperforated appendicitis: a multicity case-crossover study. *Environmental health perspectives* 2013;**121**(8): 939.
4. Tate JJT, Dawson JW, Chung SCS, Lau WY, Li AKC. Laparoscopic versus open appendicectomy: prospective randomised trial. *The Lancet* 1993;**342**(8872): 633-637.
5. Southgate E, Vousden N, Karthikesalingam A, Markar SR, Black S, Zaidi A. Laparoscopic vs open appendectomy in older patients. *Archives of Surgery* 2012;**147**(6): 557-562.
6. Adwan H, Weerasuriya CK, Endleman P, Barnes A, Stewart L, Justin T. Laparoscopic versus open appendicectomy in children: A UK District General Hospital experience. *Journal of Pediatric Surgery* 2014;**49**(2): 277-279.
7. Thomson J-E, Kruger D, Jann-Kruger C, Kiss A, Omoshoro-Jones J, Luvhengo T, et al. Laparoscopic versus open surgery for complicated appendicitis: a randomized controlled trial to prove safety. *Surgical endoscopy* 2015;**29**(7): 2027-2032.
8. Tiwari MM, Reynoso JF, Tsang AW, Oleynikov D. Comparison of outcomes of laparoscopic and open appendectomy in management of uncomplicated and complicated appendicitis. *Annals of surgery* 2011;**254**(6): 927-932.
9. Practice TDIoHPaC. The Dartmouth Atlas Project Database. 1996 - 2010.
10. Reames BN, Shubeck SP, Birkmeyer JD. Strategies for Reducing Regional Variation in the Use of Surgery A Systematic Review. *Annals of surgery* 2014;**259**(4): 616.
11. Ahmed O, Mealy K, Kelliher G, Keane F, Sorensen J. Exploring geographical variation in access to general surgery in Ireland: Evidence from a national study. *The Surgeon* 2019.
12. McPherson K, Wennberg JE, Hovind OB, Clifford P. Small-area variations in the use of common surgical procedures: an international comparison of New England, England, and Norway. *New England journal of medicine* 1982;**307**(21): 1310-1314.
13. Weeks WB, Paraponaris A, Ventelou B. Geographic variation in rates of common surgical procedures in France in 2008–2010, and comparison to the US and Britain. *Health Policy* 2014;**118**(2): 215-221.
14. Katsuno G, Nagakari K, Yoshikawa S, Sugiyama K, Fukunaga M. Laparoscopic Appendectomy for Complicated Appendicitis: A Comparison with Open Appendectomy. *World Journal of Surgery* 2009;**33**(2): 208-214.
15. Masoomi H, Mills S, Dolich MO, Ketana N, Carmichael JC, Nguyen NT, et al. Comparison of Outcomes of Laparoscopic Versus Open Appendectomy in Adults: Data from the Nationwide Inpatient Sample (NIS), 2006–2008. *Journal of Gastrointestinal Surgery* 2011;**15**(12): 2226-2231.
16. Litz CN, Ciesla DJ, Danielson PD, Chandler NM. Effect of hospital type on the treatment of acute appendicitis in teenagers. *Journal of Pediatric Surgery* 2018;**53**(3): 446-448.
17. Scoreboard MIP. Central Statistics Office statistical release. In: June; 2015.
18. Appleby J, Raleigh V, Frosini F, Bevan G, Gao H, Lyscom T. *Variations in health care: the good, the bad and the inexplicable*. King's Fund, 2011.
19. Birkmeyer JD, Reames BN, McCulloch P, Carr AJ, Campbell WB, Wennberg JE. Understanding of regional variation in the use of surgery. *The Lancet* 2013;**382**(9898): 1121-1129.
20. Chassin MR, Brook RH, Park RE, Keesey J, Fink A, Kosecoff J, et al. *Variations in the use of medical and surgical services by the Medicare population*. Rand, 1986.

21. Sauerland S, Jaschinski T, Neugebauer EAM. Laparoscopic versus open surgery for suspected appendicitis. *Cochrane Database of Systematic Reviews* 2010(10).
22. Faiz O, Clark J, Brown T, Bottle A, Antoniou A, Farrands P, et al. Traditional and laparoscopic appendectomy in adults: outcomes in English NHS hospitals between 1996 and 2006. *Annals of surgery* 2008;**248**(5): 800-806.
23. Ray-Coquard I, Philip T, Lehmann M, Fervers B, Farsi F, Chauvin F. Impact of a clinical guidelines program for breast and colon cancer in a French cancer center. *Jama* 1997;**278**(19): 1591-1595.
24. Wennberg JE. Dealing with medical practice variations: a proposal for action. *Health Affairs* 1984;**3**(2): 6-33.
25. Doumouras AG, Saleh F, Eskicioglu C, Amin N, Cadeddu M, Hong D. Neighborhood variation in the utilization of laparoscopy for the treatment of colon cancer. *Diseases of the Colon & Rectum* 2016;**59**(8): 781-788.
26. Right Iliac Fossa Pain Treatment (RIFT) Study: protocol for an international, multicentre, prospective observational study. *BMJ open* 2018;**8**(1): e017574.

Figure legend:

Figure 1 - Proportion of appendectomies conducted as laparoscopic procedures during 2014-2017 in children and adult patients

Figure 2 – Number of procedures performed during 2014-2017 on county residents

Figure 3 - Ratio of observed/expected number of episodes of appendectomy by county for children and adults.

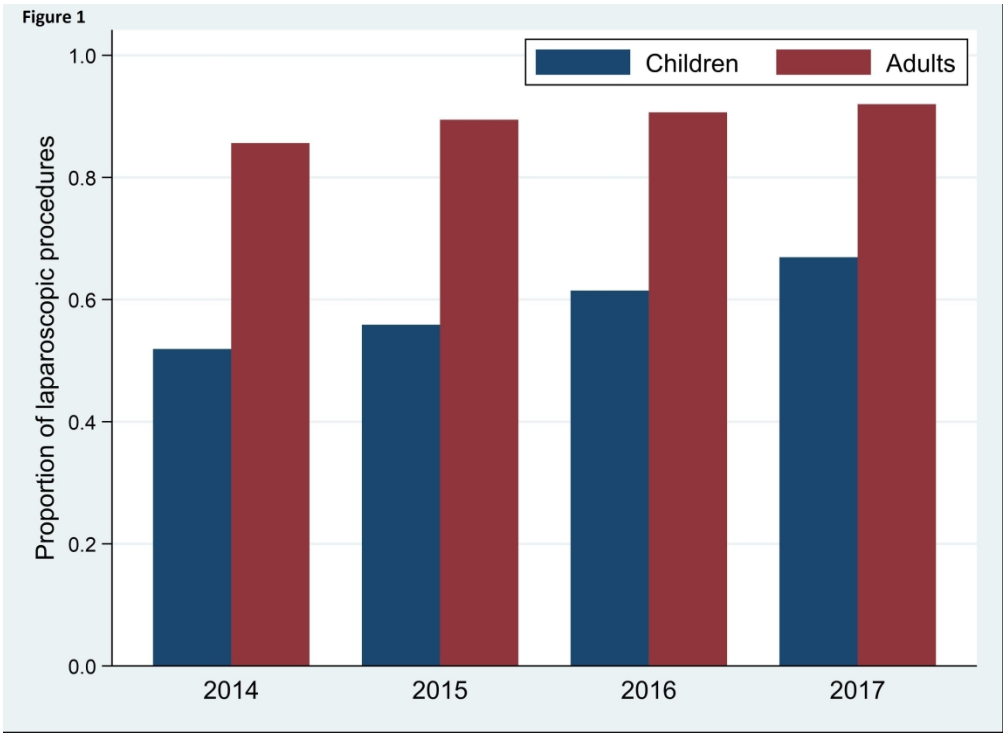
Figure 4 - Association between children and adult's ratio of observed/expected number of episodes of appendectomy by county**.**

Figure 5 - Ratio of observed/expected number of episodes of laparoscopy and open appendectomy by county for children and adults.

