



# European Heart Rhythm Association (EHRA) international consensus document on how to prevent, diagnose, and treat cardiac implantable electronic device infections—endorsed by the Heart Rhythm Society (HRS), the Asia Pacific Heart Rhythm Society (APHRS), the Latin American Heart Rhythm Society (LAHRS), International Society for Cardiovascular Infectious Diseases (ISCVID), and the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS)

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Pacemakers, implantable cardiac defibrillators, and cardiac resynchronization therapy devices are potentially lifesaving treatments for a number of cardiac conditions but are not without risk. Most concerning is the risk of a cardiac implantable electronic device (CIED) infection, which is associated with significant morbidity, increased hospitalizations, reduced survival, and increased health care costs. Recommended preventive strategies such as administration of intravenous antibiotics before implantation are well-recognized. Uncertainties have remained about the role of various preventive, diagnostic, and treatment measures such as skin antiseptics, pocket antibiotic solutions, antibacterial envelopes, prolonged antibiotics post-implantation, and others. When compared with previous guidelines or consensus statements, the present consensus document gives guidance on the use of novel device alternatives, novel oral anticoagulants, antibacterial envelopes, prolonged antibiotics post-implantation, as well as definitions on minimum quality requirements for centres and operators and volumes. The recognition that an international consensus document focused on management of CIED infections is lacking, the dissemination of results from new important randomized trials focusing on prevention of CIED infections, and observed divergences in managing device-related infections as found in an European Heart Rhythm Association worldwide survey, provided a strong incentive for a Novel 2019 International State-of-the-art Consensus document on risk assessment, prevention, diagnosis, and treatment of CIED infections.

## Keywords

Infection • Device • Extraction • Defibrillator • Pacemaker • Leads

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## Introduction

Pacemakers, implantable cardiac defibrillators (ICDs), and cardiac resynchronization therapy (CRT) devices are lifesaving treatments for a number of cardiac conditions. Device-related infection is, however, one of the most serious complications of cardiac implantable electronic device (CIED) therapy. The recognition of gaps in knowledge, reports of new important randomized trials, observed divergences in managing device-related infections,<sup>1</sup> and the lack of international consensus documents specifically focusing on CIED infections provided a strong incentive for a 2019 State-of-the-art Consensus document on management of CIED infections.

This consensus document is an international collaboration among seven professional societies/associations with a writing group consisting of cardiologists with varying subspecialties, infectious disease specialists, imaging specialist, and thoracic surgeon, from 11 countries in

**Table 1** Scientific rationale of recommendations

Consensus statement related to a treatment or procedure	Definitions of consensus statement	Statement class	Scientific evidence coding	References
Recommended/indicated or 'should do this'	Scientific evidence that a treatment or procedure is beneficial and effective. Requires at least one randomized trial or is supported by large observational studies and authors' consensus		R	
May be used or recommended	General agreement and/or scientific evidence favour the usefulness/efficacy of a treatment or procedure. May be supported by randomized trials based on small number of patients or not widely applicable		O	
Should NOT be used or recommended	Scientific evidence or general agreement not to use or recommend a treatment or procedure		E	

This categorization for the consensus document should not be considered as being directly similar to that used for official society guideline recommendations which apply a classification (I–III) and level of evidence (A, B, and C) to recommendations. The grading does not have separate levels of evidence, which instead are defined in each of the coloured heart grades.

The 'ROME' coding was applied for each consensus statement, defining existing scientific evidence; R for randomized trials, O for observational studies, M for meta-analyses, and E for expert opinion.

4 continents. A detailed literature search until May 2019 and systematic reviews of published evidence related to CIED infection topics were performed. Results of the international survey on CIED infections conducted for this purpose<sup>1</sup> and of previous registries<sup>2</sup> were considered. Consensus statements were evidence-based, derived primarily from published data and by consensus opinion after thorough deliberations, requiring at least 80% predefined consensus.

The European Heart Rhythm Association (EHRA) ranking system for consensus documents, with 'coloured hearts' providing the current status of the evidence and consequent guidance, was used for the coding of the scientific evidence for statements made (Table 1).

The document was peer-reviewed by official external reviewers representing EHRA, the participating societies, and European Society of Cardiology (ESC) Committee for Practice Guidelines (CPG). All members of the writing group as well as reviewers have disclosed potential conflicts of interest, at the end of this document.

The medical approaches discussed may include drugs or devices that are not approved by governmental regulatory agencies in all countries. The ultimate decision on management must be made by the health care provider and the patient in light of individual factors presented.

## Background and epidemiology

Infection is one of the most serious complication of CIED therapy and is associated with significant mortality, morbidity, and financial health care burden. In the Danish registry of pacemaker implantation between 1982 and 2007, the incidence of infection was 4.82/1000 device-years after a primary implantation, and 12.12/1000 device-years after replacement.<sup>3</sup> The incidence of CIED infection in the USA increased from 1.53% in 2004 to 2.41% in 2008<sup>4</sup> and a National Inpatient Sample database study showed an increase from 1.45% to

3.41% ( $P < 0.001$ ) from 2000 to 2012.<sup>5</sup> Infection rates in prospective observational studies,<sup>6,7</sup> registries,<sup>8</sup> and recent cross-over cluster PADIT- and randomized WRAP-IT trials<sup>9,10</sup> were only 0.6–1.3%, when compared with retrospective studies<sup>11,12</sup> reporting significantly higher rates (2.3–3.4%) in the first year after implantation.

## Pathogenesis and microbiology of cardiac implantable electronic device infections

Cardiac implantable electronic device infections occur via two major mechanisms. The most common is contamination of leads and/or pulse generator during implantation or subsequent manipulation.<sup>13</sup> Device erosions late after interventions may either be due to or result in pocket infection. Contamination and subsequent bacterial colonization result in pocket infection which can spread along the intravascular parts of the leads and progress to systemic infection. The second mechanism is a bloodstream infection.<sup>14</sup> Direct lead seeding can occur during bacteraemia caused by a distant infectious focus or bacterial entry via the skin, mouth, gastrointestinal, or urinary tract.

The pathogenesis of CIED infections can be related to the host, the device, or the microorganism. The patient's own skin flora can be introduced into the wound at the time of skin incision. Contamination may also occur before implantation via the air in the operating room or via the hands of anyone handling the device. Device-related factors are those affecting bacterial adherence to the generator or lead and the biofilm formation on these surfaces.<sup>15</sup> Normally non-pathogenic microorganisms such as Coagulase-negative Staphylococci (CoNS) may adhere to the CIED and establish a focus of infection. The microorganisms most frequently isolated have

**Table 2** Pathogens isolated in patients undergoing interventions for device infection from three large patient cohorts in North America, Europe, and Asia

Pathogens	Percentage of isolates		
	North America <sup>16</sup>	Europe <sup>17</sup>	Asia <sup>18</sup>
Coagulase-negative Staphylococci		69	45.2
Methicillin-resistant	18.8		
Methicillin-sensitive	18.8		
<i>Staphylococcus aureus</i>		13.8	4.1
Methicillin-sensitive	15.8		
Methicillin-resistant	15.0		
<i>Streptococcus</i> spp.	2.5		
<i>Enterococcus</i> spp.			
Vancomycin-sensitive	2.8		
Vancomycin-resistant	1.4		
<i>Cutibacterium</i> spp. (previously <i>Propionibacterium</i> spp.)		2.5	
<i>Corynebacterium</i>		5	
Gram-negative bacteria	8.9	6.1	9.1
<i>Enterobacteriaceae</i>		3	3.2
Non-fermentative bacilli, incl. <i>Pseudomonas</i> spp.		1.5	5.9
Anaerobes	1.6		
Fungi	0.9	1	0.9
Mycobacteria	0.2		

been Gram-positive bacteria (70–90%), especially CoNS (37.6% of the isolates) and *Staphylococcus aureus* (30.8%), which are far more prone to adhere to non-biological material than others (Table 2).<sup>16,17,19</sup> *Staphylococcus aureus* is the most common cause of bacteraemia and early pocket infections. Altogether, methicillin-resistant staphylococci were isolated in 33.8% of CIED infections (49.4% of all staphylococcal infections).<sup>16,18,20</sup>

## Risk factors for cardiac implantable electronic device infection

Identification of modifiable risk factors is important because it may allow for preventive measures to reduce the risk. In patients with non-modifiable risks, alternative approaches may be an option to lower the overall risk.

A meta-analysis<sup>21</sup> of pooled data including 206 176 patients summarizes the most important risk factors in Table 3. In large device registry-, health care database-, and device-cohort studies,<sup>5,22,23</sup> the importance of risk factors varied from study to study and findings were in some cases contradictory (age as an example).

Of the *patient-related factors*, end-stage renal disease was consistently associated with the highest risk, but not age or gender.<sup>21</sup> Younger age, along with prior device infection were identified as significant risks in the Danish device-cohort study.<sup>23</sup> Others identified malnutrition [odds ratio (OR) 2.44,  $P < 0.001$ ] as a strong risk factor.<sup>5</sup>

Regarding *procedure-related factors*, the presence of a haematoma was associated with an approximately nine-fold increased risk of

infection, later confirmed by the prospective BRUISE-CONTROL study.<sup>24</sup> Early reoperation for haematoma or lead dislodgement was identified as strongest risk factors for CIED infection in a device registry data.<sup>5,22</sup> Procedure duration was associated with a multifold increased risk of infection,<sup>21,23</sup> as were implantation of CRT and reoperations. Experience has an impact on outcome,<sup>25</sup> and risk of infection may be increased by allocating generator changes to inexperienced operators.

There are fewer *device-related factors* for CIED infection. Device complexity and the numbers of leads were significantly associated with increased infection risk on multivariate analysis [hazard ratio (HR) 1.26, 1.67, and 2.22 for ICD, CRT-P, and CRT-D systems, respectively vs. pacemakers,  $P \leq 0.002$  for all comparisons].<sup>23</sup>

*Risk stratification* with risk score calculations could potentially play a role in better identifying patients at risk than individual factors<sup>26,27</sup> but can currently not be recommended because the evidence of their benefit remains weak.

## Prevention

Recommended preventive measures are summarized in Table 4 and Figure 1.

### Pre-procedural measures

#### Patient selection

For patients undergoing device removal for infection, up to one half may not require device reimplantation.<sup>39</sup> Implanting an epicardial

**Table 3** Pooled effect estimates for potential risk factors predisposing to CIED infection

Factors	Prospective + retrospective studies				Prospective studies only			
	Studies (n)	Total (n)	Pooled estimate	P-value	Studies (n)	Total (n)	Pooled estimate	P-value
Patient-related factors								
ESRD <sup>a</sup>	8	3045	8.73 (3.42–22.31)	0.00001	NA			
History of device infection	4	463	7.84 (1.94–31.60)	0.004	NA			
Fever prior to implantation	3	6652	4.27 (1.13–16.12)	0.03	2	6580	5.34 (1.002–28.43)	0.05
Corticosteroid use	10	3432	3.44 (1.62–7.32)	0.001	3	1349	2.10 (0.47–9.32)	0.33
Renal insufficiency <sup>b</sup>	5	2033	3.02 (1.38–6.64)	0.006	NA			
COPD	6	2810	2.95 (1.78–4.90)	0.00003	2	2393	2.30 (0.97–5.48)	0.06
NYHA class $\geq 2$	3	2447	2.47 (1.24–4.91)	0.01	2	2393	2.77 (1.26–6.05)	0.01
Skin disorders	4	6810	2.46 (1.04–5.80)	0.04	2	6519	2.60 (0.88–7.70)	0.08
Malignancy	6	1555	2.23 (1.26–3.95)	0.006	NA			
Diabetes mellitus	18	11 839	2.08 (1.62–2.67)	<0.000001	7	9815	1.88 (1.19–2.98)	0.007
Heparin bridging	2	6373	1.87 (1.03–3.41)	0.04	NA			
CHF	6	1277	1.65 (1.14–2.39)	0.008	NA			
Oral anticoagulants	9	8527	1.59 (1.01–2.48)	0.04	3	7271	1.18 (0.44–3.11)	0.75
Procedure-related factors								
Procedure duration	9	4850	9.89 (0.52–19.25)	0.04	6	4508	13.04 (-0.64 to 26.73)	0.06
Haematoma	12	14 228	8.46 (4.01–17.86)	<0.000001	6	9715	9.33 (2.84–30.69)	0.0002
Lead repositioning	5	1755	6.37 (2.93–13.82)	0.000003	4	1659	7.03 (2.49–19.85)	0.0002
Inexperienced operator <sup>c</sup>	2	1715	2.85 (1.23–6.58)	0.01	2	1715	2.85 (1.23–6.58)	0.01
Temporary pacing	10	10 683	2.31 (1.36–3.92)	0.002	4	8683	3.29 (1.87–5.80)	0.00004
Device replacement/revision/upgrade	26	21 214	1.98 (1.46–2.70)	0.00001	8	8793	0.95 (0.49–1.87)	0.89
Generator change	20	12 134	1.74 (1.22–2.49)	0.002	6	2139	0.91 (0.37–2.22)	0.83
Antibiotic prophylaxis	16	14 166	0.32 (0.18–0.55) <sup>d</sup>	0.00005	11	10 864	0.29 (0.13–0.63)	0.002
Device-related factors								
Epicardial leads	3	623	8.09 (3.46–18.92)	0.000001	NA			
Abdominal pocket	7	4017	4.01 (2.48–6.49)	<0.000001	2	2268	5.03 (1.96–12.91)	0.0008
$\geq 2$ leads	6	1146	2.02 (1.11–3.69)	0.02	NA			
Dual-chamber device	14	45 224	1.45 (1.02–2.05)	0.04	7	12 102	1.28 (0.73–2.25)	0.38

Adapted from Polyzos et al.<sup>21</sup>

Risk parameters, which were statistically significant for retrospective and prospective data are shown. Analyses restricted to prospective data only for the same parameters (if available) are also shown.

CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; ESRD, end-stage renal disease; NA, not available; NYHA, New York Heart Association.

<sup>a</sup>Glomerular filtration rate  $\leq 15$  mL/min or haemodialysis or peritoneal dialysis.

<sup>b</sup>Glomerular filtration rate  $<60$  mL/min or creatinine clearance  $<60$  mL/min.

<sup>c</sup> $<100$  previous procedures.

<sup>d</sup>The pooled effect estimate from randomized studies was 0.26 (0.13–0.52).

system may be preferential in high-risk patients.<sup>40</sup> 'Leadless' pacemakers may be less prone to infection and can be used in high-risk patients.<sup>41,42</sup> Subcutaneous ICDs (S-ICDs) are an option in patients requiring sudden death protection.

### Lead management

The number of leads and the presence of abandoned leads are associated with increased risk for infection. The decision to abandon or extract a lead must be made on an individual basis weighing all known risks and benefits.<sup>43,44</sup>

















### Patient factors

A procedure should be delayed until a patient has been afebrile for at least 24 h.<sup>28</sup> Better glycaemic control in the perioperative period may reduce infections in surgical patients.<sup>45</sup>

### Anticoagulation and antiplatelet drugs






A 'bridging' approach with heparin is not recommended.<sup>30</sup> In patients with CHA<sub>2</sub>DS<sub>2</sub>VASc score  $<4$ , holding anticoagulation for the procedure and restarting when the bleeding risk is reduced seems prudent. In higher-risk patients (prior embolic event or mechanical valve) continuing anticoagulation with Warfarin is recommended.

**Table 4** List of recommended preventive measures for CIED infections

Consensus statement	Statement class	Scientific evidence coding	References
<i>Pre-procedural measures</i>			
Confirm indication for CIED		E	
Delay CIED implantation in patients with infection		E	28
Avoid temporary transvenous pacing and central venous lines, which should ideally be removed prior to introducing new hardware, whenever possible		O, M	21
Measures to avoid pocket haematoma are recommended (avoid heparin bridging, discontinue antiplatelets if possible)		R	21,29–31
Periprocedural use of therapeutic low-molecular-weight heparin		R, M, O	30,32,33
Perform the CIED procedure in an operating room/suite with complete sterile environment as required for other surgical implant procedures		E	34
Procedure should be performed or supervised by an operator with sufficient training and experience (Table 12)		O	35
Topical <i>Staphylococcus aureus</i> decolonization may be performed		E	
Pre-procedural skin wash may be performed		E	
Hair removal with electric clippers (not razors) is recommended		O	36
Antibiotic prophylaxis is recommended within 1 h of incision for cefazolin and flucloxacillin, within 90–120 min for vancomycin		R, M	21
A continuous surveillance programme of infection rates and associated microbiology should be set-up at the level of each implanting centre		E	—
<i>Periprocedural measures</i>			
Surgical preparation with alcoholic chlorhexidine should be used rather than povidone–iodine		R	37,38
Allow sufficient time for the antiseptic preparation to dry		E	
Adhesive iodophor-impregnated incise drapes may be used		E	
Perform the procedure with adequate surgical technique—minimize tissue damage, haemostasis, adequate wound closure		E	

Continued

**Table 4 Continued**

Consensus statement	Statement class	Scientific evidence coding	References
Antibiotic envelope in high-risk situations is recommended <sup>a</sup>		R	10
If the operator performs the prepping and draping, glove change/re-scrub or remove outer glove of a double-glove before incision		E	
Using local instillation of antiseptic and antibiotics in the pocket		R, E	9
Use of braided sutures for final skin closure		E	
<i>Post-procedural measures</i>			
Use of post-operative antibiotic therapy		R	9
Adequate dressing for 2–10 days is recommended		E	
Patient instructions on wound care should be provided		E	
Delay or reconsider indication for reintervention if possible		E	
Haematoma drainage or evacuation (unless tense, wound dehiscence is present or pain is severe)		O	24,28

CIED, cardiac implantable electronic device; E, expert opinion; M, meta-analysis; O, observational studies; R, randomized trials.

<sup>a</sup>Candidates are those as defined in the WRAP-IT study population<sup>10</sup> (patients undergoing pocket or lead revision, generator replacement, system upgrade, or an initial CRT-D implantation) and patients with other high-risk factors as outlined in Table 3, considering also the local incidence of CIED infections.

Preliminary data suggest the same for non-vitamin K antagonist oral anticoagulants.<sup>29</sup> Therapeutic low-molecular-weight heparin should be avoided.<sup>30,32,33</sup> Antiplatelet agents, especially P2Y12 inhibitors should preferably be discontinued for 5–10 days before the intervention.<sup>31</sup>

**Appropriate environment**

The standards for sterile procedures must be met as for other surgical procedures associated with implants.<sup>34</sup>

**Staff training**

All staff involved in CIED implantation must be trained in appropriate strict sterile techniques and behaviour in an operating room setting. Operators should be adequately trained.<sup>35</sup>

**Nasal swabs/*Staphylococcus aureus* decolonization of patients**

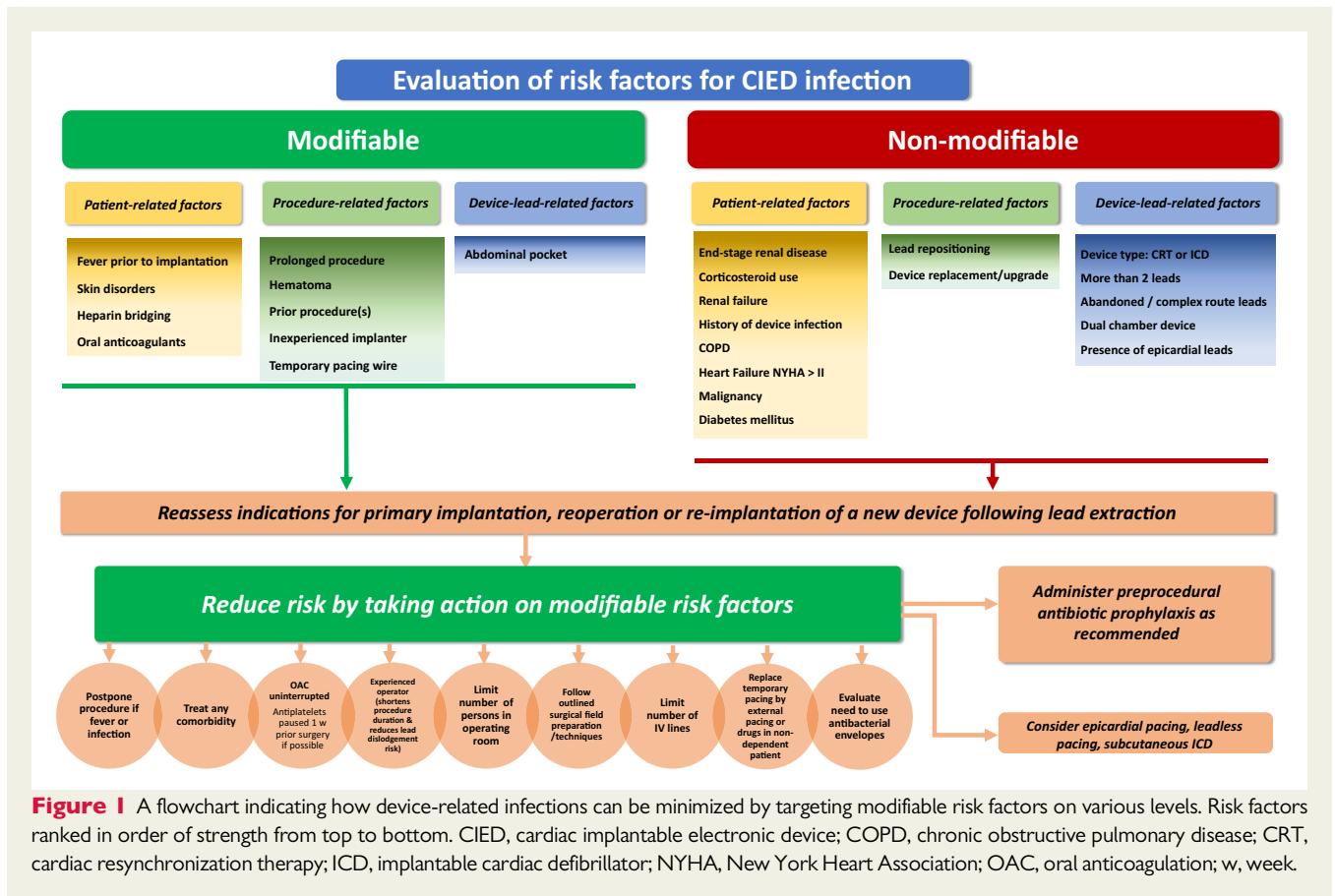
For elective procedures, *S. aureus* colonization can be detected by nasal swabs. Nasal treatment with mupirocin and chlorhexidine skin washing has been shown in some surgical studies to reduce the risk for infection.<sup>46</sup>

**Pre-procedure skin preparation**

Routine pre-surgical washing with an antimicrobial agent cannot be strongly supported.<sup>47</sup> Electric clippers with a single-use head (not razors) should be used for chest hair removal.<sup>36</sup>

**Pre-procedure antibiotic therapy**

Prophylactic systemic antibiotics are the standard of care<sup>21,48,49</sup> and should at least cover *S. aureus* species. Randomized trials have used



i.v. flucloxacillin (1–2 g) and first-generation cephalosporins such as cefazolin (1–2 g).<sup>9,48,49</sup> Vancomycin (15 mg/kg) may be used in case of allergy to cephalosporins.

## Periprocedural measures

### Patient surgical preparation

Alcoholic 2% chlorhexidine was superior to povidone–iodine for skin preparation prior to surgery<sup>37</sup> or intravascular catheter insertion<sup>38</sup> but no randomized data exist regarding CIED implantation. There is no evidence that adhesive incise drapes reduces infection rates (may increase risk of infection when non-iodophor incise drapes are used<sup>50</sup>).

### Good surgical technique

Non-powdered gloves may reduce the risk of infection by reducing local inflammation.<sup>51</sup> Vigorous pocket irrigation is important to remove devitalized tissue as well as dilute any contaminants.<sup>52</sup>

Diagnostic or therapeutic aspiration of a haematoma is contraindicated given the risk of ‘inoculating’ the pocket and causing an infection.<sup>24,28</sup> Haematoma evacuation should only be undertaken if pain is unmanageable or wound closure is threatened, ideally performed in an operating room.<sup>24,28</sup>

### Antibiotic envelope

An antibacterial mesh envelope (TYRX™, Medtronic, MN, USA), which locally releases minocycline and rifampin, significantly reduced the incidence of CIED infection in high-risk patients (WRAP-IT trial<sup>10</sup>) without a higher incidence of complications. The incidence of primary endpoints (infection resulting in system extraction or revision, long-term antibiotic therapy, or death) within 12 months after the CIED implantation was lower in patients who received the envelope (0.7%) vs. controls (1.2%) (HR 0.60, 95% confidence interval (CI) 0.36–0.98;  $P=0.04$ ).<sup>10</sup> The number of patients needed to treat to prevent one infection was high. The exclusion of higher-risk patients (immunosuppressive treatments, with vascular access, or on dialysis) may have contributed to a lower-than-expected rate of infections (1.2%) also observed in other prospective studies.<sup>6,7,9</sup> Higher infection rates (2.3–3.4%), as observed in less selected retrospective studies<sup>11,12</sup> would improve the overall cost-effectiveness of the envelope. Recommendation for the use of the antibacterial envelope is outlined in *Table 4*.

