

Acute uncomplicated diverticulitis: guidelines on diagnosis and management: is everything fine?

Abstract

The transition from intravenous (IV) antibiotic therapy to oral therapy and the observation that in patients with acute uncomplicated diverticulitis (AUD), treatment with or without antibiotics gave similar results in both hospitalized and outpatients, opened the way for out-of-hospital treatment in selected patients with CT-confirmed diagnosis. Due to economic constraints and a growing demand for hospitalization, home hospital care (HAH) and other community-based services was supported to alleviate the burden on emergency departments (EDs). This resulted in significant cost savings for the National Health Service (NHS) but, in many countries, community services are not uniformly present, leading to health care inequality. Relationships between hospital and community doctors indicate poor professional communication. Shared guidelines could lead to increased adherence. Some conditional recommendations based on low-certainty evidence related to the diagnosis and management of AUD remain controversial. Even after recovery from an episode, the question of whether to pursue conservative management or elective surgery is still open for debate. The outpatient treatment is understood as referring to both patients managed by hospital doctors and those treated by general physicians in their office. On management and outcomes of patients with AUD diagnosis in primary care there is little data. AUD treatment without antibiotics encounters resistance in many countries for multiple reasons, including low implementation and uncertain dissemination of guidelines recommendations. This would require greater control and commitment on the part of Institutional bodies and scientific societies.

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Social and health aspects in home care assistance

Since the 1940s, home care for the elderly has been a social value in Canada. However, skepticism about the capabilities of families to supply care and poor institutional planning hindered its development for decades. It was only when home treatment was found to be more cost-effective than hospitalization that the Health System began to support it, prioritizing health and cost saving over original social concerns.¹ In Ireland, the concept of outpatient treatment² took shape in the emergency departments (ED) in the last years of the past century to cope with the rapid increase in hospitalization requests for pediatric or elderly patients suffering from various acute or subacute diseases.³ The initial interest was primarily economic, with a focus on providing lower-cost out-of-hospital services as part of the Hospital-Based Home Care Program (HBPC).⁴

In the United States, home care service was very active in the 1930s but declined significantly in the 1950s. Subsequently the expansion of hospital-at-home services was due to multiple factors, including cost containment, quality of care, excessive demand for hospitalization, lack of acute inpatient services, and satisfaction among patients and their families with home treatment.⁵ Furthermore, the forecast of Medicare cost reductions made it necessary to plan and finance new hospital-based home care methods of diagnosis and treatment.^{2,5-8}

Antibiotics

In 1952 an “in office” study of patients with diverticulosis, documented by barium enema, found that 75 developed an unequivocal clinical picture of acute diverticulitis. All were treated with sulfonamides, with good results in 71. All except 4 were treated at home. Of the 4 who were hospitalized, only one required surgery. The conclusion was that if patients with diverticulitis are treated early,

they rarely require surgical intervention.⁹ Unlike studies conducted in a hospital setting, this one was carried out in private primary care and did not receive the attention it deserved.

In 1994 Sarin reported that 85% of the patients admitted who responded to the standard conservative IV antibiotic treatment, had a good outcome, with a recurrence rate of 2% per year at a median 48 months follow up. His conclusion was that in patients with conservative management, routine elective operation was not justified.¹⁰

The turning point in Europe and western countries, where diverticulitis mostly affects the left colon, came in 2007 with Hjerm's report¹¹ showing that antibiotics are not mandatory for mild diverticulitis. In hospitalized patients, conservative treatment with or without antibiotics had comparable outcomes, with recurrence or subsequent surgery rates of 28% and 29% respectively, at a mean follow-up of 30 months. However, the study was retrospective, and patients treated with antibiotics had more pronounced blood, clinical, and CT inflammatory parameters. So, the results warranted further randomized prospective studies.

In 2010, Etzioni confirmed the effectiveness of outpatient treatment in 94% of cases with initial acute diverticulitis diagnosed in ED room visit and confirmed by CT. The study found that risk factors for failure (6%), defined as a return to the emergency room or an admission for diverticulitis within 60 days, were female gender and the presence of free fluid on a CT scan.¹² Failure will then be defined in such a varied way as to constitute one of the factors of heterogeneity between studies.