Table 1 – Adult and paediatric laparoscopic and open appendectomy percentage rates..

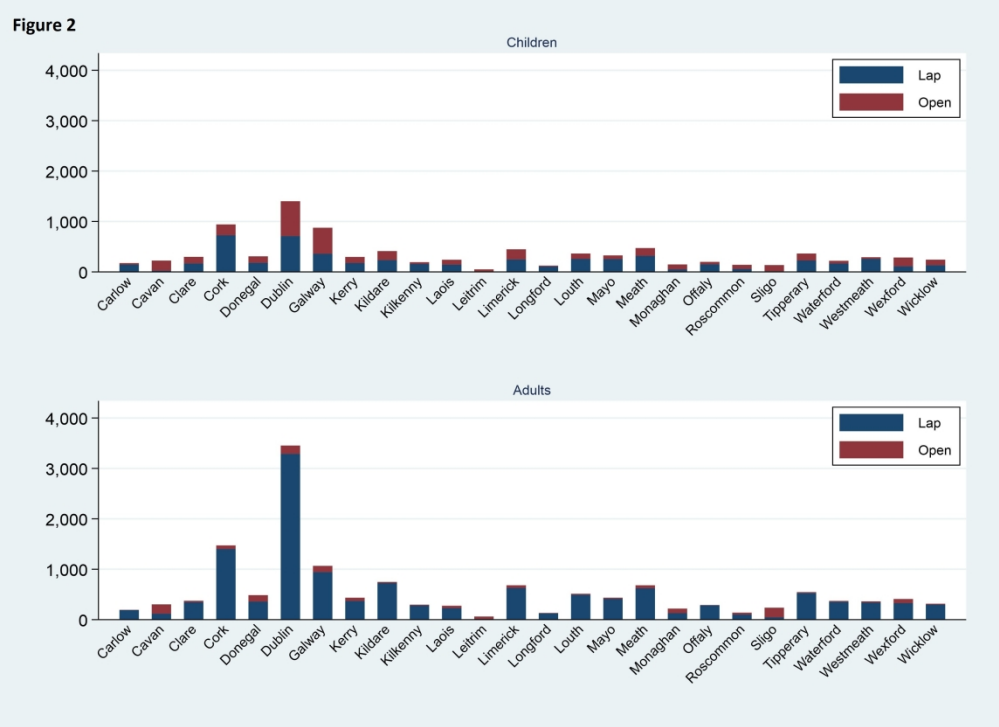
Table 2 – Variation statistics for laparoscopy, open and combined for children, adult and the whole patient population, 2014-2017.

Online supplementary table – Proportion of laparoscopic appendectomies per year by county of residence for child and adult population.



Proportion of appendectomies conducted as laparoscopic procedures during 2014-2017 in children and adult patients

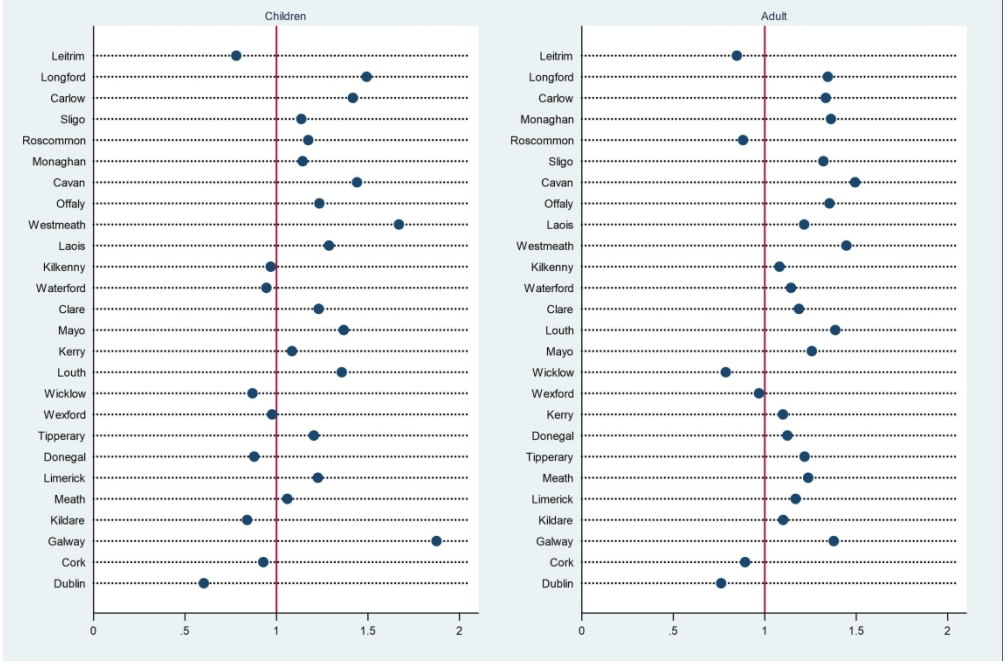
279x203mm (300 x 300 DPI)



Number of procedures performed during 2014-2017 on county residents

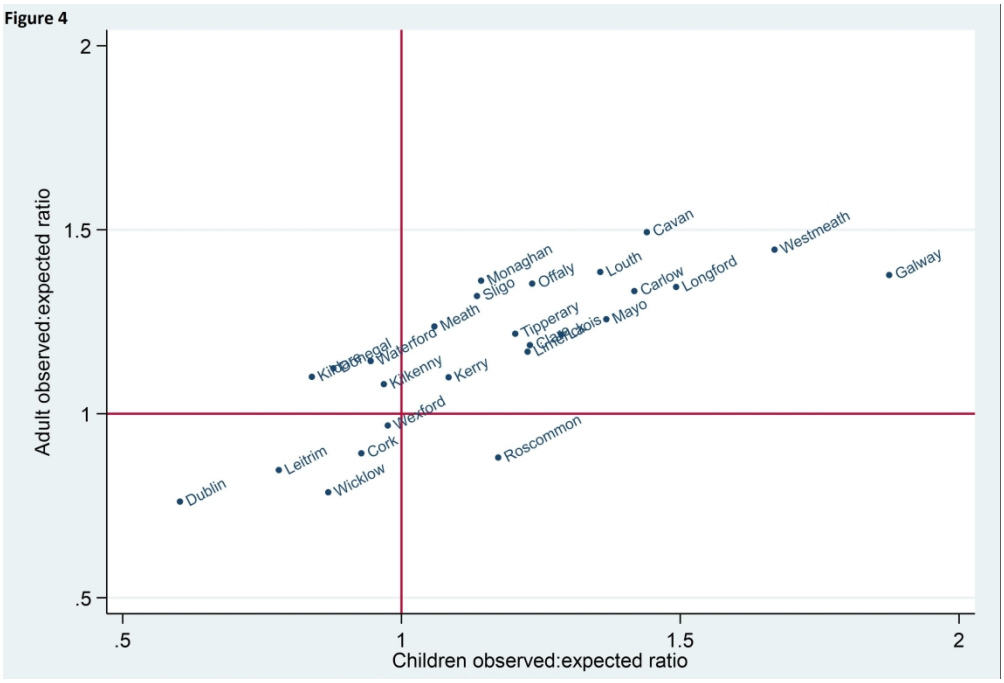
279x203mm (300 x 300 DPI)

Figure 3



Ratio of observed/expected number of episodes of appendectomy by county for children and adults.

276x190mm (300 x 300 DPI)



Association between children and adult's ratio of observed/expected number of episodes of appendectomy by county.