### Local instillation of antibiotics or antiseptics

Local instillation of antibiotics or antiseptics is not recommended. The recent PADIT trial demonstrated no benefit.<sup>9</sup>

### Capsulectomy

Even in the absence of signs of clinical infections, cultures taken at the time of generator change demonstrate a significant incidence of colonization.<sup>53</sup> The fibrous capsule inhibits the body's normal defence mechanisms and antibiotic penetration but 'capsulectomy' could also result in more pocket bleeding/haematoma and cannot be recommended as routine practice.<sup>54</sup>

### Closure

Closure in layers minimize wound tension and reduces the risk of dehiscence and infection.<sup>55</sup>

## Post-procedural measures

### Post-procedure antibiotic therapy

The recent PADIT trial,<sup>9</sup> tested the clinical effectiveness of incremental perioperative antibiotics but the primary outcome of 1-year hospitalization for device infection in the high-risk group was not statistically significant. It is therefore not recommended to administer post-operative antibiotic therapy.

### Wound care

Pressure dressing may be used for the first 24 h to avoid haematoma.

### Reintervention

All measures must be taken to avoid the need of early reintervention which dramatically increases the risk of infection.<sup>19,21,28</sup>

## Diagnosis of cardiac implantable electronic device infections and related complications

### Clinical findings

A *superficial incisional infection* involves only the skin and the subcutaneous tissue without communication with the pocket.<sup>56,57</sup> Close monitoring of the patient must be pursued in order to recognize a significant pocket infection.

*Pocket infection* is defined as an infection limited to the generator pocket. Local signs of inflammation may be mild (erythema, warmth, and fluctuation).<sup>14,57</sup> Deformation of the pocket, adherence or threatened erosion are often signs of low grade, indolent infection. Once a wound dehiscence occurs, a purulent drainage or a sinus is established, and a pocket infection is clearly present. If the generator or proximal leads are exposed, the device should be considered infected, irrespective of the results of the microbiology. Material from the pocket may be used for culture, recognizing the potential for contamination. Pocket infections may be associated with lead infections and CIED systemic infections and/or infective endocarditis.<sup>58</sup>

The diagnosis of *CIED systemic infection and infective endocarditis without local infection* may be more challenging (Table 5). Symptoms may be non-specific (fever, chills, and night sweats). Patients with CIED infection may present with embolic involvement of lungs and pleural

space<sup>60,61</sup> or with vertebral osteomyelitis and discitis. Procalcitonin test may be of value, especially if positive ( $\geq 0.05$ ).<sup>62,63</sup>

The modified Duke criteria<sup>64</sup> and the ESC 2015 criteria<sup>59</sup> for the diagnosis of infective endocarditis are the only available framework for CIED endocarditis diagnosis. In order to increase sensitivity for CIED infection diagnosis, this panel developed the 2019 International CIED Infection Criteria (Table 5).

## Identification of the causative microorganisms

Every effort should be made to obtain cultures prior to the institution of antibiotic therapy. Blood cultures should be repeated in patients with CIED and fever without clear signs of local infections and infective endocarditis (Table 6). In unstable patients with sepsis or septic shock, early empiric antibiotic therapy should be administered following two sets of blood cultures. Blood bottles must be filled properly in order to increase the sensitivity.<sup>17,65</sup> Every positive blood culture, including a single bottle with CoNS or other Gram-positive organisms, should prompt active exclusion of CIED infection with other diagnostic techniques employed (Figure 2).<sup>71</sup> In case of negative blood cultures (usually 5 days), the use of biomolecular methods (DNA amplification and/or gene sequencing) to detect fastidious or atypical pathogens<sup>19</sup> may be considered for CIED endocarditis (Table 6).<sup>67</sup> Some Gram-positive microorganisms species may require longer period of incubation, such as *Cutibacterium* (previously *Propionibacterium*) *acnes*.<sup>19</sup>

Tissue or fluid collected from the pocket via an adjacent intact portion of the skin (via a sterile needle or syringe) should only be used to make a bacterial diagnosis, not to determine the presence of a pocket infection. Entering an intact pocket should be avoided to avoid inoculation with bacteria.

During an extraction procedure, distal and proximal lead fragments, lead vegetation and generator pocket tissue should be sent for culture (Table 6).<sup>71</sup> Culture media suggested are chocolate agar incubated in 5% CO<sub>2</sub>, MacConkey agar, blood agar in anaerobic condition, and Sabouraud agar.<sup>72,73</sup> In case of pus, but no growth after 3 days, consider slow growing microorganisms including *C. acnes* and increase incubation duration. Tissue samples and sonication for the recovery of bacteria from CIED leads and tissue may be useful.<sup>68-70</sup>



## Imaging

### Echocardiography

Transthoracic echocardiography (TTE) and transoesophageal echocardiography (TEE) are both recommended to identify lead vegetations and valvular involvement in suspected CIED infections.<sup>59</sup> Transoesophageal echocardiography is superior for the detection and sizing of vegetations.<sup>74</sup> Lead masses in asymptomatic CIED carriers may be observed on TTE/TEE and do not predict CIED-related infective endocarditis over long-term follow-up.<sup>75,76</sup> Once a lead mass is identified, careful clinical assessment to rule out either infection or non-bacterial lead-thrombotic endocarditis is needed, including serial TTE/TEE or additional imaging tests.

Intracardiac echocardiography (ICE) has a high sensitivity for the detection of vegetations in cardiac devices.<sup>77,78</sup> Therefore, a vegetation seen with ICE may be considered a major criterion for diagnosis

**Table 5 Recommendations for diagnosis of CIED infections and/or infective endocarditis: the Novel 2019 International CIED Infection Criteria<sup>a</sup>**

Consensus statement	Statement class	Scientific evidence coding	Reference
'Definite' CIED clinical pocket/generator infection = generator pocket shows swelling, erythema, warmth, pain, and purulent discharge/sinus formation OR deformation of pocket, adherence, and threatened erosion OR exposed generator or proximal leads.			
'Definite' CIED/IE = presence of either two major criteria or one major + three minor criteria			
'Possible' CIED/IE = presence of either one major + one minor criteria or three minor criteria			
'Rejected' CIED/IE diagnosis = patients who did not meet the aforementioned criteria for IE			
Major criteria		 E	59
Microbiology	<p>A. Blood cultures positive for typical microorganisms found in CIED infection and/or IE (Coagulase-negative Staphylococci, <i>Staphylococcus aureus</i>)</p> <p>B. Microorganisms consistent with IE from two separate blood cultures:</p> <ol style="list-style-type: none"> <li>Viridans streptococci, <i>Streptococcus gallolyticus</i> (<i>Streptococcus bovis</i>), HACEK group, <i>S. aureus</i> or</li> <li>Community-acquired enterococci, in the absence of a primary focus.</li> </ol> <p>C. Microorganisms consistent with IE from persistently positive blood cultures:</p> <ol style="list-style-type: none"> <li>≥2 positive blood cultures of blood samples drawn &gt;12 h apart; or</li> <li>All of three or a majority of ≥4 separate cultures of blood (first and last samples drawn ≥1 h apart); or</li> <li>Single positive blood culture for <i>Coxiella burnetii</i> or phase I IgG antibody titre &gt;1:800</li> </ol>		
Imaging positive for CIED infections and/or IE	<p>D. Echocardiogram (including ICE) positive for:</p> <ol style="list-style-type: none"> <li>CIED infection: <ol style="list-style-type: none"> <li>Clinical pocket/generator infection</li> <li>Lead vegetation</li> </ol> </li> <li>Valve IE <ol style="list-style-type: none"> <li>Vegetations</li> <li>Abscess, pseudoaneurysm, intracardiac fistula;</li> <li>Valvular perforation or aneurysm;</li> <li>New partial dehiscence of prosthetic valve</li> </ol> </li> </ol> <p>E. [<sup>18</sup>F]FDG PET/CT (caution should be taken in case of recent implants) or radiolabelled WBC SPECT/CT detection of abnormal activity at pocket/generator site, along leads or at valve site</p> <p>F. Definite paravalvular leakage by cardiac CT</p>		
Minor criteria		 E	59
	<ol style="list-style-type: none"> <li>Predisposition such as predisposing heart condition (e.g. new onset tricuspid valve regurgitation) or injection drug use</li> <li>Fever (temperature &gt;38°C)</li> <li>Vascular phenomena (including those detected only by imaging): major arterial emboli, septic pulmonary embolisms, infectious (mycotic) aneurysm, intracranial haemorrhage, conjunctival haemorrhages, and Janeway's lesions</li> <li>Microbiological evidence: positive blood culture which does not meet a major criterion as noted above or serological evidence of active infection with organism consistent with IE or pocket culture or leads culture (extracted by non-infected pocket)</li> </ol>		

Green text refers to CIED-related infection criteria.

CIED, cardiac implantable electronic device; E, expert opinion; ICE, intracardiac echocardiography; IE, infective endocarditis; M, meta-analysis; O, observational studies; R, randomized trials.

<sup>a</sup>Based on merging of the modified Duke- and ESC 2015 Guidelines criteria, see text.<sup>63,64</sup>

(Table 5). Transvenous biopsy, guided by TEE, was shown to be useful to differentiate vegetation from thrombus.<sup>79</sup>

A TEE should be considered after percutaneous lead extraction in order to detect infected material, ghosts,<sup>80</sup> and potential tricuspid valve complications (Table 7). A normal echocardiography does not rule out CIED-related infective endocarditis.

#### Radiolabelled leucocyte scintigraphy, positron emission tomography and computerized tomography

Fluorine-18-fludeoxyglucose ([<sup>18</sup>F]FDG) positron emission tomography/computerized tomography (PET/CT) scanning and radiolabelled leucocyte (white blood cell, WBC) scintigraphy are complementary tools for the diagnosis of CIED-related infections

**Table 6 Recommendations for diagnosis of CIED infections by clinical findings and microbiology**

Consensus statement	Statement class	Scientific evidence coding	References
At least three sets of blood cultures should be acquired in case of clinically suspected CIED endocarditis		E, O	19,65
Samples from the pocket should be cultured but only if acquired during removal and not passing through the sinus		E, O	19,65
Suspect CIED infections in case of vertebral osteomyelitis and/or embolic pneumonia (clinical signs and symptoms of CIED systemic infections may be difficult to recognize as only fever may be present)		E, O	60,65
Cultures of extracted CIED should be performed		E, O	66
PCT may be useful in case of infective endocarditis and embolism and/or in case of <i>Staphylococcus aureus</i> CIED-related infective endocarditis		E, O	63
Increased incubation time (10–14 days) for slowly growing microorganism may be considered in case of CIED-related infective endocarditis and persistent negative blood cultures		E	67
The usefulness of sonication of CIED to enhance microbial detection during removal/extraction is still under evaluation but may be used with caution when interpreting results		E, O	68–70
Cultures from the sinus of the CIED pocket or from parts of the device exposed		E	19

