

Original Article

Acute Appendicitis: Trends in Surgical Treatment

A Population-Based Study of Over 800 000 Patients

Christian Stöß*, Ulrich Nitsche*, Philipp-Alexander Neumann, Victoria Kehl, Dirk Wilhelm, Reinhard Busse, Helmut Friess, Ulrike Nimptsch

Summary

Background: Appendectomy is the gold standard for treatment of acute appendicitis. However, recent studies favor primary antibiotic therapy. The aim of this observational study was to explore changes in the numbers of operations for acute appendicitis in the period 2010–2017, paying special attention to disease severity.

Methods: Data from diagnosis-related group statistics were used to analyze the trends, mortality, and complication rates in the surgical treatment of appendicitis in Germany between 2010 and 2017. All cases of appendectomy after a diagnosis of appendicitis were included.

Results: Altogether, 865 688 inpatient cases were analyzed. The number of appendectomies went down by 9.8%, from 113 614 in 2010 to 102 464 in 2017, while the incidence fell from 139/100 000 in 2010 to 123/100 000 in 2017 (standardized by age group). This decrease is due to the lower number of operations for uncomplicated appendicitis (79 906 in 2017 versus 93 135 in 2010). Hospital mortality decreased both in patients who underwent surgical treatment of complicated appendicitis (0.62% in 2010 versus 0.42% in 2017) and in those with a complicated clinical course (5.4% in 2010 versus 3.4% in 2017).

Conclusion: Decisions on the treatment of acute appendicitis in German hospitals follow the current trend towards non-surgical management in selected patients. At the same time, the care of acute appendicitis has improved with regard to overall hospital morbidity and hospital mortality.

Cite this as:

Stöß C, Nitsche U, Neumann PA, Kehl V, Wilhelm D, Busse R, Friess H, Nimptsch U: Acute appendicitis: trends in surgical treatment—a population-based study of over 800 000 patients. *Dtsch Arztebl Int* 2021; 118: 244–9.
DOI: 10.3238/arztebl.m2021.0118

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Appendicitis is a common global disease with a lifetime risk of 7–8% (1). The pooled incidence of appendicitis in Western Europe is estimated at 151 per 100 000 person-years (2). Appendectomy has been established as the treatment of choice for acute appendicitis (3). In recent years, the surgical treatment of acute uncomplicated appendicitis – defined as the absence of perforation or abscess – has been challenged in several randomized controlled trials. Some have proclaimed a paradigm shift and proposed antibiotics alone as first-line treatment for acute appendicitis (4–9). However, estimating the course of the disease remains problematic even with the use of diagnostic imaging (e.g., low-dose computed tomography) (9). In 14 to 40% of all cases, primary antibiotic treatment is followed by recurrence and rescue surgery. The guideline recommendations regarding conservative and surgical treatment options therefore show considerable heterogeneity (10–14).

The aim of this study was to depict trends in case numbers for surgical treatment of acute appendicitis in Germany by examining all inpatient cases from 2010 to 2017, based on full national data sets. Specifically, outcomes of care were assessed by studying indicators of complicated clinical courses and in-hospital mortality.

Methods

This retrospective observational study was based on microdata analysis of diagnosis-related group statistics for the years 2010 to 2017 via the Research Data Center of the Federal Statistical Office by means of controlled data processing (15). Details of the statistical methods can be found in the *eMethods*. The inclusion and exclusion criteria for diagnosis codes (International Statistical Classification of Diseases, 10th revision [ICD-10]) and procedure codes (German classification for operations and procedures [OPS]) are given in *eTable 1*.

Complicated appendicitis was identified by the ICD-10 codes K35.2 (with generalized peritonitis), K35.31 (localized peritonitis with perforation or rupture), and K35.32 (with peritoneal abscess). The clinical outcome was assessed in terms of in-hospital mortality and indicators of a complicated clinical course. Based on previous research, these indicators

were defined by means of the ICD-10 codes for the secondary diagnoses of septicemia or postoperative ileus and the OPS codes for blood transfusion (\geq six units), complex intensive care treatment, or mechanical ventilation for more than 24 hours (*eTable 1*) (16, 17).

Results

Characteristics of cases treated

A total of 865 688 inpatient appendectomies for acute appendicitis were performed as independent procedures in Germany during the period 2010 to 2017 and were thus included in this study. The overall number of operations per year declined linearly from 113 614 cases in 2010 to 102 464 cases in 2017, a relative overall reduction of 9.8% (*Table 1, eTable 2*).

Taking the population of Germany into consideration (18), the incidence of appendectomy in the year 2010 was 139 per 100 000 person-years. By 2017, the incidence had fallen to 124 per 100 000 person-years. Standardized by age groups to 2010, the incidence declined from 139 per 100 000 in 2010 to 123 per 100 000 in 2017 (*eTable 2*). This corresponds to a relative reduction of approximately 11.5% within 8 years. The proportion represented by the youngest age group (< 15 years) decreased during the study from an initial 20% (n = 22 273) to 15% (n = 14 944), while the group “15–35” remained stable at 46% (n = 47 331) and the group “35 or older” increased from 34% (n = 38 176) to 39% (n = 40 189).

The proportion of female patients was higher in 2010 (53%; n = 59 734) than in 2017 (50%; n = 51 173). The mean length of hospital stay went down from 5.1 days to 4.4 days during the 8-year observation period. The proportion of operations performed for uncomplicated appendicitis decreased from 82% (n = 93 135) in 2010 to 78% (n = 79 906) in 2017. Conversely, the proportion of operations for complicated appendicitis increased from 18% (n = 20 479) to 22% (n = 22 558) (*Figure 1*). This trend can also be observed in the analysis of all individual federal states of Germany, with the sole exception of Saarland, where the opposite trend was found (*eTable 3*).