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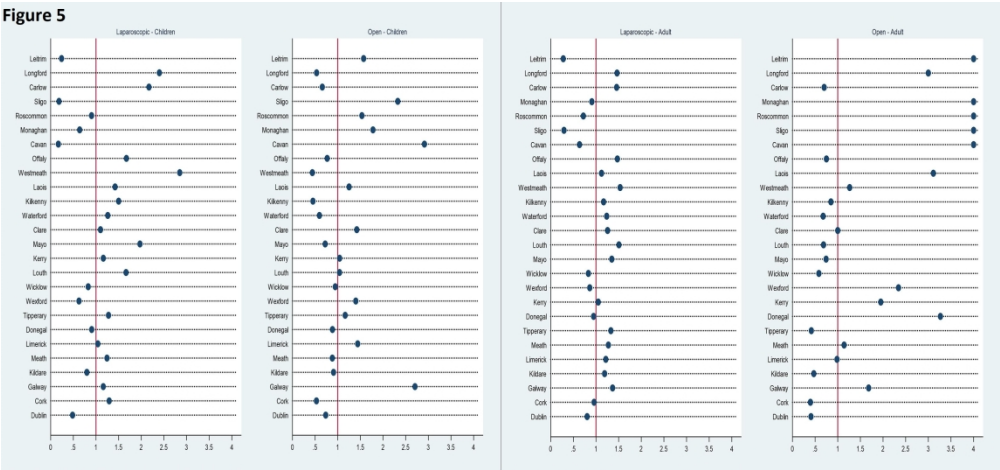
Figure 5



Ratio of observed/expected number of episodes of laparoscopy and open appendectomy by county for children and adults.

279x131mm (300 x 300 DPI)

Online Supplementary Table Proportion of laparoscopic appendectomies per year by county of residence for child and adult population

Proportion of laparoscopic procedures								
	Children				Adults			
County	**2014**	**2015**	**2016**	**2017**	**2014**	**2015**	**2016**	**2017**
Carlow	0.74	0.91	0.84	0.90	0.90	0.98	0.96	1.0
Cavan	0.11	0.14	0.08	0.13	0.22	0.51	0.44	0.5
Clare	0.56	0.43	0.59	0.65	0.90	0.94	0.88	0.97
Cork	0.65	0.76	0.8	0.87	0.93	0.96	0.97	0.95
Donegal	0.25	0.46	0.77	0.89	0.54	0.73	0.78	0.86
Dublin	0.44	0.42	0.54	0.64	0.93	0.96	0.96	0.96
Galway	0.39	0.41	0.38	0.47	0.86	0.89	0.89	0.90
Kerry	0.46	0.66	0.71	0.60	0.80	0.85	0.92	0.90
Kildare	0.49	0.62	0.64	0.56	0.97	0.97	0.98	0.98
Kilkenny	0.75	0.84	0.82	0.89	0.89	0.93	0.95	0.99
Laois	0.47	0.45	0.64	0.81	0.80	0.78	0.79	0.96
Leitrim	0.14	0.27	0.11	0.22	0.27	0.15	0.33	0.46
Limerick	0.44	0.50	0.54	0.70	0.89	0.93	0.90	0.95
Longford	0.70	0.97	0.90	0.93	0.90	0.93	0.92	0.92
Louth	0.66	0.61	0.78	0.77	0.96	0.97	0.93	0.96
Mayo	0.73	0.83	0.78	0.79	0.94	0.94	0.98	0.94
Meath	0.59	0.61	0.74	0.75	0.89	0.91	0.94	0.93
Monaghan	0.35	0.30	0.33	0.41	0.59	0.51	0.77	0.51
Offaly	0.65	0.78	0.83	0.78	0.94	0.98	1.00	0.95
Roscommon	0.42	0.39	0.50	0.47	0.69	0.68	0.75	0.865
Sligo	0.12	0.1	0.09	0.19	0.18	0.19	0.20	0.19
Tipperary	0.63	0.68	0.60	0.60	0.94	0.98	0.98	0.98
Waterford	0.75	0.80	0.77	0.74	0.92	0.94	0.98	0.96
Westmeath	0.86	0.84	0.92	0.92	0.89	0.96	0.96	0.97
Wexford	0.25	0.19	0.53	0.52	0.68	0.67	0.82	0.93
Wicklow	0.67	0.61	0.50	0.40	0.98	0.90	0.94	0.97

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*5*
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	n/a
		(*d*) If applicable, explain how loss to follow-up was addressed	n/a
		(*e*) Describe any sensitivity analyses	n/a
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7
		(b) Indicate number of participants with missing data for each variable of interest	n/a
		(c) Summarise follow-up time (eg, average and total amount)	n/a
Outcome data	15*	Report numbers of outcome events or summary measures over time	7,8,9,10,
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8,9, 10
		(*b*) Report category boundaries when continuous variables were categorized	8, 9
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8,9,10,
Discussion			
Key results	18	Summarise key results with reference to study objectives	11, 12,13,
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12
Generalisability	21	Discuss the generalisability (external validity) of the study results	12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Exploring geographic variation in acute appendectomy in Ireland: results from a national registry

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Exploring geographic variation in acute appendectomy in Ireland: results from a national registry

Authors:

Ola Ahmed, Ken Mealy, Jan Sorensen

1. Department of General Surgery, Wexford General Hospital, Wexford, Ireland

   Ms Ola Ahmed

   Trainee Surgeon

2. National Clinical Programme in Surgery, Royal College of Surgeons in Ireland, Dublin 2, Ireland; Department of General Surgery, Wexford General Hospital, Wexford, Ireland

   Mr Ken Mealy

   Consultant Surgeon

3. Healthcare Outcomes Research Centre, Royal College of Surgeons in Ireland, Dublin 2, Ireland

   Professor Jan Sorensen

   Director of the Healthcare Outcomes Research Centre

Correspondence to: Ms Ola Ahmed, Department of General Surgery, Wexford General Hospital, Wexford, Ireland

Email: olasdahmed@gmail.com

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Strengths and limitations of this study

- The study employed a large, well-defined patient population of the Republic of Ireland.
- All data was age and gender standardised as is standard when analysing geographical variation in healthcare, including the Dartmouth Atlas Project.
- The study does not include data from private hospitals, however acute appendicitis is largely managed in public hospitals regardless of medical insurance cover.
- Co-morbidities, procedural complexity and socioeconomic status were not controlled for when assessing patient characteristics.
- Future studies should expand on this study design and additional examination of regional and local variations perhaps in a risk adjusted setting should be a priority.

Abstract

Objective To explore geographic variations in Irish laparoscopic and open appendectomy procedures.

Design Analysis based on 2014-2017 administrative hospital data from public hospitals.

Setting Counties of the Republic of Ireland.

Participants Irish residents with hospital admissions for an appendectomy as the principal procedure.

Main outcome measures Age and gender standardised laparoscopic and open appendectomy rates for 26 counties. Geographic variation measured with the extremal quotient (EQ), coefficient of variation (CV) and the systematic component of variation (SCV).

Results 23,684 appendectomies were included. 77.6% (n= 18,387) were performed laparoscopically. An EQ of 8.3 for laparoscopy and 10.0 for open appendectomy was determined. A high CV was demonstrated with a value of 36.7 and 80.8 for laparoscopic and open appendectomy. A SCV of 14.2 and 124.8 for laparoscopic and open appendectomy was observed. A wider variation was determined when children and adults were assessed separately.

Conclusions The geographic distribution in rates of appendectomy varies considerably across Irish counties. Our data suggests that a patient's likelihood of undergoing a laparoscopic or open appendectomy is associated with their county of residence.

Introduction

Acute appendicitis continues to be a global disease with escalating incidence rates in rapidly developing and industrialised countries[1]. These epidemiological associations contribute to the evolving knowledge on the pathogenesis of acute appendicitis and the influences of environmental triggers[2, 3]. Modern advances in laparoscopic surgery over the past two decades have led to the demonstrable advantage of laparoscopic appendectomy over open techniques across all populations[4-6]. Laparoscopy is associated with shorter hospital length of stay, decreased analgesic requirements, and lower morbidity rates in comparison with open surgery[4, 7, 8]. However, while laparoscopic approaches are preferred in most instances, open appendectomy is still practiced in cases where laparoscopy is difficult or contraindicated.