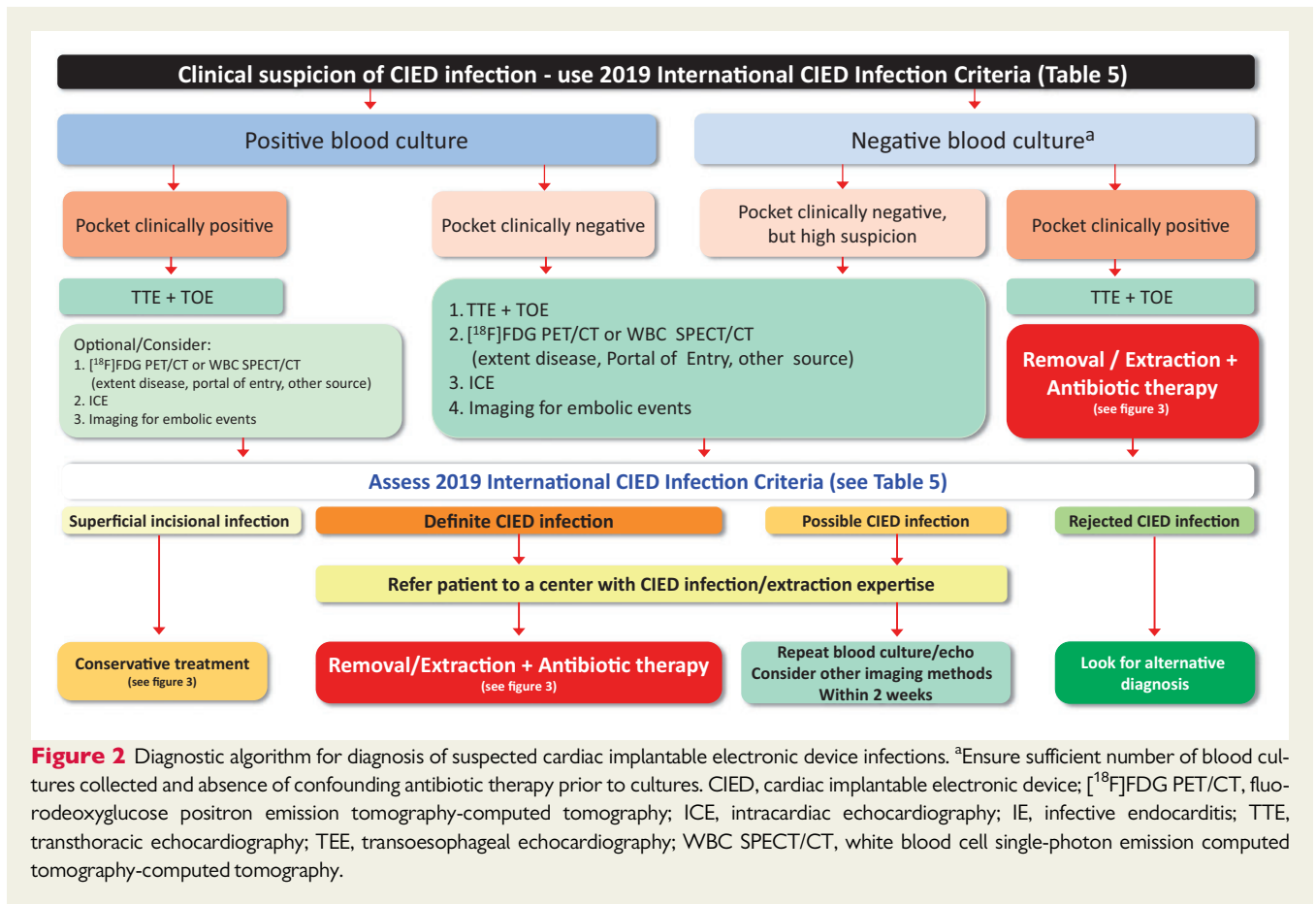
CIED, cardiac implantable electronic device; E, expert opinion; M, meta-analysis; O, observational studies; PCT, Procalcitonin; R, randomized trials.

and related complications, particularly in the subset of possible CIED infections, and may distinguish between early-onset superficial surgical site infection and a true generator pocket infection (Figure 2). When patients present with systemic infection without local findings at the generator pocket a PET/CT is useful for the diagnosis of local infection [pooled specificity and sensitivity of 93% (95% CI 84–98%) and 98% (95% CI 88–100%), respectively, and AUC of 0.98 at ROC analysis].<sup>85,99</sup> White blood cell count scintigraphy including single-photon emission tomography/computerized tomography (SPECT/CT) has high sensitivity and specificity for the detection and localization of CIED-related infections (94% and 100%, respectively).<sup>89</sup> In case of CIED-related infective endocarditis, PET/CT and WBC are very specific when tracer uptake is visualized (only if applied late after implantation), although a negative result does not completely exclude the presence of small vegetations with low metabolic activity (i.e. limited sensitivity and negative predictive value). Therefore, the diagnostic accuracy for lead infections is lower,<sup>99,100</sup> with overall pooled sensitivity of 65% (95% CI 53–76%), specificity of 88% (95% CI 77–94%), and AUC of 0.861.

Positron emission tomography/computerized tomography is particularly useful for the identification of unexpected embolic localizations and metastatic infections.<sup>84,88</sup> The identification of the infection entry site by PET/CT and WBC imaging is critical for the prevention of infective endocarditis relapse.<sup>90</sup> Positron emission tomography/computerized tomography imaging may also contribute to mortality risk stratification after lead extraction, as patients with definite CIED infection without pocket involvement on PET/CT had unfavourable outcome.<sup>101</sup>

The addition of contrast-enhanced CT to standard PET/CT protocol resulted in a high rate of reclassifications from 'possible' to 'definite' infective endocarditis in patients with suspected pulmonary embolism or CIED infections.<sup>84</sup> Pulmonary CT angiography may be useful in patients with recurrent pneumonia.<sup>91</sup> The technical aspects and the interpretation criteria for multimodality imaging has recently been published.<sup>85</sup>

Multidisciplinary team evaluations of imaging results significantly reduced the 1-year mortality<sup>98</sup> from 18.5% to 8.2%.



## Management of cardiac implantable electronic device infections

### Cardiac implantable electronic device removal

Successful treatment of definite CIED infections (systemic and localized) requires complete removal of all parts of the system and transvenous hardware, including vascular ports or permanent haemodialysis catheter.<sup>81,102,103</sup> Antibiotic therapy without device removal was associated with a seven-fold increase in 30-day mortality in multivariate analysis.<sup>104</sup> The timing of the extraction procedure should be without unnecessary delay after the diagnosis of CIED infection (Figures 2 and 3, Table 8). Transvenous lead extraction within 3 days after hospitalization results in significantly lower in-hospital mortality and shorter hospitalizations in patients with CIED infections.<sup>114</sup> Systemic infection was a predictor for increased all-cause mortality (OR 4.93, 95% CI 2.72–8.93;  $P < 0.0001$ ) in the ELECTRA registry.<sup>2</sup>

Percutaneous transvenous extraction is the method of first choice (Table 8) since major complications and mortality are significantly

lower compared with open surgical approaches.<sup>105,115</sup> Transvenous extraction procedures are even preferred in the presence of lead vegetations with a diameter of  $>10$  mm (Table 8)<sup>116,117</sup> In patients with systemic CIED infection and vegetations larger than approximately 20 mm, open surgical extraction<sup>59,81</sup> or percutaneous aspiration with a veno-venous extracorporeal circuit with an in-line filter may be considered.<sup>106,107</sup> The goal is to reduce the overall 'vegetative' burden and the risk of embolization of infectious material into the pulmonary circulation.

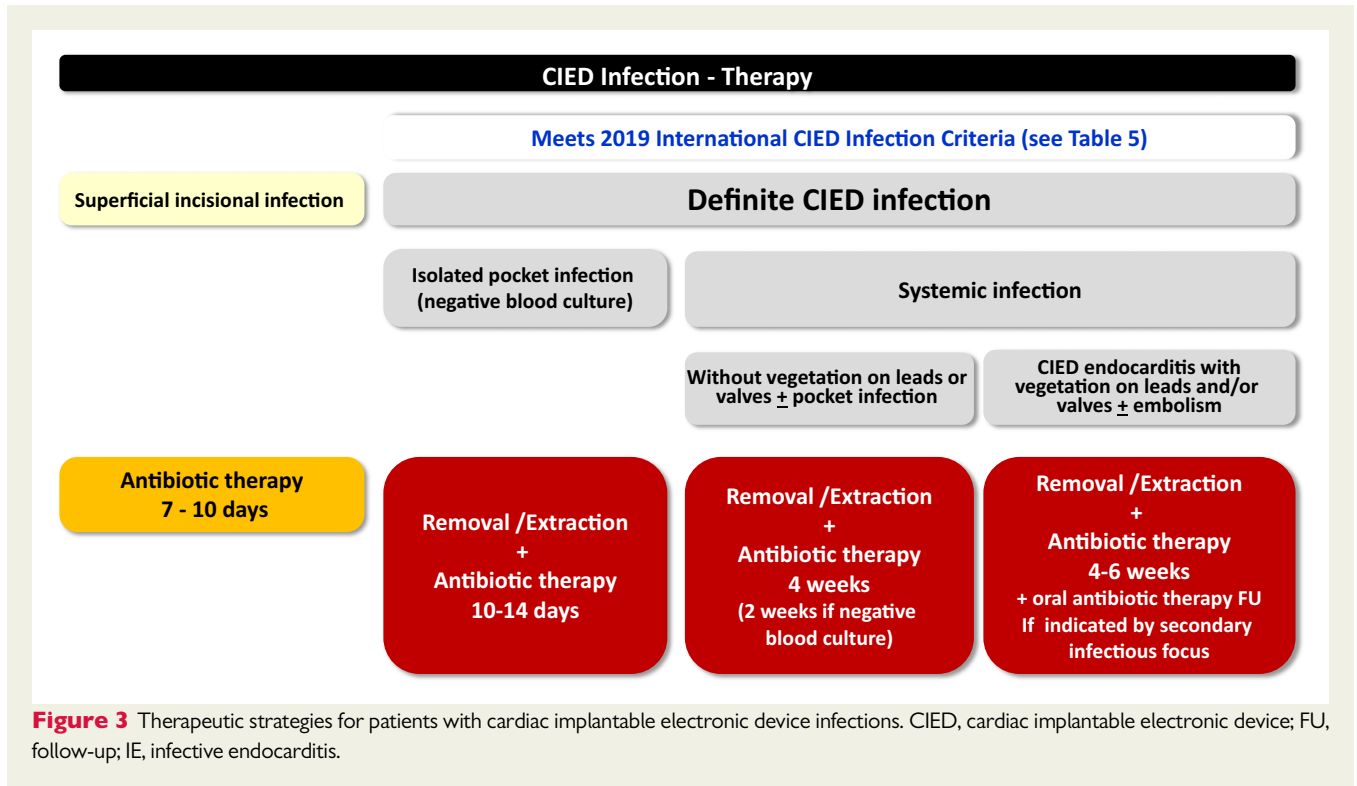
In case of infections of CIED systems with epicardial leads, complete lead removal is recommended in case of definite involvement based on individual risk-risk-analysis.<sup>115</sup> For localized pocket infection without definite involvement of the distal epicardial lead, it is reasonable to leave the distal portion by cutting the lead through a separate incision away from the device pocket.<sup>81</sup> A PET/CT scan may prove helpful.

In cases of occult bacteraemia or fungaemia the results of microbiological examination influence further therapy (Table 8). Complete CIED removal is indicated in bacteraemia or fungaemia with *S. aureus*, CoNS, *Cutibacterium* spp. and *Candida* spp., whereas it may be carried out as a second step for other bacteraemia in case of recurrent/continued bacteraemia despite appropriate antibiotic therapy

**Table 7** Recommendations for diagnosis of CIED infections by imaging<sup>59</sup>

Consensus statement	Statement class	Scientific evidence coding	Reference
TTE is recommended as the first-line imaging modality in patients with suspected CIED-related IE		O	81
A chest X-ray should be performed in all patients with suspected CIED infection		E	
TEE is recommended in suspected CIED infection with positive or negative blood cultures, independent of TTE results before an extraction, to evaluate CIED infection and IE		O	74
Repeat TTE and/or TEE within 5–7 days is recommended in case of initially negative examination when clinical suspicion of CIED-related IE remains high		O	81
TEE should be performed in CIED patients with <i>Staphylococcus aureus</i> bacteraemia		O	82,83
ICE may be considered if suspected CIED-related IE, with positive blood cultures and negative TTE and TEE results		O, E	77,78
[ <sup>18</sup> F]FDG PET/CT scanning or radiolabelled WBC scintigraphy or contrast-enhanced CT are recommended if suspected CIED-related IE, positive blood cultures and negative echocardiography (attention in imaging interpretation early after device implant)		O, M	84,85
[ <sup>18</sup> F]FDG PET/CT should be performed in case of <i>S. aureus</i> bacteraemia in CIED patients		O, E	86,87
[ <sup>18</sup> F]FDG PET/CT, radiolabelled WBC scintigraphy and/or contrast-enhanced CT is recommended for identification of unexpected embolic localizations (i.e. lung embolism) and metastatic infections		O, M	84,88,89
The identification of the infection portal of entry may be considered by [ <sup>18</sup> F]FDG PET/CT and WBC imaging in order to prevent IE relapse		O, E	84,90
Pulmonary CT angiography is recommended in patients with recurrent pneumonia		O, E	91
In patients with CIED infection treated with percutaneous lead extraction, TTE/TEE before hospital discharge are recommended to detect presence of retained segments of pacemaker lead, and to assess tricuspid valve function, RV function, and pulmonary hypertension		O	80,92,93
In case of persistent sepsis after device extraction: <ul style="list-style-type: none"> <li>• TEE is recommended to identify residual insulation material and local complications</li> <li>• [<sup>18</sup>F]FDG PET/CT, radiolabelled WBC scintigraphy and/or contrast-enhanced CT for better assessment of local extension of the infection and whole-body assessment</li> </ul>		O, M	84,94–97
A multidisciplinary team (the Endocarditis Team) is recommended for evaluation of imaging results		E	98

[<sup>18</sup>F]FDG PET/CT, fluorine-18-fludeoxyglucose positron emission tomography/computerized tomography scanning; CIED, cardiac implantable electronic device; E, expert opinion; ICE, intracardiac echocardiography; IE, infective endocarditis; M, meta-analysis; O, observational studies; R, randomized trials; RV, right ventricular; TEE, transoesophageal echocardiography; TTE, transthoracic echocardiography; WBC, white blood cell count.