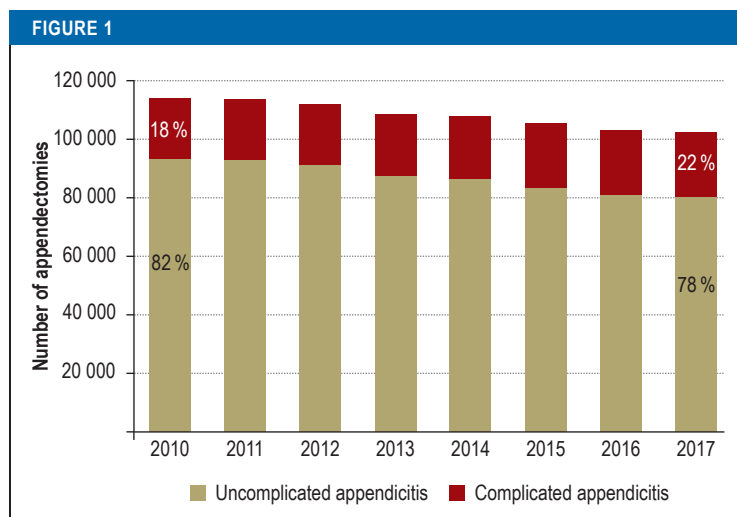
Morbidity and mortality

The mean rates for secondary diagnoses or procedures such as septicemia (0.56%), blood transfusion (0.07%), postoperative ileus (0.46%), mechanical ventilation > 24 hours (0.33%) and complex intensive care treatment (1.58%) did not change significantly. The proportion of cases with at least one of the above-mentioned surrogates for a complicated course stayed constant at 2.2–2.4% (2010: n = 2540; 2017: n = 2502). The overall in-hospital mortality rate was 0.12% (n = 118) in 2017 compared with 0.16% (n = 184) in 2010. If at least one of the indicators for a complicated course was present, the mean in-hospital mortality rate increased steeply to 4.2%. Here too, however, in-hospital mortality declined, from 5.4% (n = 136) in 2010 to 3.4% (n = 86) in 2017 (*Table 2, eTable 4*).

TABLE 1

Characteristics of inpatient cases with appendectomy as sole intervention for acute appendicitis

		2010		2017	
		n	%	n	%
Total number of inpatient cases		113 614	100.0	102 464	100.0
Incidence per 100 000 persons		139		124	
Incidence per 100 000 persons (standardized by age group, in relation to 2010)		139		123	
Age (years)	< 15	22 273	19.6	14 944	14.6
	15–35	53 165	46.8	47 331	46.2
	> 35	38 176	33.6	40 189	39.2
Sex	Female	59 734	52.6	51 173	49.9
Length of hospital stay (days)	Mean (median)	5.1 (4)		4.4 (4)	
Severity	Uncomplicated appendicitis	93 135	82.0	79 906	78.0
	Complicated appendicitis	20 479	18.0	22 558	22.0
Surgical procedure	Laparoscopic surgery	86 500	76.1	95 441	93.1
	Open surgery	23 365	20.6	4534	4.4
	Conversion	3728	3.3	2450	2.4
	Other or undefined	21	0.0	39	0.0
Type of surgery	Appendectomy	112 815	99.3	101 037	98.6
	Cecal resection	799	0.7	1427	1.4



Number of appendectomies in the period 2010–2017

The overall number of appendectomies fell by 9.8% from 113 614 cases in 2010 to 102 464 cases in 2017. The proportion of all appendectomies accounted for by complicated appendicitis increased to 22%, while that for uncomplicated appendicitis decreased to 78%.

Uncomplicated versus complicated appendicitis

The ratio of appendectomies for uncomplicated versus complicated appendicitis differed among the age groups (*eFigure*). In patients aged < 15 years, the number of appendectomies for uncomplicated appendicitis declined, while the absolute numbers of appendectomies for complicated appendicitis stayed almost constant. As a consequence, the proportion of appendectomies for complicated appendicitis rose from 14% (n = 3083) in 2010 to 19% (n = 2879) in 2017. In the intermediate age group (15–35 years) the proportion of appendectomies for complicated appendicitis increased from 9% (n = 4604) in 2010 to 11% (n = 5104) in 2017, and for patients older than 35 years the proportion was 34% (n = 12 792) in 2010 and 36% (n = 14 575) in 2017.

Of note, in-hospital mortality differed between uncomplicated appendicitis and complicated appendicitis (*eTable 5*). The in-hospital mortality rate for uncomplicated appendicitis was 0.06% (57 deaths) in 2010 and fell by 50% to 0.03% in 2017 (23 deaths) (*Figure 2a*). The in-hospital mortality rate for an acute complicated appendicitis was more than 10 times higher: 0.62% (127 deaths) in 2010, 0.42% (95 deaths) in 2017. At least one of the indicators of a complicated clinical course was present in 9.3% (n = 1897) of all patients with complicated appendicitis in 2010 and in 8.9% (n = 2001) in 2017—compared with 0.7% and 0.6%, respectively, for uncomplicated appendicitis (*Figure 2b*).

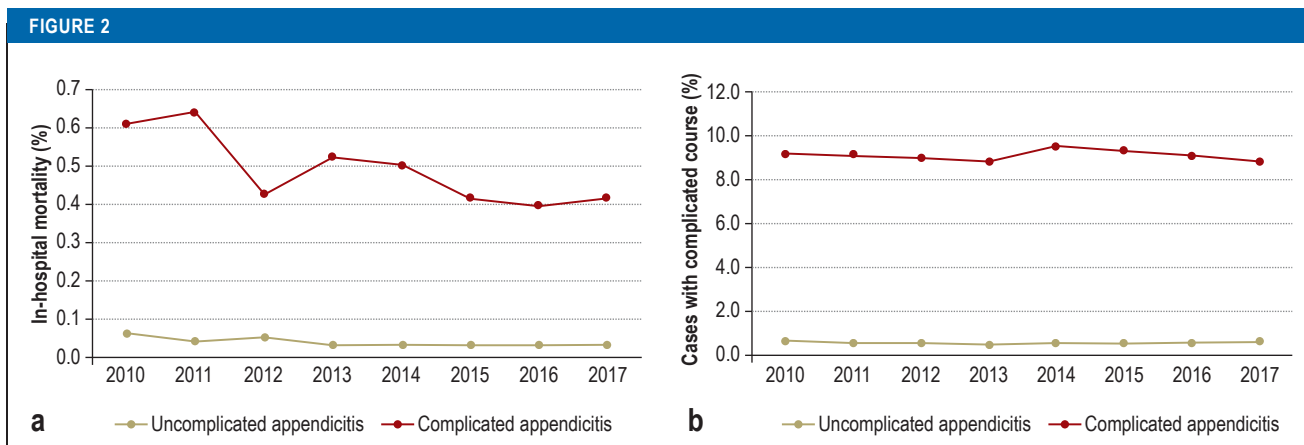
Discussion

This study demonstrates a decrease in the number of appendectomies for acute appendicitis between 2010 and 2017 in Germany (relative reduction: 9.8%; demo-