A retrospective study on AUD confirmed the effectiveness of chemotherapy in outpatient setting and found that ambulatory oral antibiotic treatment was viable in 73% of patients with CT confirmed AUD and that only 3% of them needed admission.¹³

The requirements for outpatient treatment included the ability to tolerate oral intake, the absence of signs of systemic inflammatory response, no severe comorbidities, and family or social support allowing adequate monitoring. Priority was given to the absence of immune compromise, for the high risk of severe outcomes, which required hospitalization and antibiotic treatment.^{14,15} The antibiotic treatment in AUD was gradually defined based on evidence¹⁶ concerning the efficacy and savings of the oral route,^{17–19} the type and combination of antibiotics,²⁰ and the short vs the alternative courses of 7–10 or, 14 days.^{11,12,20,21}

No antibiotic treatment

In 2012, the RCT Avod and, later, the Diabolo study, albeit with limitations, highlighted the efficacy of conservative treatment without antibiotics in AUD.^{22,23} A Cochrane review aimed to evaluate the effects of antibiotics on relevant outcomes in AUD, concluded that the newest evidence from a single RCT needed confirmation from more RCTs before it could be safely “implicated” in clinical guidelines (16). Nevertheless, at about the same time, Danish guidelines reversed the traditional indication of mandatory use of antibiotics, arguing that there was no evidence of their beneficial effect in AUD. Antibiotics were to be used only in selected cases depending on the global clinical situation. Moreover, considering that clinical diagnosis may not be accurate stated that CT scan could confirm it and define its severity and guide treatment.²⁴ Even guidelines issued by Dutch scientific societies took a stand on the adequacy of treatment without antibiotics in selected mild cases. Nevertheless, their indication was that pain, absence of vomiting and C-reactive protein >50 mg/l were highly predictive of AUD. In the absence of signs of complication imaging could be avoided.²⁵

Outpatient treatment

A subsequent review evaluating the safety and effectiveness of home treatment with oral antibiotics (with a maximum hospital stay of 24 hours and further ambulatory or HAH assistance) found that failure rates (6.5% vs. 4.6%, $p=0.32$) and recurrence rates (13.0% vs. 12.1%, $p=0.81$) were similar between outpatient and inpatient care. Failure of medical treatment included the need for prolonged antibiotic treatment or admission for radiological or surgical intervention.

A meta-analysis was not possible due to the heterogeneity of the studies, but the conclusion was that outpatient treatment without antibiotics was adequate in selected patients, with a daily saving per patient of between 690 and 1,868 euros.²⁶ These results are in line with those of previous and subsequent studies. Nevertheless, some concerns arose, especially about a trend for a higher number of overall (9.0% vs. 5.0%) or elective (7.7% vs. 4.2%) interventions in the observational group compared to the antibiotic treatment group at 24 months, as well as many limitations in the study design.²⁷ This statistically non-significant difference in sigmoid resection (5.0% vs. 2.5%, $p=0.21$) was confirmed by pooling the 12-month data from the Avod and Diabolo trials.²⁸ Moreover, a meta-analysis including only randomized trials found that elective sigmoid resection was significantly more frequent in the observational than in the antibiotic group (2.5% vs. 0.9%; $p = 0.04$) during follow-up.¹⁹

In 2018, van Dijk et al conducted a meta-analysis on 2303 people and, while supporting the effectiveness and safety of the outpatient setting (7% readmission and 0.2% emergency surgery), underlined that the studies concerned only cases of left AUD. Moreover, only the Diver trial¹⁸ was a multicenter RCT^{23,29–31} guidelines adherence.

Besides the known studies limitations it was confirmed that the potential cost reduction of outpatient treatment, between 42 and

82%, compared to hospitalized patients had not been adequately implemented in clinical practice in many countries³² and that only a few guidelines had changed their recommendations on this point.^{33–35}

As for acute diverticulitis, in the US from 2002 to 2007 emergency admission rate increased by 9.5% but only 12.2% of patients underwent urgent surgical resection equal to a 4.3% increase but, unexpectedly, elective surgery increased by 38.7%.^{36,37} Even a population-based analysis using administrative data from 2002 to 2012 reported an increase in admissions for complicated acute diverticulitis and a reduction in urgent surgery (from 28% to 16%).³⁷ In some countries, instead, this trend reversed in the same period. In Iceland, although from 1985 to 1995 the incidence of admissions and resections for sigmoid diverticulitis increased, from that year until 2014 the incidence of hospitalization for diverticulitis decreased, particularly for elderly patients.³⁸