(Table 8).<sup>14,72,102,111,112</sup> Complete CIED removal is indicated in patients with infective endocarditis without definite involvement of the CIED system.<sup>113</sup>

After device and lead removal a meticulous debridement of the device pocket with complete excision of the fibrotic capsule, removal of all non-absorbable suture material and subsequent wound irrigation with sterile saline solution, is crucial.<sup>108</sup>

Cardiac implantable electronic device patients with superficial wound infections early after implantation, device exchange or revision surgery should not undergo device and lead removal.

### Antimicrobial therapy including long-term suppressive therapy

Definitive treatment of CIED infection is early and complete removal of all parts of the system and antibiotic therapy is to be seen as a complement.<sup>103</sup> Randomized studies to guide antibiotic choice in CIED infections are lacking.<sup>19,59,65</sup> Successful salvage therapy<sup>103</sup> and long-term suppressive antibiotic therapy have been used in selected cases not candidates for device removal.<sup>118</sup>

Antibiotic treatment recommendations are summarized in Table 9. Systemic infections are further divided depending on presence of positive blood cultures and vegetations on leads and/or valves.<sup>65</sup>

For *superficial incisional infection*, a wound culture before initiation of antibiotic treatment is recommended (Table 9).

For *isolated pocket infections* empirical i.v. therapy is recommended after blood cultures have been obtained (Table 9, Figure 3). A switch to oral treatment after device removal is reasonable, but evidence-based recommendations are lacking. In pocket erosion with minimal inflammation, delayed antibiotic

therapy until after device removal and pocket cultures should be considered.

For *pocket infection with positive blood culture but without vegetation on leads or valves*, the definite treatment follows recommendations given above but the systemic involvement makes a switch to an oral antibiotic regimen inappropriate (Table 9, Figure 3). Shorter post-extraction treatment duration is considered possible by some experts.<sup>19</sup>

For *blood culture positive CIED endocarditis with vegetation on lead or valve*, the recommendations follow guidelines for infective endocarditis (Table 9).<sup>59</sup> Total treatment duration should always be at least 4 weeks. If the TEE performed after device removal shows no signs of valve vegetation, the follow-up blood cultures are negative, the clinical improvement is good and there are no pulmonary abscesses, a 2 weeks treatment duration post-device extraction can be sufficient (Figure 3).



For *bacteraemia in a CIED patient without signs of pocket infection or echocardiographic evidence of lead or valve involvement*, the antibiotic treatment follows general recommendations. Device removal should be considered even in the absence of vegetations, in case of infection with specific pathogens or relapsing bacteraemia without other source, but randomized studies are lacking.<sup>119</sup> The addition of rifampicin is not recommended in patients with *S. aureus* bacteraemia but can be considered in the presence of concomitant non-removable foreign body.<sup>120,121</sup> For *S. aureus*, CoNS, *Cutibacterium* spp. and *Candida* spp., CIED removal is generally recommended. With viridans group and beta-haemolytic *Streptococcus* spp. or *Enterococcus* spp., device removal should be considered as well as prolonged i.v. treatment (4 weeks). Even though Gram-negative bacteria are capable of

**Table 8** Recommendations for device and lead removal

Consensus statement	Statement class	Scientific evidence coding	References
In patients with definite CIED infection (systemic and local) complete device removal is recommended (including abandoned leads, epicardial leads, and lead fragments)		O	81,102,104
After diagnosis of CIED infection, the device removal procedure should be performed without unnecessary delay (ideally within 3 days)		O	104
The recommended technique for device system removal is percutaneous, transvenous extraction technique. Epicardial leads require surgical removal		O	105
In patients with systemic infection and lead vegetations of approximately >20 mm percutaneous aspiration of vegetations prior to and during transvenous lead extraction or alternatively surgical extraction may be considered		O	105–107
After device removal, meticulous debridement of the generator pocket (complete excision of the fibrotic capsule and complete removal of all non-absorbable suture material) and subsequent wound irrigation with sterile normal saline solution is recommended		E	108
Cultures of extracted CIED should be performed		E, O	66
The following wound closure methods after device removal and debridement of device pocket may be performed: <ul style="list-style-type: none"> <li>• Primary closure with or without the use of a drain</li> <li>• Delayed closure after negative pressure wound therapy</li> </ul>		E	NA
Complete CIED removal is indicated in bacteraemia or fungaemia with <i>Staphylococcus aureus</i> , CoNS, <i>Cutibacterium</i> spp. and <i>Candida</i> spp.		E	109
In bacteraemia with alpha- or beta-haemolytic <i>Streptococcus</i> spp. and <i>Enterococcus</i> spp. a complete CIED removal may be performed as first-line treatment or in case of recurrent/continued bacteraemia despite appropriate antibiotic therapy as a second step therapy		E	110
In case of bacteraemia with non-pseudomonal/Serratia Gram-negative bacteria or <i>Pneumococcus</i> spp., CIED removal should be performed in the case of recurrent/continued bacteraemia despite appropriate antibiotic therapy when there is no other identifiable source for recurrence or continued infection		E	14,72,111,112
Complete CIED removal is recommended in patients with infective endocarditis with or without definite involvement of the CIED system		E	113
Blood cultures should be taken 48–72 h after removal of an infected CIED		E	19

E, expert opinion; M, meta-analysis; NA, not available; O, observational studies; R, randomized trials.

**Table 9** International consensus recommendations for antibiotic therapy including long-term suppressive therapy<sup>a</sup>

Consensus statement	Statement class	Scientific evidence coding	References	
<b>Superficial incisional infection</b>				
Empirical treatment:		O, R	19,65	
Oral antibiotic treatment covering <i>S. aureus</i>				
Flucloxacillin oral (amoxicillin–clavulanate is an alternative)				Flucloxacillin p.o. 1 g every 6–8 h
If high MRSA prevalence: Trimethoprim–sulfamethoxazole, Clindamycin, Doxycyclin, Linezolid				(amoxicillin–clavulanate standard dose)
To be adjusted after culture result				
Duration: 7–10 days				
<b>Isolated pocket infection (negative blood cultures)</b>				
Empirical treatment:		O, R	19,59,65	
Directed at methicillin-resistant Coagulase-negative Staphylococci (CoNS) and <i>Staphylococcus aureus</i> :				Vancomycin: 30–60 mg/kg/day i.v. in 2–3 doses (Daptomycin 8–10 mg/kg i.v. o.d.)
Vancomycin (Daptomycin is an alternative)				
If systemic symptoms:				+/-
For additional Gram-negative coverage, combine with 3rd generation Cephalosporin (or a broader betalactam antibiotic) or Gentamicin				Cephalosporin: standard dose Gentamicin 5–7 mg/kg i.v. o.d. <sup>b</sup>
To be adjusted after culture result				
If sensitive staphylococcus: Flucloxacillin (1st generation cephalosporin as an alternative)	Flucloxacillin: 8 g/day i.v. in four doses (1st generation cephalosporin standard dose)			
Partial oral treatment often used				
Duration post-extraction: 10–14 days				
<b>Systemic infections</b>				
<b>Without vegetation on leads or valves ± pocket infection</b>				
Empirical treatment: (directed at methicillin-resistant staphylococci and Gram-negative bacteria):		O, R	19,59,65,81	
Vancomycin (Daptomycin is an alternative)				Vancomycin: 30–60 mg/kg/day i.v. in 2–3 doses (Daptomycin 8–10 mg/kg o.d.)
+ 3rd generation Cephalosporin (or a broader betalactam antibiotic) or Gentamicin				+ Cephalosporin: standard dose i.v. or Gentamicin 5–7 mg/kg i.v. o.d. <sup>b</sup>
To be adjusted after culture result				
If sensitive staphylococcus: Flucloxacillin iv (1st generation cephalosporin i.v. as an alternative)				Flucloxacillin i.v. dosages as above (1st generation cephalosporin standard dose i.v.)
Duration post-extraction: 4 weeks (2 weeks if negative blood culture, see text)				
<b>CIED endocarditis with vegetation on leads and/or valves + embolism</b>				
Empirical treatment:		O, R	59	
Vancomycin (Daptomycin is an alternative)				Vancomycin; 30–60 mg/kg/day i.v. in 2–3 doses (Daptomycin 8–10 mg/kg o.d.)
+ 3rd generation Cephalosporin (or a broader betalactam antibiotic) or Gentamicin				+ Cephalosporin; standard dose or Gentamicin 5–7 mg/kg i.v. o.d. <sup>b</sup>
Adjust to culture result according to ESC endocarditis guidelines 2015				
If prosthetic valve and staphylococcal infection: Rifampicin to be added after 5–7 days				Rifampicin: 900–1200 mg/day orally (or i.v.) in two doses

Continued

**Table 9 Continued**

Consensus statement	Statement class	Scientific evidence coding	References
Duration for native valve infective endocarditis: 4 weeks post-extraction, for prosthetic valve endocarditis: (4-) 6 weeks, for isolated lead vegetation: 2 weeks therapy after extraction may be sufficient (in total 4 weeks) except for <i>Staphylococcus aureus</i> infection, see text			
<b>Bacteraemia in a CIED patient without signs of pocket infection or echocardiographic evidence of lead or valve involvement</b>			
According to pathogen-specific treatment guidelines, see text		O, R	119,120
<b>Attempted salvage therapy and long-term suppressive therapy</b>			
i.v. antibiotics as in prosthetic valve endocarditis for 4–6 weeks		E	103,118
Stop antibiotic therapy under close follow-up or continue individualized long-term suppressive oral therapy, see text			

E, expert opinion; i.v., intravenous; M, meta-analysis; MRSA, methicillin-resistant *Staphylococcus aureus*; O, observational studies; o.d., once daily; p.o., per oral; R, randomized trials.

<sup>a</sup>Treatment regimens differ between countries depending on prevalence of MRSA and other circumstances—see text. Dosage recommendation needs to be adjusted for kidney function.

<sup>b</sup>For patients with normal renal function.



secondary seeding of a device,<sup>72</sup> concomitant CIED infection is uncommon in non-pseudomonal/Serratia Gram-negative or pneumococcal bacteraemia, and device removal is generally not needed.<sup>14,111,112</sup>

For attempted salvage therapy if complete device removal is not possible, long-term suppressive therapy with i.v. antibiotic following recommendations in prosthetic valve endocarditis for 4–6 weeks is reasonable (Table 9, Figure 3). If oral suppressive therapy is planned, antibiotic therapy should be chosen according to culture results.<sup>103,118</sup> In methicillin-sensitive staphylococci, oral flucloxacillin is considered an option by some experts but is not used by others due to low oral bioavailability. In methicillin-resistant *S. aureus* or CoNS, oral trimethoprim-sulfamethoxazole, clindamycin, or doxycycline are alternatives. Linezolid is not suitable for long-term treatment. Rifampicin and fusidic acid are not suitable as single therapy. A combination suppressive therapy is generally not preferred.

## Preventive strategies after cardiac implantable electronic device implantations, reimplantations, and alternative novel devices

Early follow-up in a clinical setting and patient educational programmes should be conducted for early identification of CIED-related infectious complications, including video consultations for wound inspections.