graphically adjusted relative reduction: 11.5%). Interestingly, despite the reduction in the absolute number of appendectomies, the proportion of patients with complicated appendicitis has increased. This effect was most pronounced in patients younger than 15 years (*eTable 5*). The decrease in cases reflects either a declining incidence of acute appendicitis or a decrease in the number of patients treated surgically. The latter would be consistent with the current trend towards primary antibiotic treatment in selected patients (19, 20). De Wijkerslooth et al. reported a fall in the incidence of appendectomy from 90 per 100 000 inhabitants in 2006 to 78 per 100 000 in 2015 (21). It remains unclear why the incidence in their study was significantly lower than in our and other studies (see below). Moreover, the authors were unable to determine whether the cause was a reduction in the incidence of acute appendicitis or a decrease in the number of patients treated surgically. Furthermore, improved diagnostic modalities (sonography, computed tomography, etc.) are contributing to the reduced rate of appendectomy. However, the reduction cannot be fully explained by a lower rate of negative appendectomies (22–24).

The data on the development of the incidence of appendicitis are very heterogeneous. Studies in the USA and England describe decreasing rates (25, 26), while more recent publications report stable or rising case numbers (27–30). A systematic review on the global incidence of appendicitis published in 2017 estimated the pooled incidence of appendicitis or appendectomy in western Europe at 151/100 000 person-years; since 1990 the incidence of appendectomy has decreased in western countries, while the incidence of appendicitis is stated as stable (2). Assuming that the incidence remained stable during the period we investigated, one can conclude that the observed decrease of appendectomies in Germany may be influenced by the growing number of studies which, on the basis of their results, recommend conservative treatment of 60–70% of all appendicitis patients (3, 19, 20, 31, 32). A glance at the appendectomy numbers for uncomplicated and complicated appendicitis seems to confirm this conclusion: The proportion of patients that underwent appendectomy for uncomplicated appendicitis fell from 82% (n = 93 135) in 2010 to 78% (n = 79 906) in 2017.

Since both the absolute and relative number of operations for complicated appendicitis increased, it might be supposed that an increasing number of patients treated with antibiotics were developing complicated appendicitis and required surgery. Although this cannot be supported by unambiguous data in this study, the results of a recently published randomized controlled trial suggest exactly this clinical scenario (20). This study of 1552 adult patients showed non-inferiority of antibiotic treatment; nevertheless, three out of every ten participants in the antibiotic arm of the trial had to undergo rescue appendectomy. In addition, the complication rate was correspondingly higher. In our study, the increase in the number of



Development of in-hospital mortality and proportion of cases with complicated course, stratified by severity of appendicitis (complicated versus uncomplicated) Mortality is higher for appendectomy cases with complicated appendicitis than for appendectomy cases with uncomplicated appendicitis and shows a declining trend over time (a). The proportion of cases with a complicated course is higher for appendectomy cases with complicated appendicitis than for appendectomy cases with uncomplicated appendicitis. No temporal trend is evident (b).

cecal resections from 799 (0.7%) in 2010 to 1427 (1.4%) in 2017 may be due to a delay in surgical intervention, as cecal resection is only performed when severe inflammation does not allow simple appendectomy.

Appendectomy is in principle a low-risk surgical procedure. The in-hospital mortality rate in Germany decreased from 0.16% (n = 184) in 2010 to 0.12% (n = 118) in 2017, which is comparable to mortality rates reported from other countries (0.09% to 0.25%) (33). Here, we also present data on the mortality rate stratified by disease severity. For uncomplicated appendicitis, the rate of death was 0.03% (95% confidence interval [0.02; 0.04]; n = 23) in 2017, compared to a significantly higher rate of 0.06% in 2010 ([0.05; 0.08]; n = 57). For complicated appendicitis, the mortality rate was more than 10 times higher in 2017, at 0.42% (n = 95), but also showed a downward trend (2010: 0.62%; n = 127). For those cases in which acute appendicitis—whether uncomplicated or complicated—was accompanied by at least one surrogate parameter of a complicated clinical course (i.e., septicemia, transfusion of more than six units of erythrocytes or whole blood, postoperative ileus, mechanical ventilation > 24 h, need for intensive care), the in-hospital mortality in 2017 was 3.4% (n = 86), compared with 5.4% (n = 136) in 2010. As expected, however, complicated appendicitis was more likely than uncomplicated appendicitis to involve a complicated clinical course (2017: 8.9% vs. 0.6%; 2010: 9.3% vs. 0.7%).

The present study has several limitations. Studies based on DRG statistics are subject to potential information bias introduced by inconstant coding behavior. Moreover, the distinction between non-perforated and perforated appendicitis is based on ICD-10 diagnoses. These are assigned on the basis of the surgeon’s intraoperative findings, so the distinc-

tion is open to interobserver variation (34). Cases with the clinical appearance of appendicitis and conservative treatment were excluded from the study because the respective number might have been distorted by incorrect diagnoses and multiple hospitalizations. Moreover, owing to the way in which DRG data are documented no temporal association could be established between possible subsequent procedures and diagnoses, which limits our assumptions with regard to a complicated disease course.

Given these limitations, the advantage of this study lies in the robustness of its data. Whereas study populations often represent only a statistical sample, our study included all inpatient cases in Germany who underwent surgery for acute appendicitis, corresponding to over 850 000 cases.

We therefore present not only developments in the surgical treatment of appendicitis, but also new data on in-hospital mortality of appendicitis, stratified by disease severity and clinical course. The numbers of appendectomies for appendicitis in general, and uncomplicated appendicitis in particular, fell during the study period, while the population (all residents of Germany) grew (18).

The findings of this study suggest that German hospitals are acting, albeit slowly, on the evidence of recently published studies favoring a non-operative approach in selected patients. Thus, an overall reduction of 9.8% was observed within 8 years. Advances in diagnosis may have contributed to this effect. Interestingly, the proportion of patients with complicated appendicitis treated with appendectomy increased during the period 2010 to 2017, while the use of appendectomy in those with uncomplicated appendicitis decreased. The outcome of treatment in terms of in-hospital morbidity and mortality improved during the same time span.