The increase in outpatient care reduced the number of inappropriate hospitalizations. In the US, while the number of visits for diverticulitis in the ED increased, admission rates dropped from 58.0% in 2006 to 47.1% in 2013, and bowel surgeries decreased by 33.7% in relation to visits for diverticulitis.³⁹ Data from the Italian Hospital Information System, from 2008 to 2015, found a progressive increase in hospitalizations for complicated AUD. The emergency surgery rate increased by 3.9% per year. Also in this study there was a significant increase of 38% in elective surgery.⁴⁰ According to the 2014 ASCRS guidelines,⁴¹ elective resection after AUD had to be considered only on a case-by-case basis. In the US elective sigmoidectomy continued to increase after the 2006 guidelines with an annual trend of 1.16% up to 2015. Only later there was a progressive adaptation to the new guidelines.^{42,43}

In Canada, population-based administrative data showed that elective surgery after discharge for acute diverticulitis decreased from 9.6% in 2002 to 3.9% by 2011, besides shorter stays, had produced savings.^{37,44} Thus, the reduction of hospitalizations and surgical interventions for AUD were determining factors in healthcare cost reduction, estimated at between 35% and 83% compared to traditional hospitalization.^{18,26,32,45}

Inequalities in access, treatment, and outcomes are related to economic, educational, and ethnic factors^{46,47} and are observed even in countries where medical care was guaranteed to everyone. The Swedish National Hospital Registry showed that among patients with diverticular disease, an increased risk of hospitalization, more frequent laparotomy, and complications were more frequently associated with low social status, advanced age, peripheral location, or in patients without private insurance.^{48–50} Regarding acute diverticulitis Previous studies in outpatients⁵¹ or in both inpatients and outpatients,⁵² treated without antibiotics found good results in short term follow up. Also, a population-based analysis using administrative data from 2002 to 2012 reported an increase in admissions for complicated acute diverticulitis and a decrease in urgent surgeries (from 28% to 16%) and an increase in percutaneous drainage.³⁷ However, this trend was reversed in some countries. In Iceland, the incidence of admissions and resections for sigmoid diverticulitis increased from 1985 to 1995, but from that year to 2014, the incidence of hospitalization for diverticulitis decreased, especially in older patients.³⁸

More recently, the long-term results of the AVOD trial confirmed efficacy and safety of outpatients' treatment with or without antibiotics at a median follow up of 11 years. In Van Dijk ST et al.²⁸ and the same conclusion was confirmed by another meta-analysis.⁵³ The randomized, multicenter DINAMO trial also confirmed that no antibiotic treatment is effective and no inferior to current standard treatment in AUD.⁵⁴

Subgroups

As for subgroups, the presence of significant comorbidities in outpatients treated with antibiotics did not affect outcomes in meta-analyses or single studies,^{29,45} although it should be noted that more than 80% of studies included only patients in their first acute episode, while patients with high ASA scores were excluded.³⁰

In their editorial Flum and Read point out the paucity of evidence in the literature data, the resulting weakness of guideline recommendations, and the low adherence to these recommendations. Currently, there are no global scores that have individual prognostic value for the outcome of diverticulitis. With subgroup evaluation that includes genetic data on other characteristics, it will be possible to obtain stronger evidence. The committee ASCRS CPG advocates a “large, randomized trial comparing surgery and medicine in diverticulitis (COSMID)” that has not yet recruited patients and aims to better clarify the outcomes of conservative and surgical treatment of diverticulitis. The primary endpoint is assessment of overall health at one-year follow-up.⁵⁵

It is important to note that 80% of patients with diverticula have no symptoms. Diverticulum is only an epiphenomenon of the multiple morpho-functional changes of the colon wall. However, some patients, about 20%, complain of abdominal symptoms essentially characterized by non-transient pain in the left iliac fossa, along with more nonspecific symptom or, more rarely, acute diverticulitis 10% of which is complicated or with sequelae. AI is likely to support research into individual predictive factors by processing thousands of clinical, environmental, metabolomics, and increasing genomic data.⁵⁶