There is no convincing evidence that microorganisms associated with invasive medical procedures cause infection of non-valvular

vascular devices at any time after implantation (Table 10). Therefore, antibiotic prophylaxis is not routinely recommended for CIED patients who undergo dental, respiratory, gastrointestinal, genitourinary, or cardiac procedures. Secondary prophylaxis is only recommended for patients when they undergo incision and drainage of infection at other sites or replacement of an infected device.<sup>134</sup>








No part of the removed CIED system should be reimplanted. The venous access sheath used for percutaneous removal should not be used for reimplantation of a new system. Central and peripheral lines and any other removable catheters should also be changed at this time, where feasible.

The indication for reimplantation should always be re-evaluated after a CIED removal.<sup>39,122</sup> There are no randomized trials guiding appropriate timing of reimplantation and therefore such decision must be individualized. Reimplantation should be delayed until signs and symptoms of local and systemic infection have resolved or postponed until blood cultures are negative for at least 72 h after the extraction if feasible (Table 10).<sup>39,123,135</sup> In pacemaker dependent patients, an active-fixation lead ipsi-laterally implanted (preferably not through the vein used for extraction) and connected to an externalized pacemaker could safely delay reimplantation<sup>124–127</sup> by preserving the contralateral side for definitive device reimplantation.<sup>57,81,128</sup>

Leadless pacemakers (LPMs) may represent a valid solution. In selected high-risk patients, the risk of infection with LPM appears low.<sup>42,129</sup> The device also seems safe and feasible in patients with pre-existing CIED infection and after extraction of infected leads.<sup>129,130,136</sup>

In selected patients, the reimplantation of an S-ICD significantly reduced the risk of new infections while still providing an effective defibrillation system.<sup>132,133,137</sup> While they do not offer complete protection against infection, their removal is simpler

**Table 10 Recommendations for preventive strategies after device implantation and for new reimplantations including alternative novel devices**

Consensus statement	Statement class	Scientific evidence coding	References
After device extraction, reassessment of the indication for reimplantation is recommended		O	39,122
Whenever possible, reimplantation may be avoided or delayed until symptoms and signs of systemic and local infection have resolved		O	39,123
A temporary pacemaker with ipsilateral active fixation strategy may be considered in pacemaker-dependent patients requiring appropriate antibiotic treatment before reimplantation		O	124–127
Preferred access sites for replacement device are the contralateral side, the femoral vein, or epicardially		E, O	39,128,129
Temporary pacing in patients who are not pacemaker dependent		O	28
Replacement device implantation ipsilateral to the extraction site		E	39
Alternative novel devices as LPM and S-ICD may be considered in selected patients with high infective risk or in patients in whom these devices are considered better options after a CIED infection		O	129–133

CIED, cardiac implantable electronic device; E, expert opinion; LPM, leadless pacemaker; M, meta-analysis; O, observational studies; R, randomized trials; S-ICD, subcutaneous implantable defibrillator.

and most often does not result in a life-threatening systemic infection.<sup>138</sup> While randomized trial data are still forthcoming, data from the European EFFORTLESS Registry found an infection rate (requiring device removal) of 2.4% over 3 years of follow-up.<sup>139</sup> For patients with a high risk of sudden cardiac death, a wearable defibrillator (LifeVest, Zoll) is an option as a bridge to reimplantation.

## Prognosis, outcomes, and complications of cardiac implantable electronic device infections

Cardiac implantable electronic device infection has an in-hospital or 30-day mortality of 5–8%.<sup>133,140,141</sup> The mortality is higher for patients with significant comorbidities, with CIED endocarditis rather than pocket infection,<sup>114</sup> and for patients who do not undergo complete removal of CIED hardware.<sup>118,142</sup> A delay in device removal also leads to a worse prognosis.<sup>114</sup>

The long-term mortality in patients following CIED infection is up to 1.5–2.4 times the mortality rate of non-infected patients,<sup>140,143</sup> which is 6–15% at 1 year and 14–33% at 3 years. Patients with infective endocarditis<sup>144,145</sup> and females have a higher long-term mortality




rate than males,<sup>146</sup> when adjusted for comorbid factors. The presence of end-stage renal failure confers a particularly poor prognosis.<sup>147</sup> Patients successfully treated ('cured') with complete removal of hardware and a full course of antibiotics may have a similar prognosis to patients who have never been infected.<sup>148,149</sup>

## Special considerations to prevent device-related infections (elderly, paediatrics, adult with congenital heart disease)

Elderly patients needing a pacemaker or ICD pose additional risk and considerations for infection prevention.<sup>150,151</sup> In several studies, age *per se* is not an independent predictor of infection when adjusted for other comorbidities.<sup>5,22,28,152,153</sup> Frailty, observed in CIED patients with decreased activity and common in the elderly, is associated with worse cardiovascular outcomes.<sup>154–156</sup> In a National Cardiovascular Device Registry–ICD (NCDR-ICD) study, combinations of frailty with other known risk factors for CIED infections were predictive of higher mortality.<sup>155</sup> The elderly are often at greater risk of device erosion,<sup>81,157</sup> which may be prevented using a sub-muscular approach.<sup>158</sup>

In multivariate analysis, age under 20 years had a 40% higher risk for infection<sup>3</sup> which may be due to their higher number and

**Table 11 Recommendations for prevention of infections related to device implantations in elderly, paediatric patients and in adults with congenital heart disease**

Consensus statement	Statement class	Scientific evidence coding	References
Implanting physicians should be aware of the higher CIED infection risks in frail and elderly patients. Submuscular position of PM or ICD generators is recommended in selected elderly patients with limited subcutaneous tissue to prevent device erosion		O	158
Implanting physicians should be skilled in multiple and alternative surgical approaches performed in paediatric, congenital heart disease, and ACHD patients related to a higher risk of CIED infection due to multiple procedures, lead addition and revisions, and upgrade procedures		M, O	168–172
The entirely S-ICD should be considered as an alternative to transvenous or epicardial approaches in the older child, patients with congenital heart disease, and those with limited or no venous access. Patients with a bradycardia indication, anti-tachycardia pacing, or cardiac resynchronization therapy requirements are not appropriate candidates		O	175–179

ACHD, adults with congenital heart disease; CIED, cardiac implantable electronic device; E, expert opinion; ICD, implantable cardiac defibrillator; M, meta-analysis; O, observational studies; PM, pacemaker; R, randomized trials; S-ICD, subcutaneous ICD.

complexity of device-related procedures.<sup>152,159,160</sup> Colonization of the pocket may lead to higher rates of infections with subsequent generator replacements.<sup>161</sup> The complication rates of procedures involving lead revisions or replacements are reported to be at least twice higher than that of *de novo* implants.<sup>21,22,28,162</sup> In one study of 497 children receiving pacemakers with median follow-up of 6 years, the lead failure rate was 15% and the reported infection rate after lead replacement was 1.9%.<sup>163</sup>

Data from the NCDR-ICD notes low (0.2%) acute infection rates in adults with congenital heart disease (CHD) patients.<sup>164</sup> Most infections in paediatric ages and CHD present after longer-term follow-ups and appear to be in a similar range as that reported in adults (~1–5% serious infections).<sup>3,159,165–167</sup>

The approach to device implantation poses special challenges in children and CHD patients.<sup>168–173</sup> Pooled data from the EFFORTLESS registry and the US FDA IDE trial reported no infections in the 19 CHD patients with an S-ICD compared with 1.5% system infections in the remaining 846,<sup>174</sup> confirming other favourable reports.<sup>175–179</sup>

Recommendations for prevention of infections in these patient groups are outlined in Table 11.

## Minimum quality requirements concerning centres and operator experience and volume

For implantation of pacemakers, an operator experience <100 procedures was associated with higher risk of infection in the prophylactic antibiotic era.<sup>180,181</sup> Less than 100 procedures were also associated with a higher risk of any complication.<sup>182</sup> Pocket haematoma was more common in patients implanted by operators with <100 procedures experience.<sup>183</sup> Close supervision of operators with

less than approximately 100 procedures experience seems reasonable (Table 12).

An operator volume <29 ICD implantations per year was associated with adjusted OR for infection of 2.47 (95% CI 1.18–5.17) vs. higher volume operators.<sup>184</sup> An operator volume <60 ICD procedures per year was associated with a highly increased risk of any complication [HR 10.4 (1.32–82.14)],<sup>185</sup> while an operator volume >40 pacemaker procedures per year resulted in fewer complications.<sup>186</sup> Annual operators volume <50 procedures was associated with higher risk of CIED infection (1.7% vs. 0.5%,  $P=0.02$ ).<sup>187</sup> An annual minimum operator volume of approximately 50 CIED procedures is therefore recommended (Table 12).



While infection rates were not related to centres volumes in some registries,<sup>187,188</sup> others clearly indicated an inverse relationship between infection risk for procedures and centre procedure volume.<sup>7,189</sup> Every centre should monitor and report local infection rates to a database.

## Health economics for cardiac implantable electronic devices infections and strategies to reduce costs

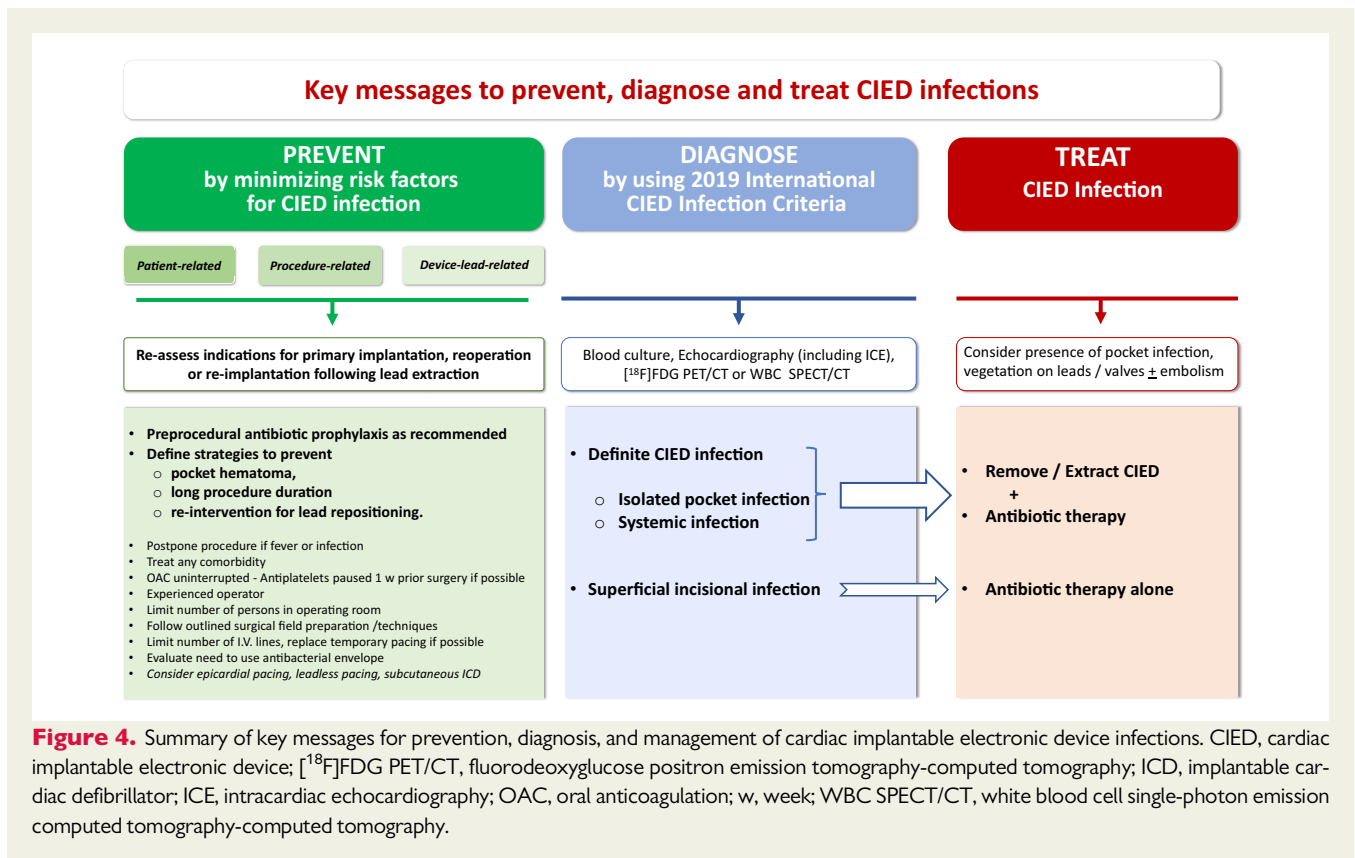
The increasing incidence of CIEDs infections, exceeding the device implantation rates<sup>4,153,190</sup> has important implications for the health care systems in view of induced health care costs.<sup>4,6,191</sup> Estimates of the costs of CIED infection are limited, with reported values of €20 623 to €23 234 in France, €36 931 in the UK, and €15 516 to €337 886 in the USA.<sup>6,11,192</sup> Any added day of in-hospital stay has huge costs.<sup>193</sup>

In Europe, reimbursement practices usually are based on diagnosis related groups and show an important variability for device

**Table 12 Recommendations on minimum volume requirements of CIED procedures for centres and operators**

Consensus statement	Statement class	Scientific evidence coding	References
Operators with less than approximately 100 CIED procedures experience should work under close supervision of more experienced operators		O, E	181–184
An annual minimum operator volume of approximately 50 CIED procedures is recommended for all operators		O, E	185–188

CIED, cardiac implantable electrical device; E, expert opinion; M, meta-analysis; O, observational studies; R, randomized trials.