TABLE 2

Morbidity and mortality of inpatient cases with appendectomy as sole intervention for appendicitis

		2010		2017	
		n	%	n	%
Total number of patients		113 614	100.0	102 464	100.0
Indicators of complicated course	Septicemia	578	0.5	727	0.7
	Blood transfusions (≥ 6 units)	108	0.1	50	0.05
	Postoperative ileus	494	0.4	537	0.5
	Mechanical ventilation > 24 h	434	0.4	309	0.3
	Complex intensive care	1796	1.6	1609	1.6
	At least one indicator of complicated course	2540	2.2	2502	2.4
In-hospital mortality (all appendectomy cases)		184	0.16	118	0.12
In-hospital mortality (among patients with at least one indicator of complicated course)		136	5.4	86	3.4

Conflict of interest statement
The authors declare that no conflict of interest exists.

Manuscript received on 17 August 2020, revised version accepted on 6 January 2021

References

- Stewart B, Khanduri P, McCord C, et al.: Global disease burden of conditions requiring emergency surgery. *Br J Surg* 2014; 101: e9–22.
- Ferris M, Quan S, Kaplan BS, et al.: The global incidence of appendicitis: a systematic review of population-based studies. *Ann Surg* 2017; 266: 237–41.
- Téoule P, de Laffolie J, Rolle U, Reißfelder C: Acute appendicitis in childhood and adolescence—an everyday clinical challenge. *Dtsch Arztebl Int* 2020; 117: 764–74.
- Bhangu A, Soreide K, Di Saverio S, Assarsson JH, Drake FT: Acute appendicitis: modern understanding of pathogenesis, diagnosis, and management. *Lancet* 2015; 386: 1278–87.
- Varadhan KK, Neal KR, Lobo DN: Safety and efficacy of antibiotics compared with appendectomy for treatment of uncomplicated acute appendicitis: meta-analysis of randomised controlled trials. *BMJ* 2012; 344: e2156.
- Styrud J, Eriksson S, Nilsson I, et al.: Appendectomy versus antibiotic treatment in acute appendicitis: a prospective multicenter randomized controlled trial. *World J Surg* 2006; 30: 1033–7.
- Eriksson S, Granstrom L: Randomized controlled trial of appendectomy versus antibiotic therapy for acute appendicitis. *Br J Surg* 1995; 82: 166–9.
- Hansson J, Korner U, Khorram-Manesh A, Solberg A, Lundholm K: Randomized clinical trial of antibiotic therapy versus appendectomy as primary treatment of acute appendicitis in unselected patients. *Br J Surg* 2009; 96: 473–81.
- Vons C, Barry C, Maitre S, et al.: Amoxicillin plus clavulanic acid versus appendectomy for treatment of acute uncomplicated appendicitis: an open-label, non-inferiority, randomised controlled trial. *Lancet* 2011; 377: 1573–9.
- Korndorffer JR, Jr., Fellingner E, Reed W: SAGES guideline for laparoscopic appendectomy. *Surg Endosc* 2010; 24: 757–61.
- Di Saverio S, Birindelli A, Kelly MD, et al.: WSES Jerusalem guidelines for diagnosis and treatment of acute appendicitis. *World J Emerg Surg* 2016; 11: 34.
- Gorter RR, Eker HH, Gorter-Stam MA, et al.: Diagnosis and management of acute appendicitis. EAES consensus development conference 2015. *Surg Endosc* 2016; 30: 4668–90.
- Vettoretto N, Gobbi S, Corradi A, et al.: Consensus conference on laparoscopic appendectomy: development of guidelines. *Colorectal Dis* 2011; 13: 748–54.
- Bakker OJ, Go PM, Puylaert JB, Kazemier G, Heij HA, Werkgroep richtlijn Diagnostiek en behandeling van acute a: [Guideline on diagnosis and treatment of acute appendicitis: imaging prior to appendectomy is recommended]. *Ned Tijdschr Geneesk* 2010; 154: A303.
- Research data centres of the Federal Statistical Office and the statistical offices of the Federal States. Diagnosis-Related Group Statistics (DRG Statistics) 2010–2017, own calculations. DOI: 10.21242/23141.2010.00.00.1.1.0 to DOI: 10.21242/23141.2017.00.00.1.1.0.
- Krautz C, Nimptsch U, Weber GF, Mansky T, Grutzmann R: Effect of hospital volume on in-hospital morbidity and mortality following pancreatic surgery in Germany. *Ann Surg* 2018; 267: 411–7.
- Nimptsch U, Mansky T: Deaths following cholecystectomy and herniotomy—an analysis of nationwide German hospital discharge data from 2009 to 2013. *Dtsch Arztebl Int* 2015; 112: 535–43.
- Federal Statistical Office (Destatis); 2020. www-genesis.destatis.de/genesis/online (last accessed on 19 April 2020).
- Salminen P, Paajanen H, Rautio T, et al.: Antibiotic therapy vs appendectomy for treatment of uncomplicated acute appendicitis: the APPAC randomized clinical trial. *JAMA* 2015; 313: 2340–8.
- CODA Collaborative, Flum DR, Davidson GH, et al.: A randomized trial comparing antibiotics with appendectomy for appendicitis. *N Engl J Med* 2020; 383: 1907–19.
- de Wijkerslooth EML, van den Boom AL, Wijnhoven BPL: Disease burden of appendectomy for appendicitis: a population-based cohort study. *Surg Endosc* 2020; 34: 116–25.
- Lu Y, Friedlander S, Lee SL: Negative appendectomy: clinical and economic implications. *Am Surg* 2016; 82: 1018–22.
- Oyetunji TA, Ong'uti SK, Bolorunduro OB, Cornwell EE, 3rd, Nwomeh BC: Pediatric negative appendectomy rate: trend, predictors, and differentials. *J Surg Res* 2012; 173: 16–20.
- Seetahal SA, Bolorunduro OB, Sookdeo TC, et al.: Negative appendectomy: a 10-year review of a nationally representative sample. *Am J Surg* 2011; 201: 433–7.
- Addiss DG, Shaffer N, Fowler BS, Tauxe RV: The epidemiology of appendicitis and appendectomy in the United States. *Am J Epidemiol* 1990; 132: 910–25.
- Kang JY, Hoare J, Majeed A, Williams RC, Maxwell JD: Decline in admission rates for acute appendicitis in England. *Br J Surg* 2003; 90: 1586–92.
- Buckius MT, McGrath B, Monk J, Grim R, Bell T, Ahuja V: Changing epidemiology of acute appendicitis in the United States: study period 1993–2008. *J Surg Res* 2012; 175: 185–90.
- Korner H, Soreide JA, Pedersen EJ, Bru T, Sondenaa K, Vatten L: Stability in incidence of acute appendicitis. A population-based longitudinal study. *Dig Surg* 2001; 18: 61–6.
- Livingston EH, Fomby TB, Woodward WA, Haley RW: Epidemiological similarities between appendicitis and diverticulitis suggesting a common underlying pathogenesis. *Arch Surg* 2011; 146: 308–14.

