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A NATIONAL EVALUATION OF THE IMPLEMENTATION OF GUIDELINE RECOMMENDATIONS TOWARDS ANTIBIOTIC PROPHYLAXIS PRIOR TO PERCUTANEOUS ENDOSCOPIC GASTROSTOMY AND JEJUNOSTOMY TUBE PLACEMENT

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Percutaneous endoscopic gastrostomy (PEG) and percutaneous endoscopic jejunostomy (PEJ) tube placement are standard procedures for artificially administered nutrition support in malnourished patients. However, minor and major complications can occur. Peristomal infections are most common, potentially leading to severe inflammation, hospitalization, and PEG/PEJ removal. Antibiotic prophylaxis is effective in preventing peristomal infections and recommended by current guidelines but does not seem to be systematically used. The present study evaluated the implementation of prophylactic antibiotics in PEG/PEJ placement in clinical routine in Germany. A web-based survey was conducted among hospitals, ambulatory health care centers, and focus practice. In total, 107 participants have finalized the questionnaire. Most participants were from major regional and maximum care facilities (36.4%), basic and standard care facilities (28.0%), as well as university facilities (23.4%). Routine antibiotic prophylaxis for every PEG/PEJ procedure is performed by 42.6%, whereas 13.9% do not apply antibiotic prophylaxis in general, and 23.8% only use it in patients with risk factors for infectious complications. This decision is based on in-house guidelines in 34.0% of participants or national recommendations 20.2%, whereas international guidelines (8.5%) and other recommendations play a minor role (4.3%). Although prophylactic antibiotics in PEG/PEJ placement is effective and recommended by current guidelines, less than half of the sites reported to routinely apply it. Given that these recommendations are based on outdated evidence, updated data is needed, and guideline recommendations need to be re-evaluated accordingly and fully implemented.

Key words: *percutaneous endoscopic gastrostomy, percutaneous endoscopic jejunostomy, antibiotic prophylaxis, enteral nutrition, guidelines, participants, surgery, infectious complications*

INTRODUCTION

Percutaneous endoscopic gastrostomy (PEG) and percutaneous endoscopic jejunostomy (PEJ) tube placement have become standard practices for long-term artificially administered nutrition support exceeding 2 to 3 weeks (1, 2). In case of malnutrition or dysphagia, which is common in patients with cancer, PEG tube feeding is an important element of patient care (1, 2). Placement of the tube is technically simple and usually well-tolerated, but minor and major complications can occur (1-3). Peristomal infections constitute the most common complications, with a reported incidence of up to 30% (4). In particular, underlying malignancy and chemotherapy or radiotherapy have been shown to be risk factors for local infections. (5, 6). Although most infections are mild and resolve upon antibiotic treatment (4), peristomal infections can lead to severe inflammation with a potential need for hospitalization,

surgery and/or PEG removal (7, 8). In addition to the impact on the clinical outcome, this is also a health economic issue due to an increase in direct and indirect healthcare costs associated with infectious complications (8).

As early as 1998, the European Society of Gastrointestinal Endoscopy (ESGE) published a guideline exclusively focusing on antibiotic prophylaxis for gastrointestinal endoscopy. Due to the increased rate of infectious complications after PEG/PEJ placement, pre-interventional antibiotic prophylaxis was recommended for patients at risk (9). The ESGE recommendations were revised and published in 2021, updating the management of peri- and post-procedural PEG/PEJ facilities. The data updated with Cochrane meta-analyses confirmed the recommendation of the antibiotic-specific guideline of 1998, so that the administration of antibiotic prophylaxis is recommended for patients at risk (3). Since the COVID pandemic, the number of immunocompromised patients with an increased risk of bacterial infections has been

rising. Konturek *et al.* demonstrated that COVID-19 patients frequently develop gastrointestinal manifestations and complaints (10). Furthermore, Iqtadar *et al.* showed that critically ill patients with COVID-19 infections are prone to secondary bacterial and fungal infections (11). Antibiotic prophylaxis therefore appears increasingly relevant for patients with a heightened risk of

infection (10, 11). Despite long-standing recommendations that antibiotic prophylaxis should be administered prior to PEG/PEJ procedures, the incidence of post-interventional infection remains very high at 21.9%, according to a study published in 2018 (6). One of the reasons for the continuing high infection rates may be the non-observance of the guidelines. To address this question, the present national survey evaluated the implementation and integration of the recommendations of the guidelines in PEG/PEJ placement in clinical routine.