**Figure 4.** Summary of key messages for prevention, diagnosis, and management of cardiac implantable electronic device infections. CIED, cardiac implantable electronic device; [<sup>18</sup>F]FDG PET/CT, fluorodeoxyglucose positron emission tomography-computed tomography; ICD, implantable cardiac defibrillator; ICE, intracardiac echocardiography; OAC, oral anticoagulation; w, week; WBC SPECT/CT, white blood cell single-photon emission computed tomography-computed tomography.

procedures,<sup>194</sup> with a substantial risk of suboptimal care.<sup>195</sup> Health technology assessment,<sup>196,197</sup> and registries are of crucial importance for optimization of care, coupling effectiveness with appropriate use of resources.<sup>2,195</sup>

## Conclusion

The lack of international consensus documents specifically focusing on CIED infections,<sup>19,59,65,81,198</sup> the gaps in knowledge, new important randomized trials, and observed divergences in managing device-related infections<sup>1</sup> provided a strong incentive for a 2019

International State-of-the-art Consensus document on the prevention, diagnosis, and management of CIED infections. The use of standardized terminology,<sup>199–201</sup> continuous surveillance programme of device infection rates at implanting centres, and improved adherence to guideline recommendations are strongly warranted (Figure 4).

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### Conflict of interest

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## References

- Traykov V, Bongiorno MG, Boriani G, Burri H, Costa R, Dagnes N, Deharo J-C, Epstein LM, Erba PA, Snygg-Martin U, Nielsen JC, Poole J, Saghy L, Starck C, Strathmore N, Blomström-Lundqvist C. Clinical practice and implementation of guidelines for the prevention, diagnosis and management of cardiac implantable electronic device infections; results of a worldwide survey under the auspices of the European Heart Rhythm Association. *Europace* 2019; **21**:1270–1279.
- Bongiorno MG, Kennergren C, Butter C, Deharo JC, Kutarski A, Rinaldi CA, Romano SL, Maggioni AP, Andarala M, Auricchio A, Kuck KH, Blomstrom-Lundqvist C; ELECTRa Investigators. The European Lead Extraction ConTrolled (ELECTRa) study: a European Heart Rhythm Association (EHRA) Registry of Transvenous Lead Extraction Outcomes. *Eur Heart J* 2017; **38**: 2995–3005.
- Johansen JB, Jørgensen OD, Møller M, Arnsbo P, Mortensen PT, Nielsen JC. Infection after pacemaker implantation: infection rates and risk factors associated with infection in a population-based cohort study of 46299 consecutive patients. *Eur Heart J* 2011; **32**:991–998.
- Greenspon AJ, Patel JD, Lau E, Ochoa JA, Frisch DR, Ho RT, Pavri BB, Kurtz SM. 16-year trends in the infection burden for pacemakers and implantable cardioverter-defibrillators in the United States 1993 to 2008. *J Am Coll Cardiol* 2011; **58**:1001–1006.
- Joy PS, Kumar G, Poole JE, London B, Olshansky B. Cardiac implantable electronic device infections: who is at greatest risk? *Heart Rhythm* 2017; **14**:839–845.
- Ahsan SY, Saberwal B, Lambiase PD, Koo CY, Lee S, Gopalamurugan AB, Rogers DP, Lowe MD, Chow AW. A simple infection-control protocol to reduce serious cardiac device infections. *Europace* 2014; **16**:1482–1489.
- Uslan DZ, Gleva MJ, Warren DK, Mela T, Chung MK, Gottipaty V, Borge R, Dan D, Shinn T, Mitchell K, Holcomb RG, Poole JE. Cardiovascular implantable electronic device replacement infections and prevention: results from the REPLACE Registry. *Pacing Clin Electrophysiol* 2012; **35**:81–87.
- Biffi M, Ammendola E, Menardi E, Parisi Q, Narducci ML, De Filippo P, Manzo M, Stabile G, Potenza DR, Zanon F, Quartieri F, Rillo M, Saporito D, Zacà V, Berisso MZ, Bertini M, Tumietto F, Malacrida M, Diemberger I. Real-life outcome of implantable cardioverter-defibrillator and cardiac resynchronization defibrillator replacement/upgrade in a contemporary population: observations from the multicentre DECODE registry. *Europace* 2019; **21**:1527–1536.
- Krahn AD, Longtin Y, Philippon F, Birnie DH, Manlucu J, Angaran P, Rinne C, Coutu B, Low RA, Essebag V, Morillo C, Redfeard D, Toal S, Becker G, Degrace M, Thibault B, Crystal E, Tung S, LeMaitre J, Sultan O, Bennett M, Bashir J, Ayala-Paredes F, Gervais P, Rioux L, Hemels MEW, Bouwels LHR, van Vlies B, Wang J, Exner DV, Dorian P, Parkash R, Alings M, Connolly SJ. Prevention of arrhythmic device infection trial: the PADIT trial. *J Am Coll Cardiol* 2018; **72**:3098–3109.
- Tarakji KG, Mittal S, Kennergren C, Corey R, Poole JE, Schloss E, Gallastegui J, Pickett RA, Evonich R, Philippon F, McComb JM, Roark SF, Sorrentino D, Sholevar D, Cronin E, Berman B, Riggio D, Biffi M, Khan H, Silver MT, Collier J, Eldadah Z, Wright DJ, Lande JD, Lexcen DR, Cheng A, Wilkoff BL. Antibacterial envelope to prevent cardiac implantable device infection. *N Engl J Med* 2019; **380**:1895–1905.
- Clementy N, Carion PL, de Leotoing L, Lamarsalle L, Wilquin-Bequet F, Brown B, Verhees KJP, Fernandes J, Deharo JC. Infections and associated costs following cardiovascular implantable electronic device implantations: a nationwide cohort study. *Europace* 2018; **20**:1974–1980.
- Ludwig S, Theis C, Brown B, Witthohn A, Lux W, Goette A. Incidence and costs of cardiac device infections: retrospective analysis using German health claims data. *J Comp Eff Res* 2018; **7**:483–492.
- Da Costa A, Lelièvre H, Pha D, Kirkorian G, Célaro M, Chevalier P, Vandenesch F, Etienne J, Touboul P. Role of the preaxillary flora in pacemaker infections. *Circulation* 1998; **97**:1791–1795.
- Uslan DZ, Sohail MR, St Sauver JL, Friedman PA, Hayes DL, Stoner SM, Wilson WR, Steckelberg JM, Baddour LM. Permanent pacemaker and implantable cardioverter defibrillator infection: a population-based study. *Arch Intern Med* 2007; **167**:669–675.
- Darouiche RO. Device-associated infections: a macroproblem that starts with microadherence. *Clin Infect Dis* 2001; **33**:1567–1572.
- Hussein AA, Baghdy Y, Wazni OM, Brunner MP, Kabbach G, Shao M, Gordon S, Saliba WI, Wilkoff BL, Tarakji KG. Microbiology of cardiac implantable electronic device infections. *JACC Clin Electrophysiol* 2016; **2**:498–505.
- Bongiorno MG, Tascini C, Tagliaferri E, Di Cori A, Soldati E, Leonildi A, Zucchelli G, Ciullo I, Menichetti F. Microbiology of cardiac implantable electronic device infections. *Europace* 2012; **14**:1334–1339.
- Wang R, Li X, Wang Q, Zhang Y, Wang H. Microbiological characteristics and clinical features of cardiac implantable electronic device infections at a tertiary hospital in China. *Front Microbiol* 2017; **8**:360–360.
- Sandoe JA, Barlow G, Chambers JB, Gammage M, Guleri A, Howard P, Olson E, Perry JD, Prendergast BD, Spry MJ, Steeds RP, Tayebjee MH, Watkin R. Guidelines for the diagnosis, prevention and management of implantable cardiac electronic device infection. Report of a joint Working Party project on behalf of the British Society for Antimicrobial Chemotherapy (BSAC, host organization), British Heart Rhythm Society (BHRS), British Cardiovascular Society (BCS), British Heart Valve Society (BHVS) and British Society for Echocardiography (BSE). *J Antimicrob Chemother* 2015; **70**:325–359.
- Jan E, Camou F, Texier-Maugein J, Whinnett Z, Caubet O, Ploux S, Pellegrin JL, Ritter P, Metayer PL, Roudaut R, Haissaguerre M, Bordachar P. Microbiologic characteristics and in vitro susceptibility to antimicrobials in a large population of patients with cardiovascular implantable electronic device infection. *J Cardiovasc Electrophysiol* 2012; **23**:375–381.
- Polyzos KA, Konstantelias AA, Falagas ME. Risk factors for cardiac implantable electronic device infection: a systematic review and meta-analysis. *Europace* 2015; **17**:767–777.
- Prutkin JM, Reynolds MR, Bao H, Curtis JP, Al-Khatib SM, Aggarwal S, Uslan DZ. Rates of and factors associated with infection in 200 909 Medicare implantable cardioverter-defibrillator implants: results from the National Cardiovascular Data Registry. *Circulation* 2014; **130**:1037–1043.
- Olsen T, Jørgensen OD, Nielsen JC, Thøgersen AM, Philbert BT, Johansen JB. Incidence of device-related infection in 97 750 patients: clinical data from the complete Danish device-cohort (1982–2018). *Eur Heart J* 2019; **40**:1862–1869.
- Essebag V, Verma A, Healey JS, Krahn AD, Kalfon E, Coutu B, Ayala-Paredes F, Tang AS, Sapp J, Sturmer M, Keren A, Wells GA, Birnie DH; BRUISE CONTROL Investigators. Clinically significant pocket hematoma increases long-term risk of device infection: BRUISE CONTROL INFECTION study. *J Am Coll Cardiol* 2016; **67**:1300–1308.
- Al-Khatib SM, Greiner MA, Peterson ED, Hernandez AF, Schulman KA, Curtis LH. Patient and implanting physician factors associated with mortality and complications after implantable cardioverter-defibrillator implantation, 2002–2005. *Circ Arrhythmia Electrophysiol* 2008; **1**:240–249.
- Mittal S, Shaw RE, Michel K, Palekar R, Arshad A, Musat D, Preminger M, Sichrovsky T, Steinberg JS. Cardiac implantable electronic device infections: incidence, risk factors, and the effect of the AigisRx antibacterial envelope. *Heart Rhythm* 2014; **11**:595–601.
- Shariff N, Eby E, Adelstein E, Jain S, Shalaby A, Saba S, Wang NC, Schwartzman D. Health and economic outcomes associated with use of an antimicrobial envelope as a standard of care for cardiac implantable electronic device implantation. *J Cardiovasc Electrophysiol* 2015; **26**:783–789.
- Klug D, Balde M, Pavin D, Hidden-Lucet F, Clementy J, Sadoul N, Rey JL, Lande G, Lazarus A, Victor J, Barnay C, Grandbastien B, Kacet S; PEOPLE Study Group. Risk factors related to infections of implanted pacemakers and cardioverter-defibrillators: results of a large prospective study. *Circulation* 2007; **116**:1349–1355.
- Birnie DH, Healey JS, Wells GA, Ayala-Paredes F, Coutu B, Sumner GL, Becker G, Verma A, Philippon F, Kalfon E, Eikelboom J, Sandhu RK, Nery PB, Lellouche N, Connolly SJ, Sapp J, Essebag V. Continued vs. interrupted direct oral anticoagulants at the time of device surgery, in patients with moderate to high risk of arterial thrombo-embolic events (BRUISE CONTROL-2). *Eur Heart J* 2018; **39**: 3973–3979.
- Birnie DH, Healey JS, Wells GA, Verma A, Tang AS, Krahn AD, Simpson CS, Ayala-Paredes F, Coutu B, Leiria TLL, Essebag V. Pacemaker or defibrillator surgery without interruption of anticoagulation. *N Engl J Med* 2013; **368**: 2084–2093.
- Kutinsky IB, Jarandilla R, Jewett M, Haines DE. Risk of hematoma complications after device implant in the clopidogrel era. *Circ Arrhythm Electrophysiol* 2010; **3**: 312–318.
- Robinson M, Healey JS, Eikelboom J, Schulman SAM, Morillo CA, Nair GM, Baranchuk A, Ribas S, Evans G, Connolly SJ, Turpie AG. Postoperative low-molecular-weight heparin bridging is associated with an increase in wound hematoma following surgery for pacemakers and implantable defibrillators. *Pacing Clin Electrophysiol* 2009; **32**:378–382.
- Du L, Zhang Y, Wang W, Hou Y. Perioperative anticoagulation management in patients on chronic oral anticoagulant therapy undergoing cardiac devices implantation: a meta-analysis. *Pacing Clin Electrophysiol* 2014; **37**:1573–1586.
- Haines DE, Beheiry S, Akar JG, Baker JL, Beinborn D, Beshai JF, Brysiewicz N, Chiu-Man C, Collins KK, Dare M, Fetterly K, Fisher JD, Hongo R, Irefin S, Lopez J, Miller JM, Perry JC, Slotwiner DJ, Tomassoni GF, Weiss E. Heart Rhythm Society expert consensus statement on electrophysiology laboratory standards: process, protocols, equipment, personnel, and safety. *Heart Rhythm* 2014; **11**: e9–e51.
- Merino JL, Arribas F, Botto GL, Huikuri H, Kraemer LI, Linde C, Morgan JM, Schali J, Simantirakis E, Wolpert C, Villard MC, Poirey J, Karaim-Fanchon S, Deront K. Core curriculum for the heart rhythm specialist. *Europace* 2009; **11**: 1–26.