Analysing regional variations in the provision of common procedures helps raise questions relating to service provision as well as identify opportunities for improving efficiency and observing best practice. The Dartmouth Atlas Project has shown wide variations of up to 10-fold for a multitude of surgical procedures across geographical sites in the United States[9]. This initiative has led to several studies of geographic variation in other countries which appear to demonstrate that a patient's likelihood of undergoing specific surgical procedures depends greatly on where they live[10-13]. Reasons for the regional variability of laparoscopic and open appendectomy are still unclear. The observed rates of open appendectomy vary widely in the literature from 6 – 35% with higher variations in the adult population[14-16]. The aim of this study was to systematically investigate the regional variation of the surgical care of acute appendicitis in the Republic of Ireland. We compare the national data of laparoscopic and open appendectomy rates for children and adults to provide a current view of regional variation rates. By analysing and comparing the patterns of utilisation of both the adult and paediatric population in Ireland, we seek to understand the extent that area of residence may influence the likelihood of undergoing either a laparoscopic or open procedure.

Methods

Data extraction

Anonymised patient data were obtained for a 4-year period from 2014 to 2017 from the National Quality Assurance and Improvement System (NQAIS). NQAIS is an online application based on the Hospital Inpatient Enquiry system (HIPE) operated by the national Health Service Executive in Ireland. Established in 1971, HIPE collects clinical and administrative data on discharges from acute Irish public hospitals. A HIPE record is created following a patient's discharge from a public hospital and offers demographic and clinical information for the episode of care. The current HIPE system only holds data for public hospitals and no national database is available on the activities in the private hospital sector. This analysis includes only patients treated in public hospitals regardless of their individual insurance status. We obtained records of all hospital episodes coded with laparoscopic appendectomy or open appendectomy as the primary procedure. From this sample we excluded episodes with primary diagnostic codes different from "Appendicitis", "Suspected appendicitis", or "Rule-out appendicitis" (i.e. not coded with K35-37 in the International Classification of Diseases Version 10 Clinical Modification (ICD-10-CM)), episodes coded as non-emergency admissions, and episodes for patients who are not residents in Ireland.

The Republic of Ireland is made up of 26 geographical subdivisions referred to as counties. These counties were used in this study to determine appendectomy rates per geographical area. County of residence is a variable in HIPE which can be utilised to determine residential status of individual persons irrespective of where the actual procedure was performed. We obtained population statistics from the 2016 census from the Central Statistical Office[17].

Patient factors considered in the analysis were age, gender and county of residence**.** Children were categorized as patients aged 14 years or younger to correspond with the 5-year age groups in the

available census data. National age and gender stratification was derived from the population of 4,761,865 referred to in the 2016-population census[17].

Statistical analysis

Data was analysed using Stata version 15.1 (StataCorp, Texas). Descriptive statistics were recorded for patient characteristics and procedure type. Continuous variables were compared using unpaired t-tests. Association of categorical variables (differences for dichotomous variables between groups) was assessed using the chi-square (X^2) test. Continuous numerical variables were reported as means and standard deviations (SD). Categorical variables were reported as proportions or percentages.

To assess relative variability we used methods described by McPhearson and colleagues[12]. These established methods of geographic variation are widely used in small-area variation studies and allow for context and comparison across geographical settings and countries[13, 18, 19]. The extremal quotient (EQ) is presented as the ratio of the highest and lowest standardised county rate. A value close to 1 indicates low variation in rates across counties. The coefficient of variation (CV) is a measure of relative variability and is calculated as the standard deviation of the county rates divided by the mean of county rates. A value greater than 0.3 is considered "highly variable" in accordance to studies by McPhearson et al with higher scores indicating greater variability[12, 20]. The systematic component of variation (SCV) is also a measure of variation. This is the difference between the random component of variation and the total variation. Homogeneity in rates between areas would result in a value of zero. A large SCV value indicates large systematic and regional variation[12]. We estimated these variability measures for the whole population and for children and adults separately.

Patient involvement

No patients were involved in setting the research question or the outcome measures, nor were they involved in the development of design or implementation of the study. No patients were asked to advise on interpretation or writing up of results.

Results

National analysis

A total of 26,760 episodes of care discharged through January 1st 2014 to December 31st 2017 were extracted. In this sample 1902 episodes were coded with diagnoses other than K35-K37; 885 episodes were coded as non-emergency admissions; 289 episodes related to non-Ireland residents. After exclusion of these episodes, our study sample included 23,684 episodes of care of which 77.6% were laparoscopic appendectomies and 22.4% were open appendectomies. 53.7% of patients were male and the mean age was 25 years (SD 15, median 20, range 0-98). These findings are summarized in Table 1.

Table 1 Number of adult and paediatric laparoscopic and open appendectomy

	Laparoscopic (n (%))	Open (n (%))	Total (n (%))	P value
Children (n=7343)				
Male	2068 (49.1%)	2140 (50.9%)	4208 (100%)	
Female	1790 (57.1%)	1345 (42.9%)	3135 (100%)	<0.01
Adult (n=16341)				
Male	7387 (86.8%)	1126 (13.2%)	8513 (100%)	
Female	7142 (91.2%)	686 (8.8%)	7828 (100%)	<0.01

The percentage of laparoscopic procedures was 52.6% among children and 88.9% among adults (statistically significant difference; OR 7.2 95% CI 6.8-7.7). Figure 1 displays the proportion of appendectomies conducted as laparoscopic procedures for 2014 to 2017 in children and adult patients. The proportion of laparoscopic procedures increased steadily during the studied years from 2014 to 2017 from 72.7% to 83.3% (trend p<0.01). For children the proportion increased from 43.9% to 61.4% (trend p<0.01).

Girls were more likely to have laparoscopic procedures than boys (57.1% vs 49.1%, OR 1.4 95% CI 1.3-1.5), and women more likely than men (91.2% vs 86.8%, OR 1.6 95% CI 1.4-1.8). A clear age gradient was observed when comparing laparoscopic and open appendectomy procedures for the whole population and for both men and women separately (Figure 2) (OR 1.016, 95%CI 1.013;1.020) The proportion of patients undergoing laparoscopic procedures reduced for older patients in both

genders (logistic regression p<0.01) and appears statistically lower for patients older than 45 years (p<0.01).

County analysis

Figure 3 displays the number of laparoscopic and open procedures performed on children and adults during the years 2014 to 2017 by county of residence. The annual appendectomy rate was estimated at 124.4 procedures per 100,000 persons and 96.5 and 27.8 for laparoscopic and open approaches respectively. The online supplementary table shows the proportion of laparoscopic appendectomies per year by county of residence for the child and adult population. The data displays a gradual increase in the number of laparoscopic procedures performed in both patient groups during the 4-year study period.

Figure 4 presents the ratio of the observed and expected number of the total appendectomy rates within different counties for both children and adults and displays the geographic dispersions determined. The expected number of procedures was estimated by relating the national age and gender procedure rate to the county population and demonstrates the inter-county discrepancies in a risk adjusted setting. A value of 1 was determined to be the national average rate to allow for comparison between geographic areas. The ratio takes a value larger than 1 when the numbers of observed procedures are higher than the expected number of procedures. This would indicate a high volume county when compared with the national average value. For children, 17/26 counties displayed a higher than average rate of appendectomy procedures. For the adult population, residents from 20/26 counties underwent appendectomy procedures at a higher rate than the national average.