30. Anderson JE, Bickler SW, Chang DC, Talamini MA: Examining a common disease with unknown etiology: trends in epidemiology and surgical management of appendicitis in California, 1995–2009. *World J Surg* 2012; 36: 2787–94.
31. Salminen P, Tuominen R, Paaanen H, et al.: Five-year follow-up of antibiotic therapy for uncomplicated acute appendicitis in the APPAC randomized clinical trial. *JAMA* 2018; 320: 1259–65.
32. Flum DR: Clinical practice. Acute appendicitis—appendectomy or the „antibiotics first“ strategy. *N Engl J Med* 2015; 372: 1937–43.
33. Faiz O, Clark J, Brown T, et al.: Traditional and laparoscopic appendectomy in adults: outcomes in English NHS hospitals between 1996 and 2006. *Ann Surg* 2008; 248: 800–6.
34. Ponsky TA, Hafi M, Heiss K, Dinsmore J, Newman KD, Gilbert J: Interobserver variation in the assessment of appendiceal perforation. *J Laparoendosc Adv Surg Tech A* 2009; 19 (Suppl 1): S15–8.

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Cite this as:

Stöß C, Nitsche U, Neumann PA, Kehl V, Wilhelm D, Busse R, Friess H, Nimptsch U: Acute appendicitis: trends in surgical treatment—a population-based study of over 800 000 patients. *Dtsch Arztebl Int* 2021; 118: 244–9. DOI: 10.3238/arztebl.m2021.0118

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[eReferences, eMethods, eFigure, eTables:](#)
www.aerzteblatt-international.de/m2021.0118

CLINICAL SNAPSHOT

Secondary Syphilis

A 35-year-old HIV-positive homosexual patient presented to the HIV outpatient clinic with fever, headache, and weight loss. Multiple painless, verrucous, papular skin eruptions, including involvement of the palms of the hands (*Figure A*), indolent ulcers on the penis shaft and scrotum (*Figure B*), inguinal lymph node swelling, and yellowish coating on the tongue were striking. The suspicion of acute *Treponema pallidum* infection was confirmed serologically (TPPA titer: 1:655 360, Western blot: IgM positive, RPR antibody titer: 1:64).



Figure A: Clavi syphilitici on the palms of the hands.



Figure B: Chancere on the penis shaft with contact chancere on the scrotum.

Due to the patient's HIV coinfection (CD4 cells 286/μl, viral load 230 copies/ml) and headache, lumbar puncture was performed. On the basis of evidence of intrathecal production of treponema-specific antibodies (specific antibody index: 19.66), neurosyphilis was confirmed. Following 14-day treatment with ceftriaxone, rapid improvement of the eruptions was seen.

In summary, these are typical findings in secondary syphilis with a chancere, lymphadenitis, verrucous exanthema and palmar involvement (clavi syphilitici), mucous membrane involvement (mucous patches), and headache as early signs of neurosyphilis. The incidence of syphilis has increased significantly in Germany since 2010 (2018: 7332 cases). A total of 85% of cases involve males who have sex with other males.

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Conflict of interest statement: The authors declare that no conflict of interest exists

Translated from the original German by Christine Rye.

Cite this as: Trawinski H, Bußler S, Lübbert C: Secondary syphilis. *Dtsch Arztebl Int* 2021; 118: 249. DOI: 10.3238/arztebl.m2021.0107

Supplementary material to:

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Dtsch Arztebl Int 2021; 118: 244–9. DOI: 10.3238/arztebl.m2021.0118

eReferences

- e1. Swart E, Gothe H, Geyer S, et al.: [Good Practice of Secondary Data Analysis (GPS): guidelines and recommendations]. *Gesundheitswesen* 2015; 77: 120–6.
- e2. Primatesta P, Goldacre MJ: Appendicectomy for acute appendicitis and for other conditions: an epidemiological study. *Int J Epidemiol* 1994; 23: 155–60.
- e3. Nimptsch U, Spoden M, Mansky T: [Definition of variables in hospital discharge data: pitfalls and proposed solutions]. *Gesundheitswesen* 2020; 82: S29–40.
- e4. Benchimol EI, Smeeth L, Guttman A, et al.: The REporting of studies conducted using observational routinely-collected health data (RECORD) statement. *PLoS Med* 2015; 12: e1001885.

eMETHODS

Study design and setting

The study presented here is a population-based retrospective study based on the diagnosis-related groups hospital discharge data of the national reimbursement system (G-DRG). The evaluation of secondary data via the German DRG system for this investigation does not require ethics committee approval (e1).

Data

Since 2004, reimbursement for inpatient services in Germany has been uniform across all hospitals calculated through a DRG reimbursement system (G-DRG). The information available for each of these inpatient cases includes age, sex, diagnoses (coded according to the International Statistical Classification of Diseases and Related Health Problems, 10th revision, German modification, ICD-10-GM), procedures (coded according to the German classification for operations and procedures, OPS), length of hospital stay, and mode of discharge. The individual inpatient data of the DRG statistics for the years 2010 to 2017 were accessed remotely via the Research Data Center of the Federal Statistical Office by means of controlled remote data processing (15).