The present data show inconsistent approaches regarding antibiotic prophylaxis in PEG/PEJ. Given that the respective guidelines are based on outdated evidence and do not contain specific recommendations for responsibilities, the present results indicate a need to update and revise guidelines to facilitate their implementation.

METHODS

The present study was based on a multi-centre web-survey on clinical nutrition among hospital departments (including *e.g.*, internal medicine, gastroenterology, and oncology), ambulatory health care centers, and focus practices. Eligible institutions were informed about the survey through paper-based newsletters and invited to participate *via* subsequent mail which included a hyperlink to the online questionnaire on the survey platform EvaSys (2019). The questionnaire consisted of 20 questions on prophylactic antibiotics for PEG/PEJ placement (see supplement). The survey was conducted over one year, beginning in May 2019 to June 2020.

The study was approved by the ethics committee of the Friedrich-Alexander-Universität Erlangen-Nürnberg in Germany. No informed written consent was needed as no patients were involved in the study.

Participating facilities

In total, 5074 persons in eligible facilities were invited to participate in the survey. Of these, 107 (2.1%) have finalized the questionnaire. The highest participation rates were achieved in Bavaria (25.2%), Baden-Württemberg (15.0%), and North Rhine-Westphalia (13.1%), followed by Hesse (8.4%), Lower Saxony (6.5%), and Saxony-Anhalt (4.7%) (*Table 1*). Most survey participants were from major regional and maximum care facilities (36.4%), basic and standard care facilities (28.0%), as well as university facilities (23.4%). The majority of those health care facilities that have been included in the study are not-for-profit and public healthcare providers (*Table 1*). Participating departments mainly included surgery, internal medicine, oncology, and gynaecology. Most of the participating departments (55.9%) had a size of less than 50 beds (*Table 1*).

Statistical analysis

Statistical analyses were performed using SPSS26. All data were analysed descriptively in univariate analyses. Categorical data are presented as absolute and relative frequencies based on the number of valid responses.

RESULTS

Percutaneous endoscopic gastrostomy and jejunostomy placement

Two thirds (64.5%) of the respondents reported that they perform PEG/PEJ-placement themselves, and one-third (29.9%) reported that their patients' PEG/PEJ placement took place in

Table 1. Structural characteristics of survey participants (PEG/PEJ sub-questionnaire population).

Data	n=107 n (%)
Federal state	
Baden-Württemberg	16 (15.0)
Lower Saxony	7 (6.5)
Bavaria	27 (25.2)
North Rhine-Westphalia	14 (13.1)
Berlin	4 (3.7)
Rhineland Palatinate	3 (2.8)
Brandenburg	4 (3.7)
Bremen	1 (0.9)
Saxony	4 (3.7)
Hamburg	4 (3.7)
Saxony-Anhalt	5 (4.7)
Hesse	9 (8.4)
Schleswig-Holstein	3 (2.8)
Mecklenburg Western Pomerania	1 (0.9)
Thuringia	4 (3.7)
Service mission	
Major regional and maximum care facilities	39 (36.4)
Basic and standard care facilities	30 (28.0)
University facilities	25 (23.4)
Oncological practice	11 (10.3)
Medical care centers	2 (1.9)
Sponsorship	
Public	34 (31.8)
Non-profit	24 (22.4)
University hospital	24 (22.4)
Private	19 (17.8)
Not specified	6 (5.6)
Department	
Internal medicine	28 (26.2)
Surgery	26 (24.3)
Oncology	17 (15.9)
ENT	9 (8.4)
Gynaecology	7 (6.5)
Radiology	5 (4.7)
Maxillofacial surgery	4 (3.7)
Urology	3 (2.8)
General medicine	2 (1.9)
Dermatology	1 (0.9)
Other	3 (2.8)
Not specified	2 (1.9)
Department size	
<50 beds	45 (42.1)
50–80 beds	25 (23.4)
>80 beds	26 (24.3)
Not specified	11 (10.3)

other clinics (*Table 2*). About one-third (30.3%) are involved in up to 20 PEG/PEJ procedures per year, one-third in up to 40 procedures per year, and about 20% in over 40 procedures per year (*Table 2*). Probes of size 15 CH (38.3%), 12 CH (21.5%), and 20 CH (17.8%) were mostly used (*Table 2*). Short-term follow-up and control after PEG/PEJ insertion (*e.g.*, traction loosening on the following day) is predominantly performed either by the physicians of the referring hospital (34.7%) or the endoscopy department (40.6%). Tube feeding application is started on the day after placement at two-thirds (67.3%) of the facilities (*Table 2*).

Antibiosis application

Routine antibiotic prophylaxis is applied for every PEG/PEJ procedure by 42.6% of participants, whereas 13.9% do not use prophylactic antibiotics in general, and 23.8% only use it in

patients with individually suspected increased risk factors of infectious complications (*Table 3, Fig. 1*). The most frequently cited risk factors in this context are immunosuppression (87.5%), *diabetes mellitus* (41.7%), and underlying malignancies (37.5%) (*Table 3*).

Responsibility for antibiotics is roughly equally distributed between the referring institution (43.8%) and the endoscopy department (53.1%) (*Table 3*). If applied, antibiotic prophylaxis is most frequently administered before the intervention (66.3%) (*Table 3*). The most frequently used antibiotics are cefuroxime (29.0%), followed by ceftriaxone (22.4%), and amoxycillin/clavulanic acid (20.7%), whereas cefazoline is rarely used (3.7%), and cefotaxime is not used at all (0%).

The decision on antibiotic prophylaxis is most frequently based on in-house recommendations (34.0%) or on national guidelines (20.2%). International guidelines (8.5%) and other recommendations play a minor role (4.3%). One-third of the

Table 2. PEG/PEJ-related and organizational characteristics of participants (sub-questionnaire).

Questionnaire	n=107 n (%)
Does your facility/department request or perform the installation of PEG/PEJ?	n'=107
No, we do not organize a PEG/PEJ system	6 (5.6)
Yes, but we connect the patient to an external facility for this purpose	32 (29.9)
Yes, we carry out the installation ourselves.	69 (64.5)
How many PEG/PEJ are requested or performed by your department in a year?	n'=99
0–20	30 (30.3)
21–40	29 (29.3)
41–60	10 (10.1)
61–80	3 (3.0)
81–100	6 (6.1)
>100	13 (13.1)
I do not know.	8 (8.1)
Which sizes of PEG/PEJ probes do you use? (multiple answers allowed)	n'=107
9 CH	9 (8.4)
10 CH	4 (3.7)
12 CH	23 (21.5)
14 CH	15 (14.0)
15 CH	41 (38.3)
16 CH	12 (11.2)
18 CH	14 (13.1)
20 CH	19 (17.8)
Other	3 (2.8)
Who is responsible in your clinic/department/facility for short-term follow-up and control after PEG/PEJ insertion (<i>e.g.</i>, traction loosening on the following day)?	n'=101
Doctors of the referring hospital	35 (34.7)
Doctors of the endoscopy department	41 (40.6)
Specialized nutrition team	10 (9.9)
Nurse	15 (14.9)
When do you start tube feeding application in routine?	n'=101
Four hours after the application	18 (17.8)
On the following day after the application	68 (67.3)
Other time	2 (2.0)
I do not know.	13 (12.9)

Table 3. Use of prophylactic antibiotics.

Questionnaire	n=107
Do you perform routine antibiotic prophylaxis for PEG/PEJ placement in your facility/department?	n'=101
Yes, always before each PEG placement.	43 (42.6)
No, generally not.	14 (13.9)
No, only in patients with a special risk profile.	24 (23.8)
I do not know.	20 (19.8)
If antibiotic prophylaxis is used only in patients with a special risk profile, which are they? (multiple answers allowed)	n'=24
Immunosuppression	21 (87.5)
<i>Diabetes mellitus</i>	10 (41.7)
Malignant primary disease	9 (37.5)
Underlying cardiovascular disease	6 (25.0)
Underlying neurological disease	3 (12.5)
Geriatric patients	2 (8.3)
Other	0
Who is responsible for antibiotic administration?	n'=96
Referring department/clinic/unit	42 (43.8)
Endoscopy department	51 (53.1)
Other	3 (3.1)
When is antibiotic administration usually performed?	n'=95
Pre-interventional	63 (66.3)
Peri-interventional	9 (9.5)
Post-interventional	4 (4.2)
I do not know.	19 (20.0)
Which of the following antibiotics do you use? (multiple answers allowed)	n'=107
Cefuroxime	31 (29.0)
Ceftriaxone	24 (22.4)
Amoxicillin/Clavulanic acid	22 (20.7)
Cefazolin	4 (3.7)
Cefotaxim	0
Other ^a	4 (3.7)
I do not know.	27 (25.2)
Which recommendation/guideline do you refer to when deciding on antibiotic prophylaxis for PEG/PEJ?	n'=94
International guideline/recommendation	8 (8.5)
DGVS recommendation	19 (20.2)
In-house guidelines	32 (34.0)
Other recommendations ^b	4 (4.3)
I do not know.	31 (33.0)

a: named once each: Ciprofloxacin, Metronidazole, Rocephin, Unacid;

b: DGEM, RKI, tumor board agreement.

respondents (33.0%) do not know which guidelines the decision on antibiotics use is based on (Table 3, Fig. 2).