Figure 5 presents the association between the ratio of observed and expected procedures for children and adults. Counties in the north-east quadrant have a higher than expected number of procedures for both children and adults. These counties demonstrate higher rates of appendectomy procedures for their entire populations. There appears to be a strong association between the ratio

for children and adults indicating that counties with a higher ratio for children also have a higher ratio for adults. Counties in the south-west quadrant have a lower than expected number of procedures for both children and adults. Using similar reasoning, counties with lower rates of paediatric appendectomy procedures appeared to have low rates for the adult population also. Only four counties have a different pattern. Roscommon is the only county where children have more than the expected episodes of care and adults have fewer than the expected episodes of care, while the reverse appears for Kilkenny, Waterford, Donegal and Kildare. These remaining four counties display high rates in the adult population but lower than average rates in the paediatric patient group.

Figure 6 displays the ratio of observed and expected procedures for laparoscopic and open procedures for children and adults separately. Wide population dispersions are demonstrated in children for both laparoscopic and open appendectomy. In 16/26 counties children underwent laparoscopic appendectomy at rates higher than the national average, indicating areas with high utilisation. Children from 13/26 counties underwent higher rates of open appendectomy procedures than the rest of the general population. Similarly, adults in 16/26 counties had higher rates of laparoscopic procedures than the rest of the national population, and adults from 12/26 counties underwent higher rates of open appendectomy procedures. Wide dispersions are particularly evident in the adult population with open appendectomy.

Table 2 displays the statistical measures of variation for the combined population and children and adults separately. The extremal quotient was 8.3 for laparoscopic and 10.0 for open appendectomy, demonstrating greater geographic variation for open appendectomy. The coefficient of variation was high for both laparoscopic and open appendectomy; 36.7 for laparoscopic and 80.8 for open procedures, in accordance with the McPhearson interpretations[12]. This demonstrates greater geographic variability in the application of open appendectomy cases. The systematic component of variation was also high for both procedures; 14.2 for laparoscopy and 124.8 for open appendectomy.

Table 2. Variation statistics for laparoscopy, open and combined for children, adult and the whole patient population, 2014-2017.

Population/procedure	Number of episodes 2014-2017	Standardised number of episodes per 100.000 population	Extremal Quotient	Coefficient of Variation	Systematic Component of Variation
Children					
Laparoscopy	3858	383.3	16.9	55.1	41.6
Open	3485	346.2	6.5	55.3	38.2
Combined	7343	729.5	3.2	24.3	9.3
Adult					
Laparoscopy	14529	386.9	7.1	33.3	10.6
Open	1812	48.3	25.7	128.4	502.0
Combined	16341	435.1	2.1	18.9	4.5
Whole population					
Laparoscopy	18387	386.1	8.3	36.7	14.2
Open	5297	111.2	10.0	80.8	124.8
Combined	23684	497.4	2.2	19.6	5.6

Extremal quotient = max(standardised episode rate i)/min(standardised episode rate i).

Coefficient of variation = standard deviation (standardised episode rate i) / mean (standardised episode rate i) *100.

Systematic component of variations = $1/k \left(\sum (O_i - E_i)^2 / E_i^2 - \sum 1/E_i \right) * 100$ where k is number of counties, O_i is observed number of episodes and E_i is expected number of episodes determined by indirect standardisation.

Discussion

This study documents a substantial geographic variation in the operative management of acute appendicitis in the Republic of Ireland. To our knowledge, there have been no population-based studies exploring emergency appendectomy variations at a county level in Ireland. While some level of disparity is to be expected, large variations particularly in emergency interventions can indicate potential inequity and inefficiency in the use of sophisticated healthcare systems, and thus indicate variations in access and use of surgical services. Similar to the Dartmouth Atlas project, our data demonstrates that a person's likelihood of undergoing a laparoscopic or open appendectomy is related to their county of residence[9].

Laparoscopic appendectomy is favoured because of its benefits in analgesic requirements post - operatively, shorter length of hospital stay, lower post-operative mortality, and faster return to normal activities[4, 7, 8, 21, 22]. Unsurprisingly, most of the cases in our data were performed laparoscopically. As with most observational data, causality cannot be determined. Historical research suggests that the variations in the utility of surgical services may result from clinical uncertainty or heterogeneity in medical literature[23, 24]. One potential hypothetical and important reason for the variations could be individual surgeon skill and practice. The current study did not control for specific surgeon factors and may reflect a lack of laparoscopic skills or capacity in certain areas and explain the higher statistical variability for open procedures. Variations in laparoscopic surgery rates are not unheard of. An analyses by Doumouras et al suggested that laparoscopic training may influence the rate of laparoscopic practices in some hospitals[25]. While our study did not evaluate larger teaching hospitals separately, there may be an inherent geographic variation in laparoscopic expertise outside of tertiary referral centres and may also reflect variation in consultant and trainee surgeon performance as the principle operator; a factor not examined in this study.

In this study laparoscopic appendectomy utilisation appears lower in children and may indicate a deficiency in the paediatric surgery skillset available in the country and an unfamiliarity in operating on children amongst general surgeons. Multiple reports have stressed the need to provide high

quality paediatric surgery services to address the challenges and demands of paediatric patients which may be unavailable in hospitals were adult surgery appears to dominate. The findings of this study suggest a potential difference in expertise in relation to paediatric surgery in Ireland. This would parallel with the reality that most district or general hospitals in Ireland lack a specialised paediatric surgeon on site and thus cases are performed by adult surgeons. These findings suggest a potential difference in expertise in relation to paediatric surgery in Ireland.

There are some limitations to this study. As with other studies including data from administrative databases, the reliability of results is based on the accuracy and completeness of systematic coding and data input. We attempt to overcome potential miscoding information by including a large population cohort of patients over a four-year period. We have not accounted for laparoscopic cases that were converted to open due to the potential inclusion of duplicate numbers and inherent miscoding errors. Co-morbidities, procedural complexity and socioeconomic status were also not controlled for when assessing patient characteristics. However, despite these limitations our findings demonstrate concerning conclusions relating to the provision of emergency appendectomy in the Republic of Ireland for both children and adults. The analysis provides some important implications for health care providers and surgeons in analysing the extent of geographic variation and the disparity in management of a common condition. While we cannot explain the wide variations seen, further analysis at an individual county level with the assessment of more in-depth patient characteristics may uncover opportunities to eliminate variations and ultimately improve the delivery of care and patient outcomes. We also await the results of the multi-institutional Right Iliac Fossa Treatment (RIFT audit) study to further analyse the variation in the management strategies of patients presenting with RIF pain to centres across the United Kingdom, Ireland, Italy, Portugal and Spain[26].

Conclusion

Geographic variation analyses can help characterise the overall performance of a health system and determine whether patients receive equal treatment for equal needs. This is the first Irish study to systematically explore the rates and geographical disparity of acute laparoscopic and open appendectomy procedures and help bridge a pre-existing knowledge gap on the topic. The high appendectomy rates seen in several counties in this study may suggest an imbalance in the provision of a common acute surgical procedure in the Republic of Ireland. Some populations appear more likely to undergo laparoscopic procedures than other populations with considerable geographical disparity observed within a relatively small country. Large statistical variability in the paediatric population may also reflect a discrepancy in surgical paediatric care in areas where these procedures are largely performed by surgeons specialising in adult care. Based on these results, we recommend future studies to focus on the practicality of this and further analysis into the structure of emergency paediatric surgery particularly in district hospitals. Despite the limitations, our study suggests a need for more effective decision-making and planning to ensure consistency and decrease the variability in the management of acute appendicitis.

Contributors: OA conceived and designed the study, analysed the data and drafted and revised the paper. JS designed the study, prepared and analysed the data, drafted and revised the paper. KM interpreted the results and revised the paper. All authors had full access to all the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. OA is the guarantor and affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as originally planned (and, if relevant, registered) have been explained.

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Competing interests: All authors declare no conflicts in interests in the preparation of this study and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Ethical approval: Ethics board approval was not required for the study.

Data sharing: All data has been included either in the main manuscript or as a supplementary file. The authors do not withhold any other data.