36. Tanner J, Norrie P, Melen K. Preoperative hair removal to reduce surgical site infection. *Cochrane Database Syst Rev* 2011;**11**:CD004122.
37. Darouiche RO, Wall MJ Jr, Itani KM, Otterson MF, Webb AL, Carrick MM, Miller HJ, Awad SS, Crosby CT, Mosier MC, Alsharif A, Berger DH. Chlorhexidine-alcohol versus povidone-iodine for surgical-site antisepsis. *N Engl J Med* 2010;**362**:18–26.
38. Mimoz O, Lucet JC, Kerforne T, Pascal J, Souweine B, Goudet V, Mercat A, Bouadma L, Lasocki S, Alfandari S, Friggeri A, Wallet F, Allou N, Ruckly S, Balayn D, Lepape A, Timsit JF. Skin antisepsis with chlorhexidine-alcohol versus povidone iodine-alcohol, with and without skin scrubbing, for prevention of intravascular-catheter-related infection (CLEAN): an open-label, multicentre, randomised, controlled, two-by-two factorial trial. *Lancet* 2015;**386**:2069–2077.
39. Sohail MR, Uslan DZ, Khan AH, Friedman PA, Hayes DL, Wilson WR, Steckelberg JM, Stoner S, Baddour LM. Management and outcome of permanent pacemaker and implantable cardioverter-defibrillator infections. *J Am Coll Cardiol* 2007;**49**:1851–1859.
40. Asif A, Carrillo R, Garisto J-D, Lopera G, Ladino M, Barakat U, Eid N, Salman L. Epicardial cardiac rhythm devices for dialysis patients: minimizing the risk of infection and preserving central veins. *Semin Dial* 2012;**25**:88–94.
41. El-Chami MF, Soejima K, Piccini JP, Reynolds D, Ritter P, Okabe T, Friedman PA, Cha Y-M, Stromberg K, Holbrook R, Fagan DH, Roberts PR. Incidence and outcomes of systemic infections in patients with leadless pacemakers: data from the Micra IDE study. *Pacing Clin Electrophysiol* 2019;**42**:1105–1110.
42. El-Chami MF, Clementy N, Garweg C, Omar R, Duray GZ, Gornick CC, Leyva F, Sagi V, Piccini JP, Soejima K, Stromberg K, Roberts PR. Leadless pacemaker implantation in hemodialysis patients: experience with the Micra transcatheter pacemaker. *JACC Clin Electrophysiol* 2019;**5**:162–170.
43. Pokorney SD, Mi X, Lewis RK, Greiner M, Epstein LM, Carrillo RG, Zeitler EP, Al-Khatib SM, Hegland DD, Piccini JP. Outcomes associated with extraction versus capping and abandoning pacing and defibrillator leads. *Circulation* 2017;**136**:1387–1395.
44. Hussein AA, Tarakji KG, Martin DO, Gadre A, Fraser T, Kim A, Brunner MP, Barakat AF, Saliba WI, Kanj M, Baranowski B, Cantillon D, Niebauer M, Callahan T, Dresing T, Lindsay BD, Gordon S, Wilkoff BL, Wazni OM. Cardiac implantable electronic device infections: added complexity and suboptimal outcomes with previously abandoned leads. *JACC Clin Electrophysiol* 2017;**3**:1–9.
45. de Vries FE, Gans SL, Solomkin JS, Allegranzi B, Egger M, Dellinger EP, Boermeester MA. Meta-analysis of lower perioperative blood glucose target levels for reduction of surgical-site infection. *Br J Surg* 2017;**104**:e95–e105.
46. Bode LGM, Kluytmans J, Wertheim HFL, Bogaers D, Vandenbroucke-Grauls C, Roosendaal R, Troelstra A, Box ATA, Voss A, van der Tweel I, van Belkum A, Verbrugh HA, Vos MC. Preventing surgical-site infections in nasal carriers of *Staphylococcus aureus*. *N Engl J Med* 2010;**362**:9–17.
47. Franco L, Cota GF, Pinto TS, Ercole FF. Preoperative bathing of the surgical site with chlorhexidine for infection prevention: systematic review with meta-analysis. *Am J Infect Control* 2017;**45**:343–349.
48. de Oliveira JC, Martinelli M, Nishioka SA, Varejão T, Uipe D, Pedrosa AA, Costa R, D'Avila A, Danik SB. Efficacy of antibiotic prophylaxis before the implantation of pacemakers and cardioverter-defibrillators: results of a large, prospective, randomized, double-blinded, placebo-controlled trial. *Circ Arrhythm Electrophysiol* 2009;**2**:29–34.
49. Da Costa A, Kirkorian G, Chucherat M, Delahaye F, Chevalier P, Cerisier A, Isaak K, Touboul P. Antibiotic prophylaxis for permanent pacemaker implantation: a meta-analysis. *Circulation* 1998;**97**:1796–1801.
50. Webster J, Alghamdi A. Use of plastic adhesive drapes during surgery for preventing surgical site infection. *Cochrane Database Syst Rev* 2015;**4**:CD006353.
51. Suding P, Nguyen T, Gordon I, Wilson SE. Glove powder increases *Staphylococcus aureus* abscess rate in a rat model. *Surg Infect (Larchmt)* 2010;**11**:133–135.
52. NICE Guideline Updates Team. Surgical site infections: prevention and treatment. *NICE Guideline No 125*. London, UK: National Institute for Health and Care Excellence; 2019.
53. Kleemann T, Becker T, Strauss M, Dyck N, Weisse U, Saggau W, Burkhardt U, Seidl K. Prevalence of bacterial colonization of generator pockets in implantable cardioverter defibrillator patients without signs of infection undergoing generator replacement or lead revision. *Europace* 2010;**12**:58–63.
54. Lakkireddy D, Pillarisetti J, Atkins D, Biria M, Reddy M, Murray C, Bommana S, Shanberg D, Adabala N, Pimentel R, Dendi R, Emert M, Vacek J, Dawn B, Berenbom L. Impact of pockeT rEvision on the rate of Infection and other Complications in patients rEquiring pocket mAnipulation for generator replacement and/or lead replacement or revisioN (MAKE IT CLEAN): a prospective randomized study. *Heart Rhythm* 2015;**12**:950–956.
55. Grubb B, Welch M, Karabin B, Foster W, Zhang D, Kanjwal K. Initial experience with a technique for wound closure after cardiac device implantation designed to reduce infection and minimize tissue scar formation. *Am J Ther* 2012;**19**:88–91.
56. Klug D, Wallet F, Lacroix D, Marquie C, Kouakam C, Kacet S, Courcol R. Local symptoms at the site of pacemaker implantation indicate latent systemic infection. *Heart* 2004;**90**:882–886.
57. Bongioni MG, Burri H, Deharo JC, Starck C, Kennergren C, Saghy L, Rao A, Tascini C, Lever N, Kutarski A, Fernandez Lozano I, Strathmore N, Costa R, Epstein L, Love C; ESC Scientific Document Group. 2018 EHRA expert consensus statement on lead extraction: recommendations on definitions, endpoints, research trial design, and data collection requirements for clinical scientific studies and registries: endorsed by APHRS/HRS/LAHS. *Europace* 2018;**20**:1217–1217.
58. Knigina L, Kuhn C, Kutschka I, Oswald H, Klein G, Haverich A, Pichlmaier M. Treatment of patients with recurrent or persistent infection of cardiac implantable electronic devices. *Europace* 2010;**12**:1275–1281.
59. Habib G, Lancellotti P, Antunes MJ, Bongioni MG, Casalta JP, Del Zotti F, Dulgheru R, El Khoury G, Erba PA, lung B, Miro JM, Mulder BJ, Plonska-Gosciniak E, Price S, Roos-Hesselink J, Snygg-Martin U, Thuny F, Tornos Mas P, Vilacosta I, Zamorano JL; ESC Scientific Document Group. 2015 ESC Guidelines for the management of infective endocarditis: the Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by: european Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). *Eur Heart J* 2015;**36**:3075–3128.
60. Klug D, Lacroix D, Savoye C, Goullard L, Grandmougin D, Hennequin JL, Kacet S, Lekieffre J. Systemic infection related to endocarditis on pacemaker leads: clinical presentation and management. *Circulation* 1997;**95**:2098–2107.
61. Acoub P, Leprince P, Nataf P, Hausfater P, Dorent R, Wechsler B, Bors V, Pavie A, Piette JC, Gandjbakhch I. Pacemaker infective endocarditis. *Am J Cardiol* 1998;**82**:480–484.
62. Lennerz C, Vrazic H, Haller B, Braun S, Petzold T, Ott I, Lennerz A, Michel J, Blažek P, Deisenhofer I, Whittaker P, Kolb C. Biomarker-based diagnosis of pacemaker and implantable cardioverter defibrillator pocket infections: a prospective, multicentre, case-control evaluation. *PLoS One* 2017;**12**:e0172384.
63. Cornelissen CG, Frechen DA, Schreiner K, Marx N, Krüger S. Inflammatory parameters and prediction of prognosis in infective endocarditis. *BMC Infect Dis* 2013;**13**:272.
64. Li JS, Sexton DJ, Mick N, Nettles R, Fowler VG Jr, Ryan T, Bashore T, Corey GR. Proposed modifications to the duke criteria for the diagnosis of infective endocarditis. *Clin Infect Dis* 2000;**30**:633–638.
65. Baddour LM, Epstein AE, Erickson CC, Knight BP, Levison ME, Lockhart PB, Masoudi FA, Okum EJ, Wilson WR, Beerman LB, Bolger AF, Estes NA 3rd, Gewitz M, Newburger JW, Schron EB, Taubert KA; American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee; Council on Cardiovascular Disease in Young; Council on Cardiovascular Surgery and Anesthesia; Council on Cardiovascular Nursing; Council on Clinical Cardiology; Interdisciplinary Council on Quality of Care; American Heart Association. Update on cardiovascular implantable electronic device infections and their management: a scientific statement from the American Heart Association. *Circulation* 2010;**121**:458–477.
66. Dy Chua J, Abdul-Karim A, Mawhorter S, Procop GW, