

## Infective endocarditis: prevention and antibiotic prophylaxis

Swiss Society for Infectious Diseases, Swiss Society for Cardiology, Swiss Society for Paediatric Cardiology, Paediatric Infectious Disease Group of Switzerland

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### Summary

The Swiss societies of Infectious Diseases, Pediatric Cardiology and Cardiology and the Pediatric Infectious Disease Group of Switzerland present the current update on infective endocarditis prophylaxis in a joint initiative. The major focus of the revised recommendations is a comprehensive prevention campaign for all patients at risk for infective endocarditis. Antibiotic prophylaxis is recommended only for individuals at high risk. Within this high-risk group there is a ranking order, and the conditions are presented accordingly. Antibiotic prophylaxis is no longer recommended for patients with unrepaired ventricular septal defects and patent ductus arteriosus. Recommendations for antibiotic prophylaxis for the prevention of infective endocarditis are categorized in dental and non-dental interventions.

### Background and approach to guideline update

The Swiss Society for Infectious Diseases (SSI), with the support of the Federal Office of Public Health, initiated a platform for clinical practice guidelines in 2017. The goal of these guidelines is to optimise and possibly reduce antibiotic use in Switzerland [1]. After considerable revision of the previous guidelines on infective endocarditis prophylaxis by the American Heart Association in 2007, the Swiss recommendations were revised and published in 2008 [2]. The SSI and the Swiss Society of Cardiology together with the Swiss Society for Paediatric Cardiology and the Paediatric Infectious Disease Group of Switzerland are presenting the current update as a joint initiative. Following the standard procedure of establishing SSI guide-

lines, the expert group reviewed existing and published international guidelines and selected one of them as the designated reference guidelines. For the subject “Prevention of Infective Endocarditis”, the recommendations of the European Society of Cardiology (ESC) 2015 were selected [3]. Deviations in the wording of the text and adaptation of the recommendations in accordance with the Swiss health care system were formulated by the expert group and concisely presented as the “Swiss Guideline Digest”. This summary is freely available on the web (<https://ssi.guidelines.ch/> → Infective Endocarditis/Prevention).

### Prevention and prophylaxis

Traditionally, either the term “antibiotic prophylaxis” or “endocarditis prophylaxis” is used to mean the administration of an antimicrobial agent prior to an intervention (e.g., in dental medicine). The goal of antibiotic prophylaxis is the rapid elimination of a transitory bacteraemia that can occur during an intervention. Hence, the aim is to reduce the risk of developing infective endocarditis. Several studies have indicated, however, that only a small proportion of cases of infective endocarditis are associated with a previous dental intervention and that the association of infective endocarditis with skin or mucosal injuries through daily activities appears to have a much higher impact on the total number of infective endocarditis cases. This observation prompted the providers of national and international guidelines to focus on general prevention strategies, including comprehensive patient education about the potential risks of developing an infective endocarditis and recommenda-

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tions for skin and dental hygiene precautions. Thus, the terminology “prevention and prophylaxis” is important and should be used in future.

### Antibiotic prophylaxis is indicated for only one risk group

Depending on the severity of the heart disease and valvulopathy, the risk for infective endocarditis is categorised as moderate (or intermediate) or high [4]. After the indication for antibiotic prophylaxis was restricted to only one risk group (i.e., those at high risk for infective endocarditis), studies from England reported a reduction in antibiotic prescriptions and an increase in the incidence of infective endocarditis [5, 6]. Consequently, the results of these studies were discussed again, and broadening the indication for antibiotic prophylaxis was also considered [7, 8]. Conversely, other studies during the same period did not observe an increase in the incidence of infective endocarditis [9, 10]. Moreover, recent large epidemiological studies in the United States [11] and Europe [12] demonstrated that – despite changes in antibiotic prophylaxis guidelines – the incidence of infective endocarditis remained stable from 1998 to 2013 and 1990 to 2014, respectively. In agreement with the ESC 2015 guidelines, the Swiss expert group recommends antibiotic prophylaxis only for individuals at high risk and hence, for only one risk group. This recommendation has been valid in Switzerland since 2008 and continues to be so.