Inclusion criteria

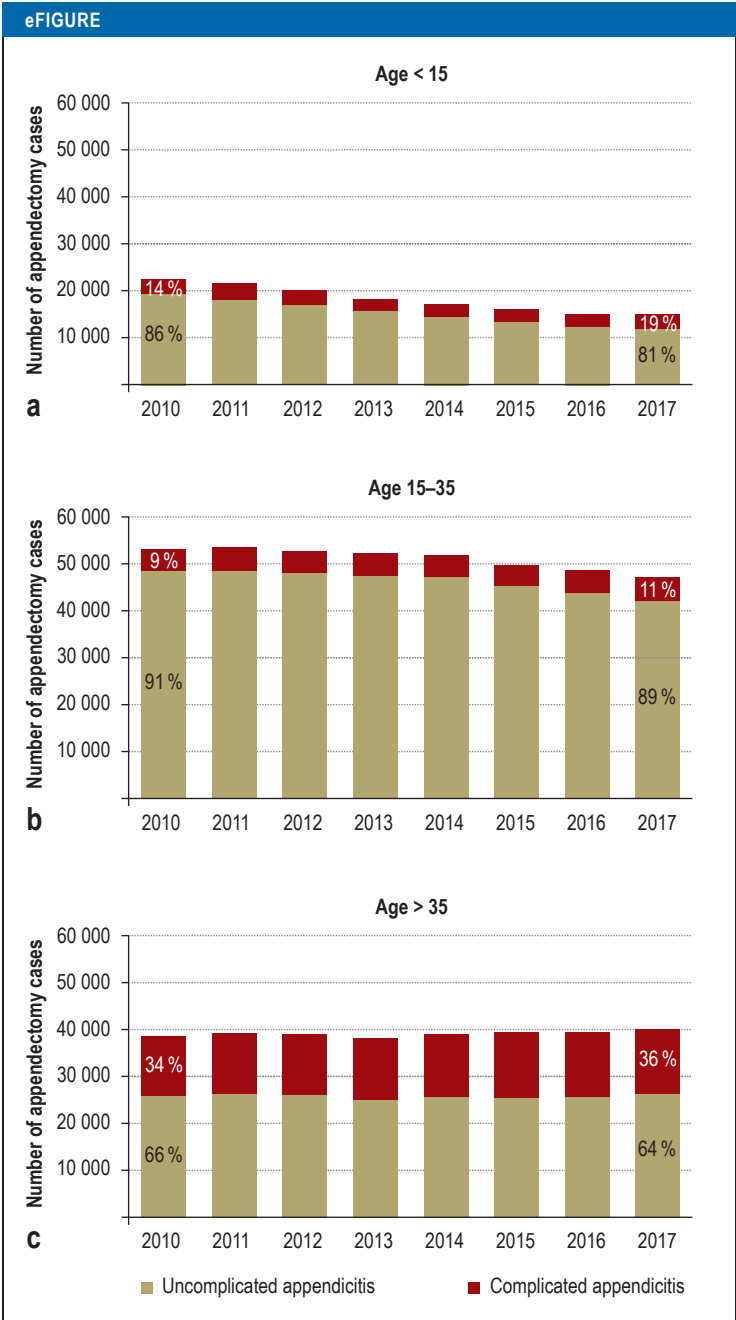
The units of analysis were inpatient cases who underwent appendectomy as sole intervention for appendicitis. These cases were identified by a principal diagnosis of appendicitis in combination with the OPS code for appendectomy or cecal resection. The inclusion and exclusion criteria for the diagnosis and procedure codes are given in *eTable 1*. Due to the nature of the data, no histological diagnoses were included in this analysis.

Stratification and outcome variables

Complicated appendicitis was identified by a principal diagnosis code of acute appendicitis with generalized (K35.2) or localized peritonitis with perforation or rupture (K35.31) or acute appendicitis with peritoneal abscess (K35.32). In accordance with previously published age distributions in patients with acute appendicitis, the study population was divided into three groups: < 15 years, 15–35 years, and > 35 years (e2). The clinical outcome was assessed in terms of in-hospital mortality and indicators of a complicated clinical course. Based on previous research, these indicators were defined by the ICD-10 codes for the secondary diagnoses septicemia and postoperative ileus, the procedure codes for blood transfusions (≥ 6 units), complex intensive care, or mechanical ventilation > 24 hours (*eTable 1*) (16, 17). These indicators were designed to identify serious complications or procedures required for serious complications while being widely unaffected by variation in coding behavior (e3).

Statistical methods

This study follows the REporting of studies Conducted using Observational Routinely collected health Data (RECORD) statement checklist (e4). All calculations were performed using SAS Version 9.3 (SAS Institute Inc., Cary, NC, USA). Data were analyzed descriptively for every year of observation and are expressed as absolute and relative frequencies. Development of appendectomy case numbers over time was analyzed separately for uncomplicated and complicated appendicitis and stratified by age group and hospital size. Additionally, in-hospital mortality and indicators of clinical course were stratified according to uncomplicated or complicated appendicitis.



The development of absolute case numbers for appendectomy, stratified by age group.

eTABLE 1

Definition of patient population and stratification variables

	Inclusion criteria	Exclusion criteria
Patient population		
All inpatient cases with appendectomy as sole intervention for acute appendicitis	PD ICD-10 K35, K36, K37 and OPS 5-470, 5-455.3	OPS 5-471, 5-479
Severity		
Uncomplicated appendicitis	PD ICD-10 K35.30, K35.8, K36, K37	
Complicated appendicitis	PD ICD-10 K35.2, K35.31, K35.32	
Surgical approach		
Open	OPS 5-470.0, 5-455.31	OPS 5-470.2, 5-455.37
Laparoscopic	OPS 5-470.1, 5-455.35	OPS 5-470.0, 5-470.2, 5-455.31, 5-455.37
Conversion	OPS 5-470.2, 5-455.37	
Other or undefined	OPS 5-470.x, 5-470.y	OPS 5-470.0, 5-470.1, 5-470.2, 5-455.31, 5-455.35, 5-455.37
Type of surgery		
Appendectomy	OPS 5-470	OPS 5-455.3
Cecal resection	OPS 5-455.3	
Indicators of complicated course		
Septicemia	SD ICD-10 A40, A41, R57.2, R65	
Blood transfusions, ≥ 6 units	OPS 8-800.1, 8-800.c1-cr	
Postoperative ileus	SD ICD-10 K91.3	
Mechanical ventilation > 24 h	Mechanical ventilation for > 24 h (separate data field)	
Complex intensive care	OPS 8-980, 8-98d, 8-98f (from 2013)	

ICD, International Statistical Classification of Diseases; OPS, German classification for operations and procedures (*Operationen- und Prozedurenschlüssel*); PD, principal diagnosis; SD, secondary diagnosis

eTABLE 2

Characteristics of inpatient cases with appendectomy as sole intervention for appendicitis