Despite the economic benefits, adherence to outpatient treatment has been slow and inconsistent, although in a meta-analysis between 40% and 62.6% of patients were enrolled for this management after an assessment in the ED.^{31,57} In a 2011 web-based survey of gastroenterologists and surgeons in the Netherlands, 90% of respondents treated mild diverticulitis without antibiotics, and most of them “would consider” outpatient treatment.⁵⁸ and in Sweden, adherence to outpatient management without antibiotics increased from 20% to 60% between 2011 and 2014, with good clinical outcomes and a reduction in healthcare costs.^{51,58,59}

Reality shows large discrepancies on this issue. While in Ireland in 2014-16 the national Hospital In-Patient Inquiry (HIPE) reported that only 4.6% of diverticulitis admitted were complicated, in a single institution 40.5% of diverticulitis admitted had complications.⁶⁰

In a recent consensus conference of the European Association of Endoscopic Surgery (EAES) and the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) on the management of acute diverticulitis. Approximately 88% of members agreed with the recommendation that AUD can be treated with mild symptoms on an outpatient basis; 65% stated that this was already their daily practice; in contrast, 20.80% disagreed that this would likely change their practice, while 59.12% agreed with the recommendation to consider trying no antibiotic therapy in immunocompetent individuals with AUD and 50% disagreed that this would likely lead to a change in their practice.⁶¹

Health care services in the community and HAH

As mentioned earlier, attempts have been made to reduce disparities in health care. Over time, many forms of home, clinical, or community-based care services have emerged, varying both between

and within countries: Health Homes, Nursing Centers, Outpatient Parenteral Antibiotic Therapy (OPAT), Health Homes, community health centers and other modalities that are integrated into the various health care systems.

Instead, at the 2023 World Congress in Barcelona, it was reaffirmed HAH peculiarity as an acute hospital service with a responsible hospitalist supported by a multidisciplinary team; patients are treated at home as if they were in hospital; diagnostic services can be accessed urgently; remote monitoring of patients can be provided through home therapies and remote patient monitoring. Unlike other hospital services, support extends to 24 hours a day, expanding patient eligibility.⁶²

The development of international platforms, such as The World Hospital at Home Community, has facilitated the sharing of new experiences and the implementation of new solutions for home care. The cost-benefit ratio is beneficial for both the healthcare system and the patient and his family. However, this activity must be understood as one of other hospital and community services. The lack of integration between these services could mean that the imbalances observed in hospitalization remain in the outpatient setting.⁶³

Reorganization of services and common procedures are a prerequisite for better and uniform health care and compliance with the guidelines. In Italy, the proposed differentiated regional autonomies, with an inconsistent financial commitment and local organization, risk disregarding the principle of equal social and health care throughout the national territory.⁶⁴ Another aspect to consider is the distinction between the roles of hospital physicians and community-based physicians as poor interprofessional collaboration is often observed. Joint participation in the development of the guidelines would undoubtedly improve adherence.

Regarding outpatient treatment, recent guidelines update two aspects, concerning diagnosis (imaging) and treatment in the outpatient setting (with or without antibiotics). A review of the guidelines on these two aspects shows indications that are not consistent.

Imaging

Regarding the CT scan, the American Gastroenterological Association (AGA) Clinical Practice Update⁶⁵ reported as the first best practice advise that imaging should be considered to confirm the diagnosis in patients without current documentation because the clinical diagnosis alone may be incorrect.^{66,67} However, this rule has problems with applicability in primary care; Imaging requires hospital access or community facilities, which are absent or inadequate in many countries.

Although recommendations vary in strength,⁶⁸⁻⁷⁰ the guidelines emphasize the importance of performing a CT scan or US examination to confirm the diagnosis. The European Society of Coloproctology (ESCP)⁶⁸ guidelines also consider imaging “essential” for treatment decisions in both secondary and primary care. The American College of Physicians (ACP) instead suggests CT scan “when diagnostic uncertainty” exists” (conditional recommendation; low certainty evidence).⁷¹