### What is new in comparison to the recommendations in 2008?

Among those in the high-risk group, patients with a history of infective endocarditis and with a prosthetic heart valve, or with a history of heart valve reconstruction and use of foreign body material, have the highest risk of infection [4]. Therefore, the indications for antibiotic prophylaxis in the high-risk group are presented in a specific ranked order. A few indications for antibiotic prophylaxis, previously listed in the 2008 recommendations, were removed because of lack of evidence. These indications include ventricle septum defect or open ductus arteriosus without surgery.

#### Populations at high risk for infective endocarditis

1. Patients with a previous episode of infective endocarditis.
2. Patients with any prosthetic valve (biological or mechanical), including a transcatheter valve (transcatheter valve implantation), or those in whom any prosthetic material was used for cardiac valve repair.
3. Patients with congenital heart disease (CHD):

Any type of cyanotic CHD (i.e., unrepaired CHD).

Any type of CHD repaired with prosthetic material, whether placed surgically or by percutaneous techniques. ⇒ At risk for up to 6 months *after* the procedure.

Any type of CHD repaired with prosthetic material, whether placed surgically or by percutaneous techniques. ⇒ At lifelong risk if residual shunt persists or

if residual finding persists *after* the procedure (e.g., incomplete tissue ingrowth of prosthetic material).

4. There is no evidence to recommend antimicrobial prophylaxis for cardiac transplant recipients who develop cardiac valvulopathy. The indication should be discussed on a case-by-case basis. The patient should contact their transplant specialist to evaluate the indication *prior* to an elective intervention.

#### Dental and non-dental interventions

Antibiotic prophylaxis recommendations for interventions related to ear-nose-throat surgery, the skin, the respiratory tract, the gastrointestinal tract and the urogenital tract are not part of the specific antibiotic endocarditis prophylaxis recommendations for two reasons. First, most abdominal and gynaecological surgical interventions are performed in a hospital setting, and Swissnos has published recommendations for perioperative antibiotic prophylaxis [13] that apply to all patients, including those with an elevated risk for infective endocarditis. A few exceptions for high-risk patients are published on the SSI website (<https://ssi.guidelines.ch/> → Infective Endocarditis/Prevention, Box 3), such as antibiotic treatment for incision of a skin abscess, or antimicrobial agent options for abdominal surgery (i.e., amoxicillin/clavulanic acid instead of cefuroxime or cefazolin to cover activity against *Enterococcus* spp.). Second, the Swiss Society for Gastroenterology published specific antibiotic prophylaxis recommendations for endoscopic interventions [14]. For these reasons, recommendations for an endocarditis card (similar to an allergy passport carried by patients) is limited to dental interventions. For non-dental interventions, we refer to published recommendations of various societies [13, 14] and those of the SSI (list below and <https://ssi.guidelines.ch/> → Infective Endocarditis/Prevention).

#### Dental procedures

Antibiotic prophylaxis is not recommended for local anaesthetic injections in non-infected tissues, treatment of superficial caries, removal of sutures, dental X-rays, placement or adjustment of removable prosthodontic or orthodontic appliances or braces, the period following the shedding of deciduous teeth, or superficial trauma to the lips and oral mucosa.

Antibiotic prophylaxis should only be administered for dental procedures with a tendency to bleed:

- requiring manipulation of the gingival or periapical region of the teeth
- perforation of the oral mucosa

#### Antibiotic prophylaxis prior to dental intervention and dental hygiene\*

The antibiotic prophylaxis should be taken 1 hour prior to the intervention.

Amoxicillin

- Adults: 2 g p.o.
- Children: 50 mg/kg (maximum dose 2 g) p.o.

Alternatives in the case of penicillin allergy

- Adults: cefuroxime-axetil 1 g p.o. in patients with delayed hypersensitivity reaction
- Children: cefuroxime-axetil 50 mg/kg p.o. (maximum dose 1 g) in patients with delayed hypersensitivity reaction
- Adults: clindamycin 600 mg p.o. in patients with immediate hypersensitivity reaction
- Children: clindamycin 20 mg/kg p.o. (maximum dose 600 mg) in patients with immediate hypersensitivity reaction

In the case of inability to swallow the antibiotic pill

- Adults: amoxicillin 2 g i.v.
- Children: amoxicillin 50 mg/kg i.v. (maximum dose 2 g)

Alternatives in the case of penicillin allergy and inability to swallow the antibiotic pill

- Adults: cefazolin 1 g i.v. or ceftriaxone 2 g i.v. in patients with delayed hypersensitivity reaction
- Children: cefazolin 25 mg/kg i.v. (maximum dose 1 g) or ceftriaxone 50 mg/kg i.v. (maximum dose 2 g) in patients with delayed hypersensitivity reaction
- Adults: clindamycin 600 mg i.v. or vancomycin 1 g i.v. in patients with immediate hypersensitivity reaction
- Children: clindamycin 20 mg/kg i.v. (maximum dose 600 mg) or vancomycin 20 mg/kg i.v. (maximum dose 1 g) in patients with immediate hypersensitivity reaction

\* There will be a separate antibiotic card for adults and children.