	2010		2011		2012		2013		2014		2015		2016		2017		
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	
Total number of inpatient cases	113 614	100.0	113 975	100.0	111 957	100.0	108 437	100.0	107 322	100.0	104 922	100.0	102 997	100.0	102 464	100.0	
Incidence per 100 000 persons	139		142		139		134		132		128		125		124		
Incidence per 100 000 persons (standardized by age group, in relation to 2010)	139		142		139		134		132		127		124		123		
Age (years)	< 15	22 273	19.6	21 451	18.8	19 991	17.9	18 256	16.8	16 893	15.7	15 891	15.1	15 139	14.7	14 944	14.6
	15–35	53 165	46.8	53 537	47.0	53 171	47.5	52 412	48.3	51 967	48.4	50 151	47.8	48 692	47.3	47 331	46.2
	> 35	38 176	33.6	38 987	34.2	38 795	34.7	37 769	34.8	38 462	35.8	38 880	37.1	39 166	38.0	40 189	39.2
Gender	59 734	52.6	60 236	52.9	58 890	52.6	57 071	52.6	56 563	52.7	53 715	51.2	51 944	50.4	51 173	49.9	
Length of hospital stay (days)	5.1 (4)		4.9 (4)		4.8 (4)		4.7 (4)		4.6 (4)		4.6 (4)		4.6 (4)		4.4 (4)		
Severity	Uncomplicated appendicitis	93 135	82.0	92 911	81.5	90 824	81.1	87 574	80.8	86 559	80.7	83 362	79.5	81 140	78.8	79 906	78.0
	Complicated appendicitis	20 479	18.0	21 064	18.5	21 133	18.9	20 863	19.2	20 763	19.3	21 560	20.5	21 857	21.2	22 558	22.0
Surgical approach	Laparoscopic	86 500	76.1	91 633	80.4	93 663	83.7	93 697	86.4	95 378	88.9	95 053	90.6	94 687	91.9	95 441	93.1
	Open	23 365	20.6	18 582	16.3	14 777	13.2	11 578	10.7	9009	8.4	6992	6.7	5578	5.4	4534	4.4
	Conversion	3728	3.3	3688	3.2	3441	3.1	3118	2.9	2908	2.7	2848	2.7	2704	2.6	2450	2.4
	Other or undefined	21	0.0	72	0.1	76	0.1	44	0.0	27	0.0	29	0.0	28	0.0	39	0.0
Type of surgery	Appendectomy	112 815	99.3	113 121	99.3	111 046	99.2	107 427	99.1	106 216	99.0	103 612	98.8	101 670	98.7	101 037	98.6
	Cecal resection	799	0.7	854	0.7	911	0.8	1010	0.9	1106	1.0	1310	1.2	1327	1.3	1427	1.4

eTABLE 3

Inpatient cases of uncomplicated and complicated appendicitis per federal state (patient's place of residence)

	2010		2011		2012		2013		2014		2015		2016		2017		
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	
Germany	Uncomplicated appendicitis	93 135	82.0	92 911	81.5	90 824	81.1	87 574	80.8	86 559	80.7	83 362	79.5	81 140	78.8	79 906	78.0
	Complicated appendicitis	20 479	18.0	21 064	18.5	21 133	18.9	20 863	19.2	20 763	19.3	21 560	20.5	21 857	21.2	22 558	22.0
Schleswig-Holstein	Uncomplicated appendicitis	2702	80.4	2820	80.1	2736	79.1	2731	80.4	2736	79.5	2605	78.3	2490	76.9	2372	77.4
	Complicated appendicitis	657	19.6	702	19.9	721	20.9	664	19.6	706	20.5	722	21.7	750	23.1	691	22.6
Hamburg	Uncomplicated appendicitis	1831	83.6	1822	81.7	1831	82.4	1795	81.7	1837	82.5	1667	82.5	1658	79.7	1633	79.7
	Complicated appendicitis	360	16.4	409	18.3	392	17.6	401	18.3	391	17.5	354	17.5	421	20.3	415	20.3
Lower Saxony	Uncomplicated appendicitis	10 008	82.0	9756	81.8	9302	80.5	9022	79.8	9025	81.0	8522	79.1	8152	78.9	8150	78.8
	Complicated appendicitis	2204	18.0	2169	18.2	2257	19.5	2282	20.2	2121	19.0	2251	20.9	2179	21.1	2199	21.2
Bremen	Uncomplicated appendicitis	527	77.6	542	79.0	595	78.7	573	77.1	541	77.4	550	77.0	492	74.3	525	76.1
	Complicated appendicitis	152	22.4	144	21.0	161	21.3	170	22.9	158	22.6	164	23.0	170	25.7	165	23.9
North Rhine-Westphalia	Uncomplicated appendicitis	21 957	82.6	21 532	81.9	21 329	81.7	20 169	80.9	19 840	81.1	19 563	80.4	19 019	79.8	18 426	78.7
	Complicated appendicitis	4610	17.4	4766	18.1	4771	18.3	4751	19.1	4632	18.9	4762	19.6	4806	20.2	4989	21.3
Hesse	Uncomplicated appendicitis	6383	80.8	6449	81.1	6355	80.3	6097	79.7	6127	80.4	5969	78.2	5945	78.0	5952	78.3
	Complicated appendicitis	1521	19.2	1507	18.9	1561	19.7	1552	20.3	1498	19.6	1667	21.8	1679	22.0	1653	21.7
Rhineland-Palatinate	Uncomplicated appendicitis	4670	82.1	4530	81.1	4323	80.8	4281	81.4	3988	80.1	3917	78.3	3756	78.7	3812	77.7
	Complicated appendicitis	1019	17.9	1057	18.9	1026	19.2	978	18.6	992	19.9	1087	21.7	1019	21.3	1094	22.3
Baden-Württemberg	Uncomplicated appendicitis	11 035	80.7	11 154	80.3	10 890	79.5	10 780	79.5	10 528	77.9	10 154	78.2	9975	77.5	10 223	76.9
	Complicated appendicitis	2639	19.3	2737	19.7	2804	20.5	2786	20.5	2989	22.1	2833	21.8	2895	22.5	3072	23.1
Bavaria	Uncomplicated appendicitis	15 508	83.8	15 944	83.1	15 633	82.9	14 903	83.0	14 746	82.8	13 990	81.1	13 176	79.7	13 086	78.8
	Complicated appendicitis	3001	16.2	3246	16.9	3234	17.1	3062	17.0	3057	17.2	3267	18.9	3362	20.3	3527	21.2
Saarland	Uncomplicated appendicitis	834	78.0	939	78.8	978	80.9	928	78.1	860	78.0	840	78.7	887	80.0	847	78.3
	Complicated appendicitis	235	22.0	252	21.2	231	19.1	260	21.9	242	22.0	227	21.3	222	20.0	235	21.7
Berlin	Uncomplicated appendicitis	3458	79.4	3435	80.8	3341	80.6	3318	80.3	3415	80.2	3110	78.0	3128	76.7	3160	76.5
	Complicated appendicitis	897	20.6	818	19.2	805	19.4	814	19.7	842	19.8	876	22.0	950	23.3	970	23.5
Brandenburg	Uncomplicated appendicitis	2651	80.9	2562	80.1	2600	80.9	2424	80.6	2386	79.2	2233	77.3	2269	77.6	2246	76.3
	Complicated appendicitis	627	19.1	641	19.9	613	19.1	583	19.4	625	20.8	656	22.7	656	22.4	698	23.7
Mecklenburg-Western Pomerania	Uncomplicated appendicitis	1479	79.9	1483	78.7	1508	79.7	1429	79.2	1472	79.8	1418	78.5	1397	78.1	1258	74.7
	Complicated appendicitis	372	20.1	401	21.3	384	20.3	376	20.8	372	20.2	389	21.5	391	21.9	427	25.3
Saxony	Uncomplicated appendicitis	4074	82.1	3960	81.6	3926	80.8	3755	79.8	3681	80.1	3617	78.2	3467	78.0	3338	76.3
	Complicated appendicitis	891	17.9	892	18.4	930	19.2	950	20.2	917	19.9	1008	21.8	977	22.0	1037	23.7