DISCUSSION

Despite the recommendation in the guidelines to administer antibiotic prophylaxis to high-risk patients before inserting a PEG/PEJ, the present study shows that this is not systematically implemented in clinical work. Despite national and international guideline recommendations, less than half of the participants implement these recommendations and apply

antibiotic prophylaxis in general. Another quarter use them only irregularly in patients with risk factors for infectious complications without paying special attention to the underlying disease. The most common risk factors mentioned by the participants in this context are general immunosuppression, *diabetes mellitus*, and malignancies, which are well described in literature (5, 6). The non-standardised application of antibiotic prophylaxis, despite the recommendation to administer it to every, *e.g.* cancer patient, could be one of the reasons for the still existing post-interventional infection rates (12). Two-thirds of the respondents involved in the study perform PEG/PEJ placements

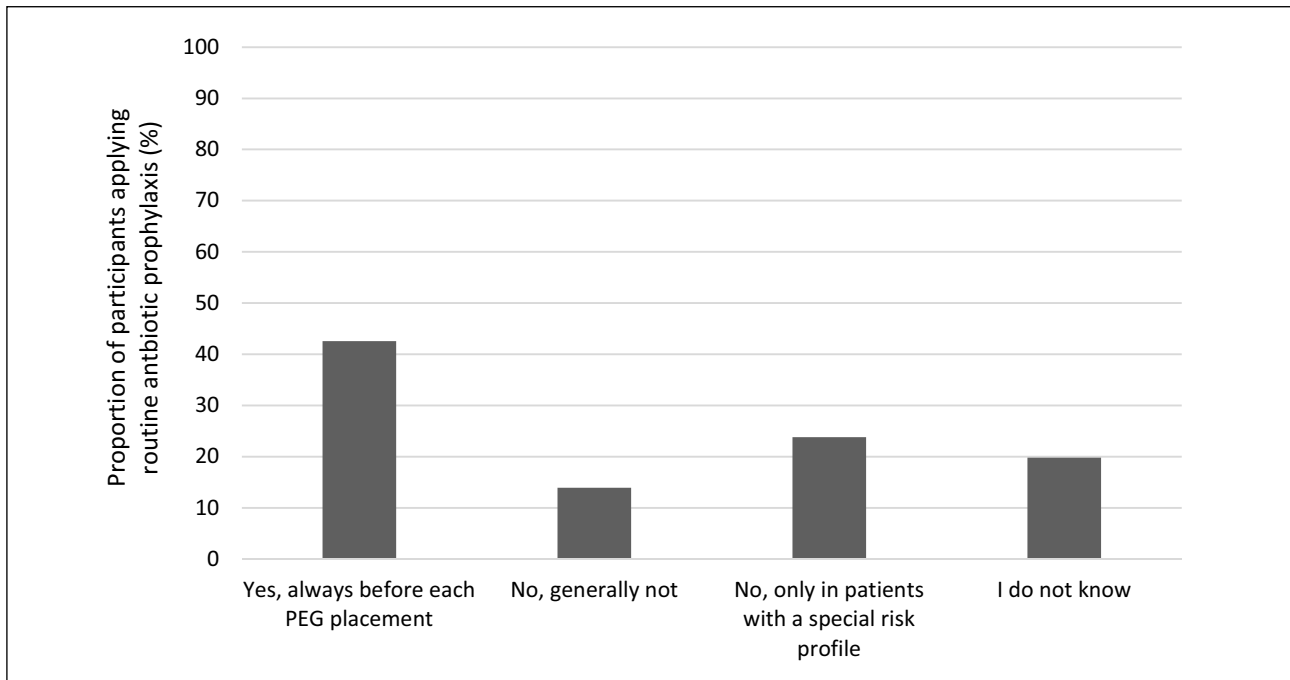


Fig. 1. Frequency of application of routine antibiotic prophylaxis for percutaneous endoscopic gastrostomy (PEG) and jejunostomy (PEJ) placement.

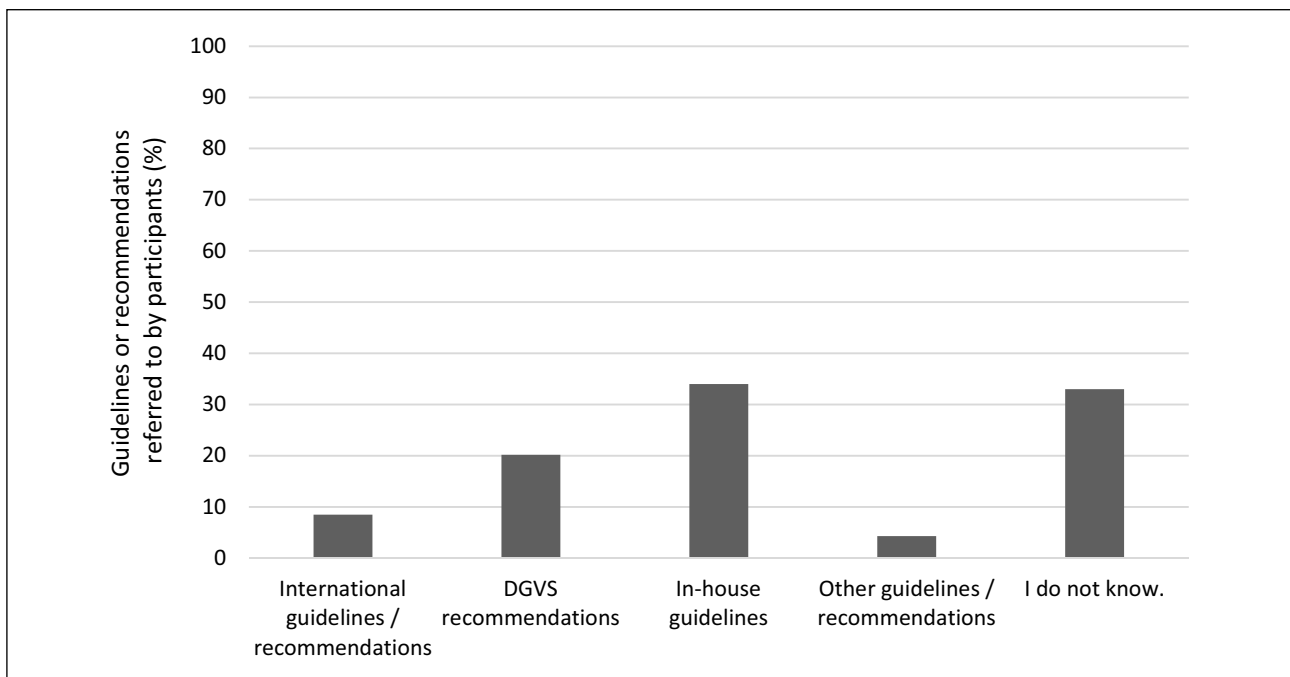


Fig. 2. Guidelines or recommendations referred to regarding antibiotic prophylaxis.

themselves, but in only half of the cases the endoscopy department is responsible for the administration of antibiotics. In most of the other cases, the referring department is responsible for application of antibiotics. One third of the participated clinics stated that they carry out less than 20 PEG/PEJ placements per year. Thus, the procedure may not be part of the daily routine in some of these facilities, and a lack of awareness of the current recommendations for invasive endoscopic procedures might play a role here. A standard operating procedure seems to be important in the complex structure of clinical work to implement official guidelines. Such

standardized processes may also have to be implemented and specified in the guidelines to ensure their use in clinical work.

Depending on who is responsible for preoperative management, guidelines from different professional associations may be consulted. The ESGE 2021 guideline as well as national guidelines as the DGVS guideline in Germany recommend antibiotic prophylaxis for all PEG/PEJ patients (3, 9, 13). In contrast, the guideline of the European Society for Clinical Nutrition and Metabolism (ESPEN), published in 2005, states that routine antibiotic prophylaxis is not obligatory in all cases (1). The latest version of this guideline does not comment on

issue of antibiotic prophylaxis. There is only a recommendation on how to handle infections after tube placements (14). The guideline for nutritional support in the homecare and outpatient sector of the German Society for Nutritional Medicine (Deutsche Gesellschaft für Ernährungsmedizin (DGEM)), which has been issued in 2013, is in accordance with the ESPEN guideline and does not support a general recommendation for antibiotic prophylaxis (14). However, the ESPEN 2005 guideline in addition refers to the ESGE recommendation of 1998 and adds that in case of doubt or outside experienced centres a generous decision in favour of antibiotic prophylaxis is recommended (1).

In order to ensure the implementation of recommendations and guidelines in clinical work, it would be advantageous if certain treatment recommendations could only be worked on by a defined working group or subject-specific societies. Otherwise, uncertainties arise in the use of recommendations. According to our survey, only one fifth of the participants reported to follow the national and international guidelines. The other participants stated that they followed internal clinic recommendations or other recommendations whose sources or references could not be named. Lack of defined structures for implementing evidence-based recommendations, could be a reason for inconsistent handling of antibiotic prophylaxis.

Of note, the 2021 ESGE recommendation for general antibiotic prophylaxis is based on a Cochrane meta-analysis including rather old evidence published mostly 20 to 25 years ago. This implies that systematic re-evaluation of antibiotic prophylaxis in PEG/PEJ placement is urgently needed to allow for development of new recommendations based on new evidence that resembles today's clinical practice settings.

The differing guideline recommendations highlight the controversy regarding antibiotic prophylaxis. This controversy might be astonishing given that a meta-analysis by the Cochrane collaboration summarizing evidence from RCTs supports the general application of antibiotics for PEG/PEJ placement for the "pull" method. For the "push" method, a more recent RCT has found no significant difference between a prophylaxis group and a control group (15). The clinical practice guidelines recently published the Korean Society of Gastrointestinal Endoscopy recommend the administration of prophylactic antibiotics at least once before tube placement in patients undergoing PEG using the pull method (16). On the other hand, there are no recommendations concerning other PEG/PEJ tube placement methods such as e.g. computed tomography (CT)-guided PEG/PEJ tube placement (17) or placement under ultrasonographic and fluoroscopic guidance (18). Further recent data suggesting that infection rates below 10% can be achieved with antibacterial gauzes instead of systemic antibiotics is derived from retrospective data and historical controls only (19). Overall, most clinical evidence is in favour of antibiotic prophylaxis. However, this evidence on antibiotic prophylaxis is either outdated or insufficient, i.e., lacks prospective, controlled trial settings. A systematic re-assessment of antibiotic prophylaxis in current clinical settings followed by a re-evaluation of guideline recommendations would be preferable.

In addition to the clinical point-of-view, which focusses on patients' benefits from antibiotic prophylaxis due to a lower rate of infection-related complications, there are also socioeconomic aspects worth to consider. An analysis by Kulling *et al.* based on seven randomised controlled trials also found prophylactic antibiotics a cost-effective strategy (8). The authors reported that the average cost of prophylactic antibiotics was approximately 13 US dollar and led to expected cost savings of approximately 77 US dollar per PEG (8). Although these data are based on the US health care system and have been published 20 years ago, they highlight the cost-saving potential of routine antibiotic prophylaxis. This effect can be assumed to be relevant in other

healthcare settings as well and further research should be undertaken to explore health economic benefits from a German point of view.

The choice of antibiotics for prophylaxis in German facilities, if applied, was in accordance with the recommendations. The 2021 ESGE guideline recommends using a single intravenous dose of a beta-lactam antibiotic or suitable alternatives in case of allergy (3). The DGVS guideline recommends the use of cephalosporines or penicillin (13). According to our survey, half of the participants use cephalosporine, and one fifth use amoxycillin with clavulanic acid. The optimal adjustment to the recommendations can be explained by the fact that the administration of antibiotics for skin germs has been established.

Taken together, clinical and public health aspects support the use of antibiotic prophylaxis. Against this background it surprises that half of the sites involved in PEG/PEJ do not follow the guideline recommendations. However, a lack of guideline implementation has been previously identified as a general problem in medical care across various disease areas (20). The reasons are supposed to be multifactorial and include personal factors (related e.g., to physicians' knowledge and attitude), guideline-related factors (related e.g., to guideline access or layout), and external factors (related e.g., to organisational constraints, lack of collaboration or lack of resources) (21). Jin *et al.* point out that half of the doctors don't use the guidelines due to lack of education and training (22).

The implementation of the guidelines could possibly be facilitated, if the responsible departments and specialists in the guidelines would be specifically named. The hospitals are also responsible for training their employees regularly and updating the internal hospital SOPs with the guidelines and emphasizing the underlying references.

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