## Non-dental interventions

### Ear-nose-throat procedures

- Antimicrobial perioperative prophylaxis is not recommended for tonsillectomy in patients without risk for infective endocarditis. There is no evidence-based recommendation for antimicrobial perioperative prophylaxis in patients with risk for infective endocarditis.
- Tonsillectomy is associated with bacteraemia in a considerable proportion of patients undergoing this procedure. There is no evidence that antimicrobial perioperative prophylaxis prevents infective endocarditis in patients at risk for infective endocarditis. The majority of the expert group favours perioperative antimicrobial prophylaxis for tonsillectomy in patients at high risk for infective endocarditis. The agent should contain activity against microorganisms belonging to the oral flora.

- The expert group clearly categorises this statement as an opinion and not as a guideline recommendation. The expert group also states that the number of opinions does not correlate with the level of evidence.

### Respiratory tract procedures

- Antibiotic prophylaxis is not recommended for bronchoscopy, laryngoscopy, or transnasal or endotracheal intubation.
- For invasive procedures to treat an established infection (e.g., drainage of abscess), an empirical antibiotic regimen containing anti-staphylococcal activity (*Staphylococcus aureus*) should be used.

### Gastrointestinal/genitourinary procedures

- Antibiotic prophylaxis is not recommended for gastroscopy, colonoscopy, low-risk laparoscopic procedures on the biliary tract (see also recommendations for antimicrobial perioperative prophylaxis of Swissnoso 2015), cystoscopy, vaginal or caesarean delivery, or transoesophageal echocardiography.
- In the case of an established infection, an empiric antibiotic regimen containing anti-enterococcal activity should be used.
- If antibiotic therapy is indicated to prevent wound infection or sepsis associated with a gastrointestinal or genitourinary tract procedure, antimicrobial perioperative or peri-interventional prophylaxis containing anti-enterococcal activity should be used (see table 1, dose recommendations are based on normal renal and liver function).

### Skin and soft tissue procedures

- Antibiotic prophylaxis is not recommended for any procedure.
- For surgical procedures on infected skin/skin structures (e.g., incision of a skin abscess), empirical antibiotic should contain an agent with activity against staphylococci and beta-haemolytic streptococci.

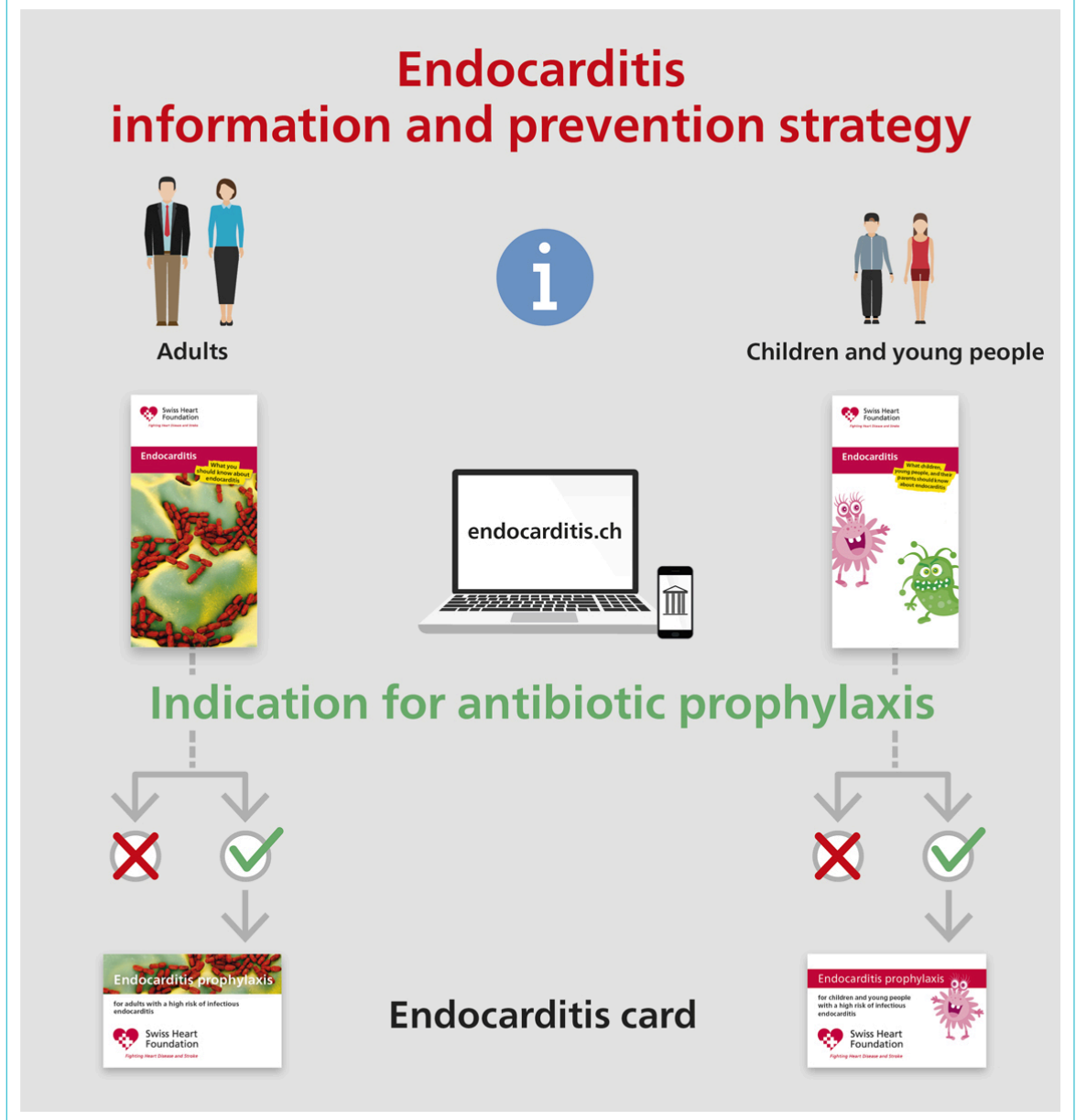
### Cardiac or vascular interventions

- Preoperative screening for nasal carriage of *S. aureus* is recommended before elective cardiac surgery in order to treat carriers.
- Systematic local treatment without screening for *S. aureus* is not recommended.
- Potential sources of infection (e.g., dental focus) should be treated/removed  $\geq 2$  weeks prior to the intervention.

**Table 1:** Perioperative or peri-interventional antimicrobial prophylaxis for gastrointestinal/genitourinary procedures.

Perioperative antimicrobial prophylaxis	No allergy to penicillin	Allergy to penicillin
Adults: 30–60 min before procedure, single dose	Amoxicillin/clavulanate 2.2 g i.v.	Vancomycin 1 g i.v. plus gentamicin* 3 mg/kg i.v. (or ciprofloxacin 400 mg i.v.) plus metronidazole 500 mg i.v.
Children: 30–60 min before procedure, single dose	Amoxicillin/clavulanate 50/5 mg/kg i.v. (maximum 2.2 g i.v.)	Vancomycin 20 mg/kg i.v. (maximum 1 g i.v.) plus gentamicin 2.5 mg/kg (maximum 80 mg) i.v. plus metronidazole 10 mg/kg i.v. (maximum 500 mg i.v.)

– \* As an alternative to gentamicin, another aminoglycoside (e.g., amikacin) can be administered. Kindly contact your institutional infectious diseases physician.

**Figure 1:** Information and prevention strategy: prevention campaign for all patients at risk for infective endocarditis.

- Perioperative antibiotic prophylaxis is recommended before placement of a pacemaker or implantable cardioverter defibrillator.
- Perioperative antibiotic prophylaxis should be administered to patients undergoing surgical or transcatheter implantation of a prosthetic valve, intravascular prosthetic device, or other foreign material (e.g., graft implantation for endovascular aneurysm repair).
- Prophylaxis should be started immediately before the procedure and repeated if the procedure is prolonged. Prophylaxis should not be prolonged for more than 48 hours.