In contrast to the American Society of Colon and Rectal Surgeons (ASCRS) (70), WSES suggests a staged approach beginning with a US examination, whereas the German guidelines⁷² advocate that imaging should be performed when diverticulitis is suspected. NICE and the guidelines of the Italian National Guideline System^{73,74} recognize the diagnostic value of early imaging and the possibility of immediate

initiation of adequate therapy and outpatient setting. Finally, the greatest dissent is found in the EAES and SAGES). Regarding the recommendation of selective imaging in patients suspected of having AUD, 42% of members stated that this was already their practice and 18% would change their practice. In contrast, 45% did not think it was likely that their practice would change.⁶¹ However, even on this topic is likely that current attitudes toward imaging will soon change due to AI support.⁷⁵

In primary care, on the other hand, imaging is not considered essential for clinical suspicion of mild AUD imaging, although some concerns are expressed. The most common objection is that in most studies, diagnoses were confirmed by imaging. In primary care setting it is difficult to quickly perform CT in the context of the NHS. Sonography, which would be easier to obtain and would be an alternative to CT in primary care, has objective diagnostic limitations out of specialized departments.^{70,76} Thus, blood tests can be quite informative, when performed.

Outpatient treatment with oral antibiotics proved to be a viable and effective option in 2/3 of patients presenting to the hospital with AUD, and this approach was successful in 94%. Complication and recurrence rates were like those obtained in hospitalized patients treated with IV antibiotics.⁷⁷ According to ACP and AGA, the efficacy of antibiotic treatment on the left side AUD is similar between outpatients and inpatients with low evidence. There is still insufficient evidence for some important clinical outcomes such as treatment failure, mortality, or emergency surgery.

The quality of evidence is low, and more studies are needed to obtain more precise effect estimates.^{71,78} Future studies should also consider the antibiotic spectrum to limit bacterial resistance, side effects, and costs.⁷⁹ Otherwise, WSES and ASCRS indicate that selected patients with uncomplicated diverticulitis can be treated without antibiotics (strong recommendation based on high-quality evidence, 1A). The result of the survey in which SAGES participated was particularly divergent. In addition, the assessment of the German guidelines⁷² is that in mild cases, even if CT is not performed, it is not clear why antibiotics should be given because their efficacy is not evident in AUD. For AGA, antibiotic treatment can be used selectively and not routinely in immunocompetent patients with mild AUD uncomplicated diverticulitis.

Recent guidelines recommend a wait-and-see approach with initial patient monitoring. Clear fluids or a light meal and analgesics are usually recommended, and in many cases, physicians are already using this observational approach without antibiotics.

Primary care

Most cases of AUD, which are visited to the doctor's office, refer to patients with mild symptoms, often only pain, can eat and move, and have help at home. In these cases, there should be no problem prescribing analgesics and a liquid or light diet for 24 hours, with a warning to report if the symptoms worsen. This treatment is widely used in northern Europe and other countries, but not elsewhere. Not surprisingly, many physicians consider giving antibiotics when diverticulitis is suspected.

Among the different reasons there is that not prescribing antibiotics in an acute phase would seem a paradox for doctors frequently prescribing them for mild symptoms. This widespread practice has also led patients to expect such treatment. Another reason is the fear of medicolegal aspects, considering that their prescription is still usual

treatment for patients with diverticula. However, there are individual situations in which GPs must decide whether to use antibiotics or not, such as in the presence of "significant" comorbidities. It is unclear whether and when heart disease or T2 diabetes - which account for 50% of comorbidities⁵⁷ or chronic obstructive pulmonary disease (COPD), which "increases the risk of infection", require antibiotics. On this point, there is often poor interprofessional collaboration between primary care physicians and other health care professionals, which is a barrier to adherence to the guidelines.⁸⁰

More detailed recommendations are needed to avoid doctors using antibiotics as the default option when in doubt. Moreover, when necessary, which antibiotics, dosage and duration of treatment should be suggested in guidelines?

The patients most seen in the office are the mildest cases for whom unnecessary referral can be avoided. But what happens next? We do not know how many of them had imaging, were referred to a specialist, received antibiotics or were hospitalized. Nonetheless, they are unlikely to have a worse outcome than patients referred to the hospital and discharged as outpatients. In the absence of confirmatory tests, it is not known how many cases are actually diverticulitis so there are no relevant data on their diagnosis, treatment, and outcome.

Indirect data comes from a study of patients who were presented to the ED or to outpatient clinics. In the two approaches an urgent CT scan was performed in 85% versus 15%; an abnormal EBC count was found in 69% versus 35%; and inpatient admission within 24 hours occurred in 30% versus 3.5% of patients' respectively.⁸¹

An Italian study of primary care physicians in patients with diverticular disease found that about 13% were referred to specialists. Of symptomatic diverticular patients, 3.4% had an admission related to diverticular problems. Only 13% had a previous diagnosis of diverticular disease. Nevertheless, rifaximin was prescribed in 61% of cases and ciprofloxacin in 7.6%.⁸²

In a small recent study evaluating compliance with NICE guidelines on antibiotic prescription, was carried out an electronic search. Among diagnoses of diverticulosis or diverticular disease, in 42% of the visits, presenting complaints were considered as "suspicious of diverticulitis." In further (one or more) consultations, antibiotics were prescribed in 68% of cases; approximately 12% of visits resulted in a referral for surgical evaluation, and blood tests were required in 19.3% of cases. Of note, only 3.5% of cases returned within 48 hours as recommended, while 3.5% of patients worsened and were hospitalized.⁸³ Although these are sparse data, adherence to guidelines seems to be very low, especially regarding antibiotics. The authors question whether diverticulitis should be managed in primary care.

The answer would be complex given that these cases are very frequent and that low adherence to guidelines, particularly about antibiotic use, is not new, is ubiquitous and can be observed in both hospital and primary care settings, although for different reasons.⁸⁰ Indeed, to assess compliance with NICE guidelines for antibiotic use in CT-confirmed AUD in the ED was found that all 20 patients with a National Early Warning Score (NEWS) of low risk were prescribed antibiotics. The conclusion in this case was the need for greater awareness of the guidelines.⁸⁴

Furthermore, to evaluate antibiotic use in primary care, prescriptions in patients with diverticular disease were monitored for 8.9 years after acute or non-acute hospitalization and in matched

inpatient controls. The result was that antibiotic use in primary care not only doubled over the years after an acute admission compared with controls but was also higher before admission.⁸⁵

Implementation and dissemination

The problem of inadequate adherence to guidelines affects the levels of the health care system, the organization, and the individual.

A recent “review of systematic reviews” aimed to identify the most frequently cited barriers and facilitators to the implementation of adherence to clinical practice guidelines in primary care. Among the six categories identified, the most frequently cited barriers included suboptimal healthcare network and interprofessional communication, applicability, motivation, and time.⁸⁶ Implementation refers to the adoption of new procedures or the application of new evidence that simplifies a process and allows for improved efficiency by reducing errors, time, and costs. However, the process is not quick. The time in which 5-10% of recommendations enter clinical practice is calculated as 17 years.⁸⁷

Implementation activities include, among others, many educational programs and feedback mechanisms. This assumes that the process of disseminating guidelines was adequate. Dissemination occurs, among many channels, through publication in “reputable” journals, medical conferences, and meetings, in institutional and professional organizations, in the media, and through professional channels.⁸⁸ It should be considered, however, that less prestigious journals can also be a good vehicle for disseminating inaccurate messages.

In a recent article, Hawkins addresses the specific issue of antibiotic treatment in AUD and asks a rhetorical question, “Why are we still using antibiotics for uncomplicated diverticulitis in North America?”⁸⁹

The question is pertinent, but circumscribed, because it is the same old question asked in other countries.⁹⁰ for example in Italy, where the use of antibiotics is higher than the European average. Among the many valid explanations, he and others cite I would like to focus on dissemination⁹¹ through medical conferences and meetings, where the message conveyed sometimes sounds unclear. It will be difficult to change the habit of diffuse antibiotic treatment when people with diverticula are cyclically prescribed antibiotics: in 61% of cases after acute diverticulitis, in 47% of cases with abdominal pain diagnosed as SUDD, and even in 20.6% of asymptomatic people in which some diverticula were discovered by accident.⁹² Considering that the latter group has a diverticulitis risk of 4.3% during an 11-year follow-up period, equivalent to 6 cases per 1000 patient-years and even lower when only confirmed cases are considered,⁹³ it is legitimate to wonder whether the dissemination was appropriate and in accordance with the guidelines or whether the message was misperceived by the audience. Institutional and professional organizations could curb this “unbalanced force”.

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