	2010		2011		2012		2013		2014		2015		2016		2017	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Saxony-Anhalt	2376	81.0	2374	79.8	2333	80.5	2268	80.5	2350	81.5	2315	79.4	2311	78.8	2131	77.5
	559	19.0	601	20.2	564	19.5	549	19.5	532	18.5	602	20.6	623	21.2	617	22.5
Thuringia	2672	84.8	2688	84.9	2581	84.0	2551	83.0	2448	82.8	2313	81.9	2326	82.4	2155	79.6
	479	15.2	479	15.1	493	16.0	523	17.0	509	17.2	510	18.1	498	17.6	552	20.4
Other country or unknown	970	79.1	901	78.8	563	75.2	550	77.2	579	76.3	579	75.8	692	72.8	592	73.2
	256	20.9	243	21.2	186	24.8	162	22.8	180	23.7	185	24.2	259	27.2	217	26.8

eTABLE 4

Morbidity and mortality of inpatient cases with appendectomy as sole intervention for appendicitis

	2010		2011		2012		2013		2014		2015		2016		2017	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Total number of patients	113 614	100.0	113 975	100.0	111 957	100.0	108 437	100.0	107 322	100.0	104 922	100.0	102 997	100.0	102 464	100.0
Septicemia	578	0.5	533	0.5	545	0.5	535	0.5	578	0.5	650	0.6	677	0.7	727	0.7
Blood transfusions (≥ 6 units)	108	0.1	104	0.1	90	0.1	77	0.1	75	0.1	52	0.05	59	0.1	50	0.05
Postoperative ileus	494	0.4	468	0.4	473	0.4	454	0.4	509	0.5	526	0.5	521	0.5	537	0.5
Mechanical ventilation > 24 h	434	0.4	399	0.4	384	0.3	346	0.3	320	0.3	363	0.3	329	0.3	309	0.3
Complex intensive care	1796	1.6	1806	1.6	1693	1.5	1678	1.5	1744	1.6	1690	1.6	1697	1.6	1609	1.6
At least one indicator of complicated course	2540	2.2	2496	2.2	2432	2.2	2346	2.2	2512	2.3	2501	2.4	2521	2.4	2502	2.4
In-hospital mortality (all appendectomy cases)	184	0.16	174	0.15	138	0.12	139	0.13	134	0.12	112	0.11	114	0.11	118	0.12
In-hospital mortality (among patients with at least one indicator of complicated course)	136	5.4	131	5.3	105	4.3	106	4.5	107	4.3	86	3.4	81	3.2	86	3.4

eTABLE 5

Appendectomy case numbers, mortality, and morbidity, stratified by severity of appendicitis (uncomplicated or complicated)

	2010		2011		2012		2013		2014		2015		2016		2017		
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	
Total number of patients	113 614	100.0	113 975	100.0	111 957	100.0	108 437	100.0	107 322	100.0	104 922	100.0	102 997	100.0	102 464	100.0	
Hospital size	≤ 20 000 cases per year	83.0	60 583	82.6	56 367	82.5	52 161	81.9	49 421	81.7	45 547	80.6	42 771	80.1	41 943	79.6	
	> 20 000 cases per year	12 839	17.0	12 735	17.4	11 988	17.5	11 551	18.3	11 095	19.4	10 988	19.9	10 655	10 744	20.4	
Age (years)	< 15	19 190	86.2	18 379	85.7	17 067	85.4	15 418	84.5	14 184	84.0	13 188	83.0	12 328	81.4	12 065	80.7
	15–35	3083	13.8	3072	14.3	2924	14.6	2838	15.5	2709	16.0	2703	17.0	2811	18.6	2879	19.3
Mortality*1	> 35	48 561	91.3	48 791	91.1	48 325	90.9	47 634	90.9	47 283	91.0	45 205	90.1	43 809	90.0	42 227	89.2
	In-hospital mortality	57	0.06	38	0.04	47	0.05	28	0.03	29	0.03	21	0.03	27	0.03	23	0.03
Complicated course*2	At least one indicator of complicated course	127	0.62	136	0.65	91	0.43	111	0.53	105	0.51	91	0.42	87	0.40	95	0.42
		643	0.7	569	0.6	515	0.6	492	0.6	524	0.6	478	0.6	510	0.6	501	0.6
	1897	9.3	1927	9.2	1917	9.1	1854	8.9	1988	9.6	2023	9.4	2011	9.2	2001	8.9	

*1 The percentages given indicate the proportion of the total quantity

*2 The percentages given indicate the proportion of the subset of uncomplicated (complicated) appendicitis per year