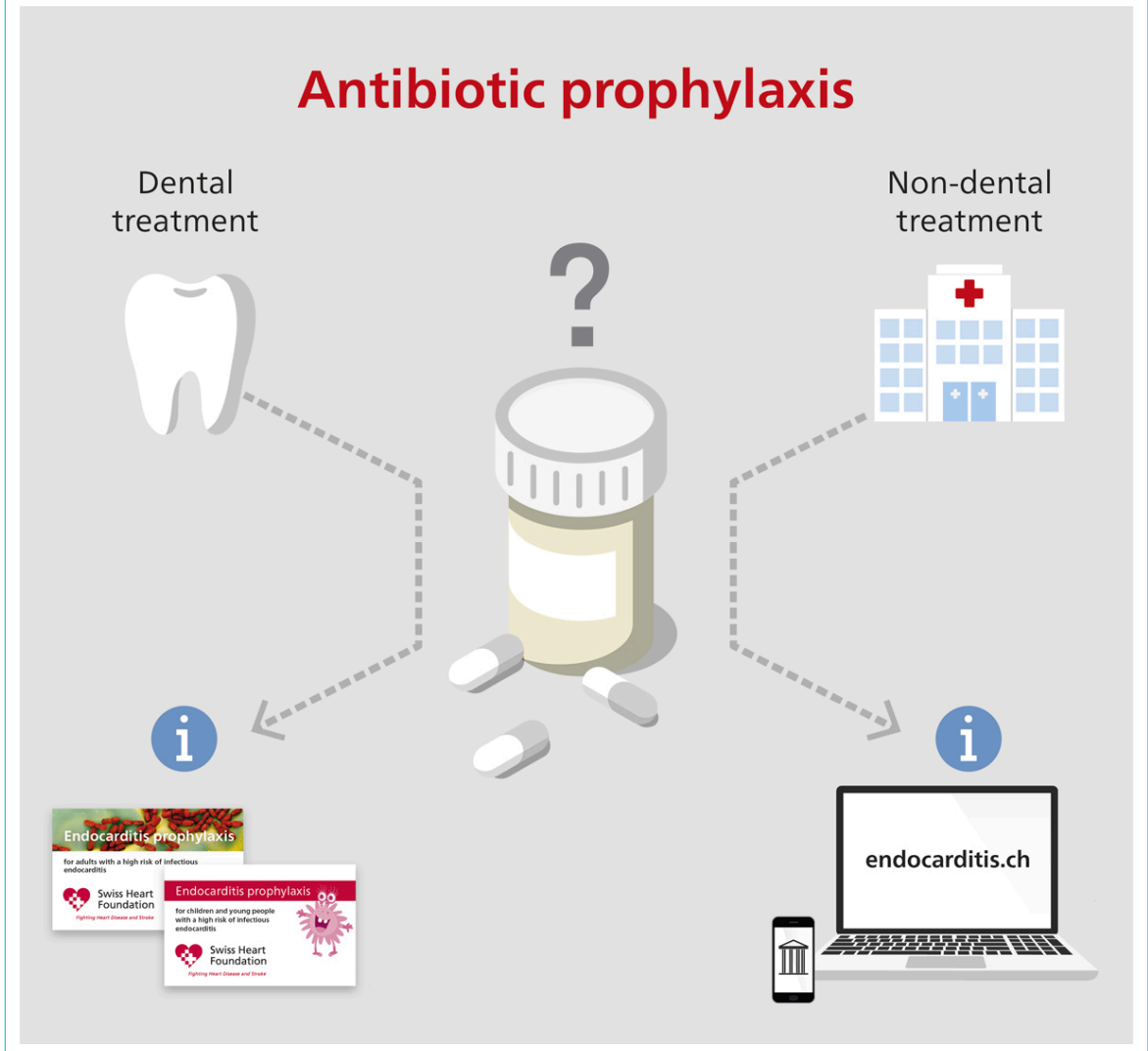
### Areas of uncertainty

While developing the Swiss Digest recommendations, the members of the expert group discussed the following areas of uncertainty thoroughly.

### Heart transplantation

Antibiotic prophylaxis in cardiac transplant recipients who develop cardiac valvulopathy is not supported by evidence and is not recommended by the ESC [3]. Conversely, the International Society for Heart and Lung Transplantation (ISHLT, 2010) recommends prophylaxis in cardiac transplant recipients who develop cardiac valvulopathy [15]. Transplant patients have a high risk of developing tricuspid regurgitation [16]; nonetheless, only a few (heterogeneous) publications are available on tricuspid regurgitation and the risk of developing infective endocarditis [17, 18]. The rationale for the ISHLT recommendations (expert opinions and consensus statement) relies on the observation of severe clinical courses with a high mortality rate in transplant patients with infective endocarditis [19]. The expert group confirms that there is no scientific evidence to support a recommendation for or against antibiotic prophylaxis in cardiac transplant patients who develop valvulopathy. The majority of the expert group members follow the recommendations of the ESC 2015 [3]. At the same time, the ex-

**Figure 2:** Patients with the highest risk for infective endocarditis require antibiotic prophylaxis prior to dental interventions. Only these patients will also receive a separate antibiotic card. For non-dental interventions, specific recommendations can be found on the corresponding websites.



pert group states that it is not meaningful to express a generalisable recommendation in Switzerland for a relatively small patient population with (different) complex disease histories. Because all heart transplant patients are followed up in specialised institutions, it is the responsibility of the treating transplant physician to prescribe antibiotic prophylaxis prior to the intervention, as evaluated on a case-by-case basis.

### Tonsillectomy

Bacteraemia occurs frequently during tonsillectomy [20–23]. However, perioperative antibiotic prophylaxis is not recommended for tonsillectomy in patients without risk for developing infective endocarditis [13, 24]. Because of the lack of evidence, the ESC has not published any recommendations for patients with risk factors for developing infective endocarditis. The majority of the expert group favour the administration of antimicrobial prophylaxis in high-risk patients who are undergoing tonsillectomy [2, 23, 25]. The antimicrobial agent must have activity against organisms belonging to the oral microbiome (e.g., amoxicillin 2 g or amoxicillin/clavulanic acid 2.2 g in adults, and 50 mg/kg [maximum dose 2.2 g] in children intravenous-

ly 30 minutes prior to incision). However, because of lack of evidence, the expert group clearly categorises this statement as expert opinion and not as guideline recommendations.

### Information and communication strategy

The endocarditis prophylaxis recommendations presented herein differ in only minor points in comparison to those published in 2008. The revised recommendations mainly relied on a comprehensive prevention campaign for all patients at risk for infective endocarditis (fig. 1).

The information strategy includes the following key elements:

- Knowledge transfer to increase awareness of good dental and skin hygiene.
- Education about symptoms consistent with infective endocarditis and appropriate steps to take when these symptoms occur (i.e., contact the doctor, obtain a blood culture sample prior to administration of antibiotic therapy).

Considering that the rapid diagnosis and correct treatment of infective endocarditis can be life-saving, patient education is a central element in the prevention strategy. For this reason, the Swiss expert group is collaborating with the Swiss Heart Foundation. An information flyer that illustrates the most important issues about infective endocarditis has been generated and is being distributed to all patients at risk for infective endocarditis (fig. 1). The purpose of this flyer is patient education and as a supportive instrument for caregivers and providers in the field of heart disease. Patients at highest risk for infective endocarditis require antibiotic prophylaxis prior to certain dental interventions, and only these patients will receive an antibiotic card (fig. 1). Different versions of flyers and cards are available for adults and children. For non-dental interventions, specific recommendations can be found on the corresponding websites (fig. 2). Additional patient information can also be found on the following websites: <https://www.endocarditis.ch> [German] and <https://www.endocardite.ch> [French]. Development of an educational movie is in progress.

#### Acknowledgment

We are indebted to the Swiss Heart Foundation for the excellent collaboration and generous support regarding public information. We thank Prof. Dr. med. dent. Michael Bornstein, Department of Oral Health and Medicine, University Centre for Dental Medicine Basel UZB, University of Basel, Basel, Switzerland, for his support on aspects of dental medicine.

A German and French version of this article has been published in the journal *Swiss Medical Forum* (<https://doi.org/10.4414/smf.2021.08717>) and <https://doi.org/10.4414/fms.2021.08717>.

#### Disclosure statement

No financial support and no other potential conflicts of interest relevant to this article were reported.

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