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References

1. Ferris M, Quan S, Kaplan BS, Molodecky N, Ball CG, Chernoff GW, et al. The Global Incidence of Appendicitis: A Systematic Review of Population-based Studies. *Annals of surgery* 2017;**266**(2): 237-241.
2. Kaplan GG, Dixon E, Panaccione R, Fong A, Chen L, Szyszkowicz M, et al. Effect of ambient air pollution on the incidence of appendicitis. *Canadian Medical Association Journal* 2009;**181**(9): 591-597.
3. Kaplan GG, Tanyingoh D, Dixon E, Johnson M, Wheeler AJ, Myers RP, et al. Ambient ozone concentrations and the risk of perforated and nonperforated appendicitis: a multicity case-crossover study. *Environmental health perspectives* 2013;**121**(8): 939.
4. Tate JJT, Dawson JW, Chung SCS, Lau WY, Li AKC. Laparoscopic versus open appendicectomy: prospective randomised trial. *The Lancet* 1993;**342**(8872): 633-637.
5. Southgate E, Vousden N, Karthikesalingam A, Markar SR, Black S, Zaidi A. Laparoscopic vs open appendectomy in older patients. *Archives of Surgery* 2012;**147**(6): 557-562.
6. Adwan H, Weerasuriya CK, Endleman P, Barnes A, Stewart L, Justin T. Laparoscopic versus open appendicectomy in children: A UK District General Hospital experience. *Journal of Pediatric Surgery* 2014;**49**(2): 277-279.
7. Thomson J-E, Kruger D, Jann-Kruger C, Kiss A, Omoshoro-Jones J, Luvhengo T, et al. Laparoscopic versus open surgery for complicated appendicitis: a randomized controlled trial to prove safety. *Surgical endoscopy* 2015;**29**(7): 2027-2032.
8. Tiwari MM, Reynoso JF, Tsang AW, Oleynikov D. Comparison of outcomes of laparoscopic and open appendectomy in management of uncomplicated and complicated appendicitis. *Annals of surgery* 2011;**254**(6): 927-932.
9. Practice TDIoHPaC. The Dartmouth Atlas Project Database. 1996 - 2010.
10. Reames BN, Shubeck SP, Birkmeyer JD. Strategies for Reducing Regional Variation in the Use of Surgery A Systematic Review. *Annals of surgery* 2014;**259**(4): 616.
11. Ahmed O, Mealy K, Kelliher G, Keane F, Sorensen J. Exploring geographical variation in access to general surgery in Ireland: Evidence from a national study. *The Surgeon* 2019.
12. McPherson K, Wennberg JE, Hovind OB, Clifford P. Small-area variations in the use of common surgical procedures: an international comparison of New England, England, and Norway. *New England journal of medicine* 1982;**307**(21): 1310-1314.
13. Weeks WB, Paraponaris A, Ventelou B. Geographic variation in rates of common surgical procedures in France in 2008–2010, and comparison to the US and Britain. *Health Policy* 2014;**118**(2): 215-221.
14. Katsuno G, Nagakari K, Yoshikawa S, Sugiyama K, Fukunaga M. Laparoscopic Appendectomy for Complicated Appendicitis: A Comparison with Open Appendectomy. *World Journal of Surgery* 2009;**33**(2): 208-214.
15. Masoomi H, Mills S, Dolich MO, Ketana N, Carmichael JC, Nguyen NT, et al. Comparison of Outcomes of Laparoscopic Versus Open Appendectomy in Adults: Data from the Nationwide Inpatient Sample (NIS), 2006–2008. *Journal of Gastrointestinal Surgery* 2011;**15**(12): 2226-2231.
16. Litz CN, Ciesla DJ, Danielson PD, Chandler NM. Effect of hospital type on the treatment of acute appendicitis in teenagers. *Journal of Pediatric Surgery* 2018;**53**(3): 446-448.
17. Scoreboard MIP. Central Statistics Office statistical release. In: June; 2015.
18. Appleby J, Raleigh V, Frosini F, Bevan G, Gao H, Lyscom T. *Variations in health care: the good, the bad and the inexplicable*. King's Fund, 2011.
19. Birkmeyer JD, Reames BN, McCulloch P, Carr AJ, Campbell WB, Wennberg JE. Understanding of regional variation in the use of surgery. *The Lancet* 2013;**382**(9898): 1121-1129.
20. Chassin MR, Brook RH, Park RE, Keesey J, Fink A, Kosecoff J, et al. *Variations in the use of medical and surgical services by the Medicare population*. Rand, 1986.

21. Sauerland S, Jaschinski T, Neugebauer EAM. Laparoscopic versus open surgery for suspected appendicitis. *Cochrane Database of Systematic Reviews* 2010(10).
22. Faiz O, Clark J, Brown T, Bottle A, Antoniou A, Farrands P, et al. Traditional and laparoscopic appendectomy in adults: outcomes in English NHS hospitals between 1996 and 2006. *Annals of surgery* 2008;**248**(5): 800-806.
23. Ray-Coquard I, Philip T, Lehmann M, Fervers B, Farsi F, Chauvin F. Impact of a clinical guidelines program for breast and colon cancer in a French cancer center. *Jama* 1997;**278**(19): 1591-1595.
24. Wennberg JE. Dealing with medical practice variations: a proposal for action. *Health Affairs* 1984;**3**(2): 6-33.
25. Doumouras AG, Saleh F, Eskicioglu C, Amin N, Cadeddu M, Hong D. Neighborhood variation in the utilization of laparoscopy for the treatment of colon cancer. *Diseases of the Colon & Rectum* 2016;**59**(8): 781-788.
26. Right Iliac Fossa Pain Treatment (RIFT) Study: protocol for an international, multicentre, prospective observational study. *BMJ open* 2018;**8**(1): e017574.

Figure legend:

Figure 1 - Proportion of appendectomies conducted as laparoscopic procedures during 2014-2017 in children and adult patients

Figure 2 – Age and gender distribution for laparoscopic and open appendectomy.

Figure 3 – Number of procedures performed during 2014-2017 on county residents

Figure 4 - Ratio of observed/expected number of episodes of appendectomy by county for children and adults.

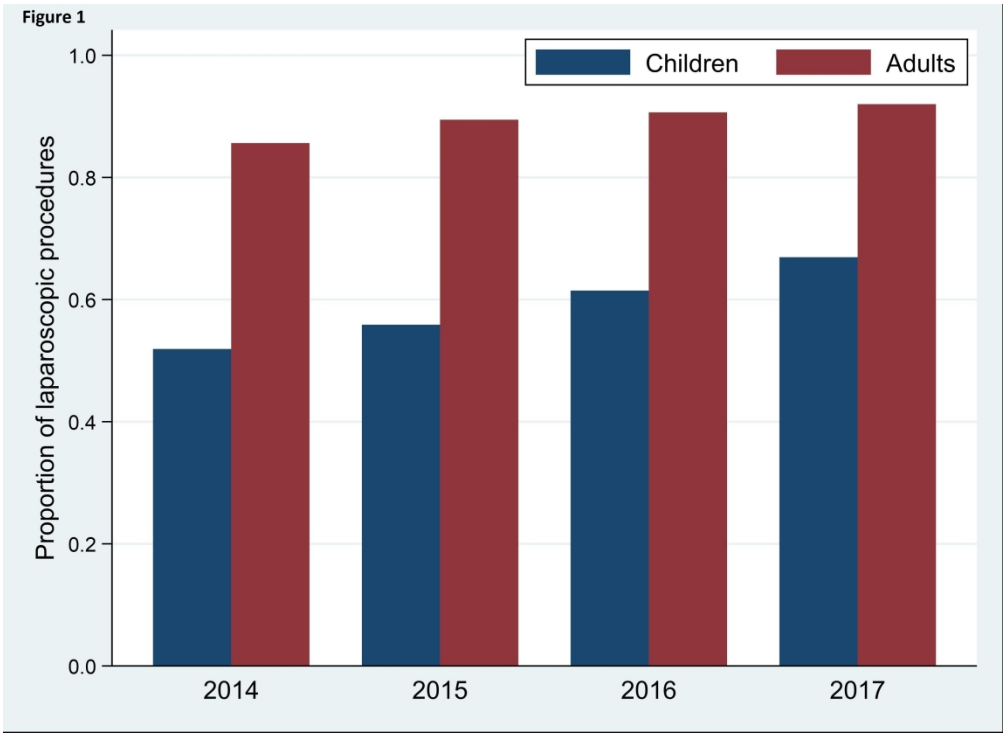
Figure 5 - Association between children and adult's ratio of observed/expected number of episodes of appendectomy by county**.**

Figure 6 - Ratio of observed/expected number of episodes of laparoscopy and open appendectomy by county for children and adults.

Table 1 – Adult and paediatric laparoscopic and open appendectomy percentage rates..

Table 2 – Variation statistics for laparoscopy, open and combined for children, adult and the whole patient population, 2014-2017.

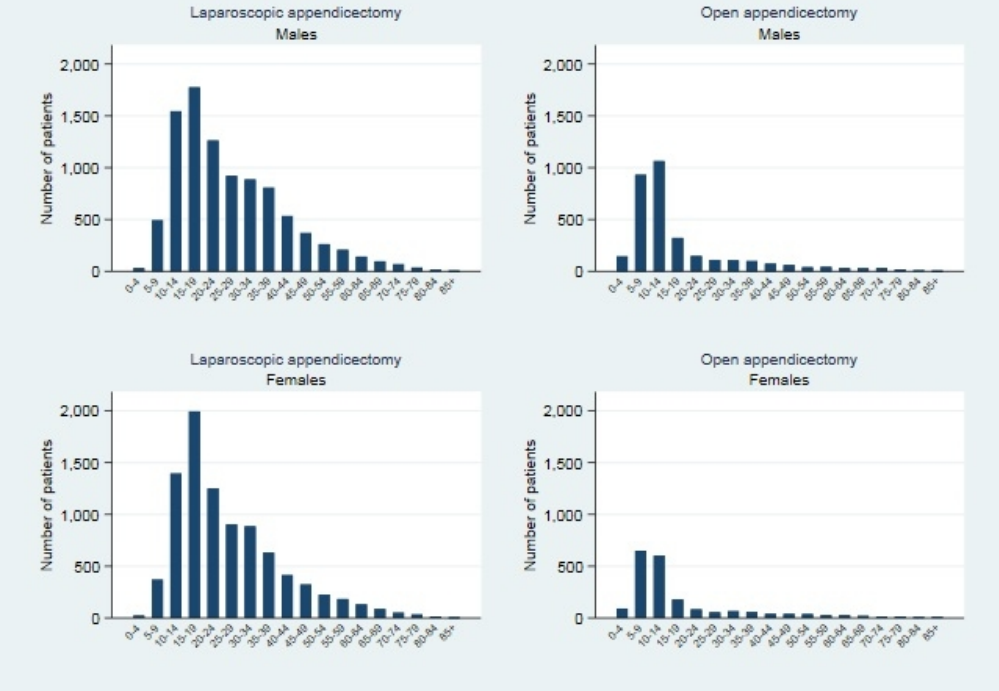
Online supplementary table – Proportion of laparoscopic appendectomies per year by county of residence for child and adult population.



Proportion of appendectomies conducted as laparoscopic procedures during 2014-2017 in children and adult patients

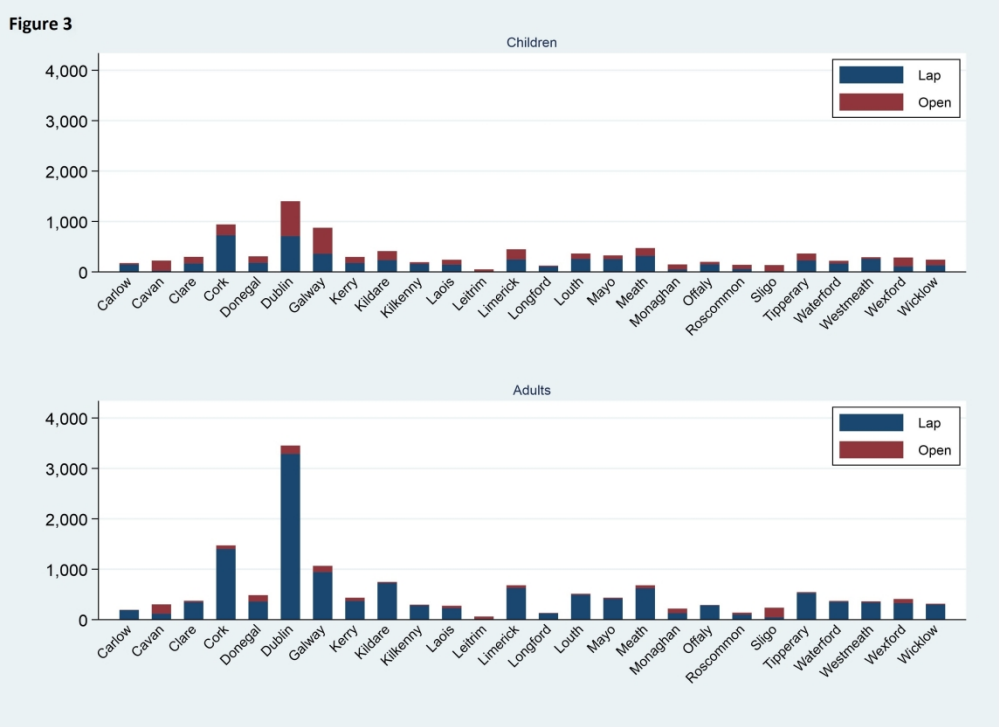
279x203mm (300 x 300 DPI)

Figure 2



Age and gender distribution for laparoscopic and open appendectomy.

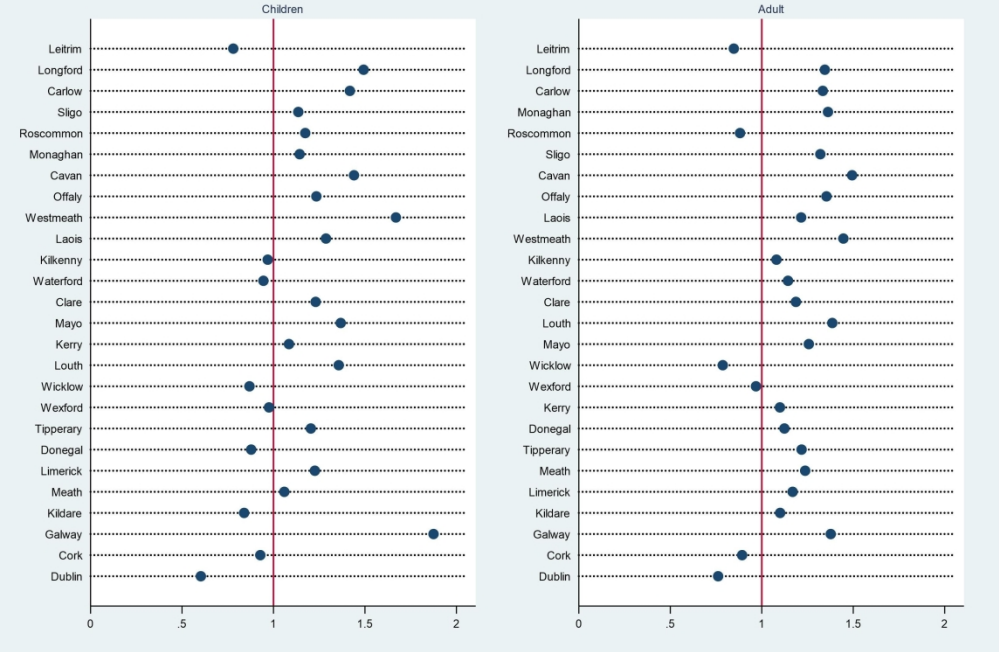
169x123mm (96 x 96 DPI)



Number of procedures performed during 2014-2017 on county residents

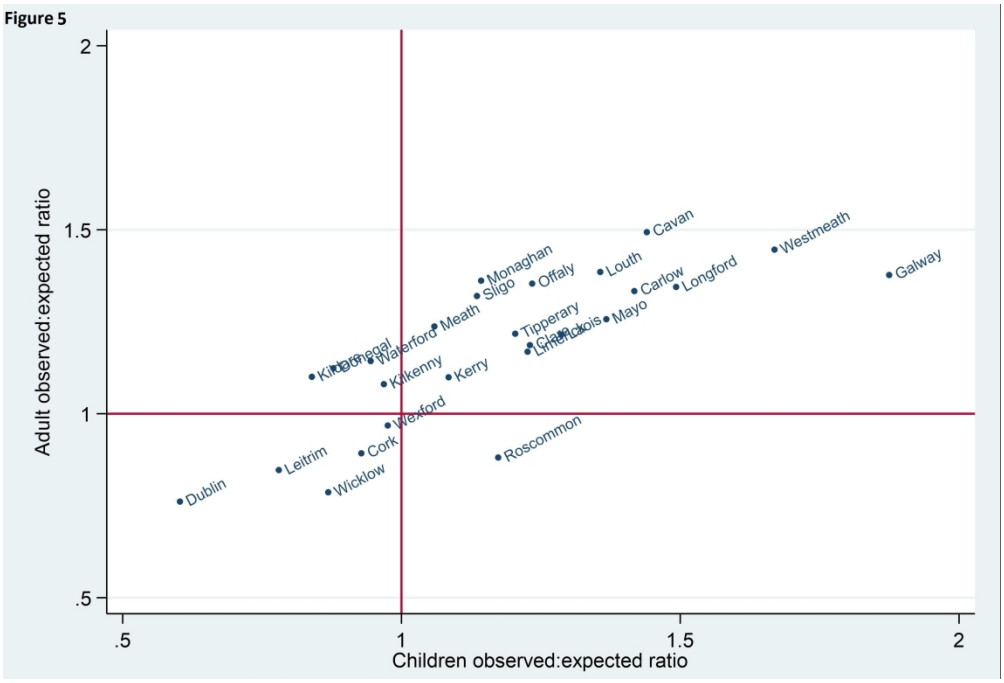
279x203mm (300 x 300 DPI)

Figure 4



Ratio of observed/expected number of episodes of appendectomy by county for children and adults.

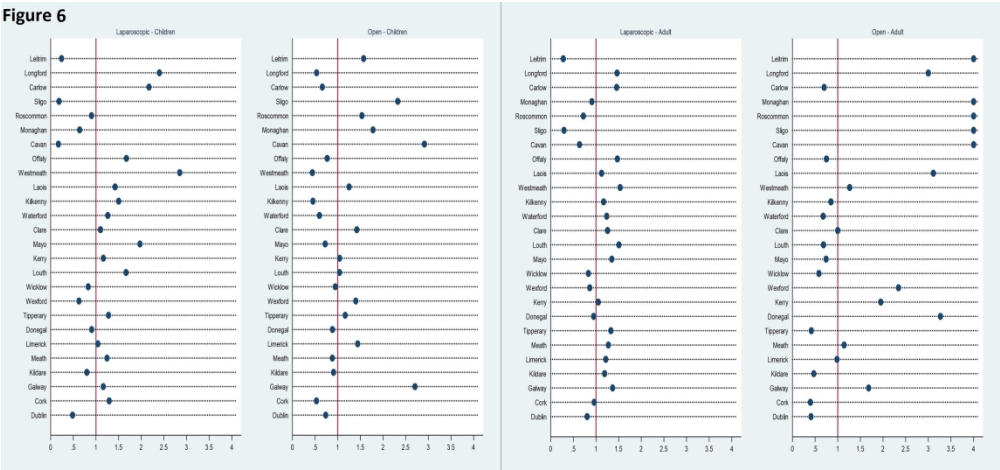
276x190mm (300 x 300 DPI)



Association between children and adult's ratio of observed/expected number of episodes of appendectomy by county.

279x188mm (300 x 300 DPI)

Figure 6



Ratio of observed/expected number of episodes of laparoscopy and open appendectomy by county for children and adults.

279x131mm (300 x 300 DPI)

Online Supplementary Table Proportion of laparoscopic appendectomies per year by county of residence for child and adult population

Proportion of laparoscopic procedures								
	Children				Adults			
County	**2014**	**2015**	**2016**	**2017**	**2014**	**2015**	**2016**	**2017**
Carlow	0.74	0.91	0.84	0.90	0.90	0.98	0.96	1.0
Cavan	0.11	0.14	0.08	0.13	0.22	0.51	0.44	0.5
Clare	0.56	0.43	0.59	0.65	0.90	0.94	0.88	0.97
Cork	0.65	0.76	0.8	0.87	0.93	0.96	0.97	0.95
Donegal	0.25	0.46	0.77	0.89	0.54	0.73	0.78	0.86
Dublin	0.44	0.42	0.54	0.64	0.93	0.96	0.96	0.96
Galway	0.39	0.41	0.38	0.47	0.86	0.89	0.89	0.90
Kerry	0.46	0.66	0.71	0.60	0.80	0.85	0.92	0.90
Kildare	0.49	0.62	0.64	0.56	0.97	0.97	0.98	0.98
Kilkenny	0.75	0.84	0.82	0.89	0.89	0.93	0.95	0.99
Laois	0.47	0.45	0.64	0.81	0.80	0.78	0.79	0.96
Leitrim	0.14	0.27	0.11	0.22	0.27	0.15	0.33	0.46
Limerick	0.44	0.50	0.54	0.70	0.89	0.93	0.90	0.95
Longford	0.70	0.97	0.90	0.93	0.90	0.93	0.92	0.92
Louth	0.66	0.61	0.78	0.77	0.96	0.97	0.93	0.96
Mayo	0.73	0.83	0.78	0.79	0.94	0.94	0.98	0.94
Meath	0.59	0.61	0.74	0.75	0.89	0.91	0.94	0.93
Monaghan	0.35	0.30	0.33	0.41	0.59	0.51	0.77	0.51
Offaly	0.65	0.78	0.83	0.78	0.94	0.98	1.00	0.95
Roscommon	0.42	0.39	0.50	0.47	0.69	0.68	0.75	0.865
Sligo	0.12	0.1	0.09	0.19	0.18	0.19	0.20	0.19
Tipperary	0.63	0.68	0.60	0.60	0.94	0.98	0.98	0.98
Waterford	0.75	0.80	0.77	0.74	0.92	0.94	0.98	0.96
Westmeath	0.86	0.84	0.92	0.92	0.89	0.96	0.96	0.97
Wexford	0.25	0.19	0.53	0.52	0.68	0.67	0.82	0.93
Wicklow	0.67	0.61	0.50	0.40	0.98	0.90	0.94	0.97

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*5*
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	n/a
		(*d*) If applicable, explain how loss to follow-up was addressed	n/a
		(*e*) Describe any sensitivity analyses	n/a
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7
		(b) Indicate number of participants with missing data for each variable of interest	n/a
		(c) Summarise follow-up time (eg, average and total amount)	n/a
Outcome data	15*	Report numbers of outcome events or summary measures over time	7,8,9,10,
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8,9, 10
		(*b*) Report category boundaries when continuous variables were categorized	8, 9
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8,9,10,
Discussion			
Key results	18	Summarise key results with reference to study objectives	11, 12,13,
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12
Generalisability	21	Discuss the generalisability (external validity) of the study results	12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.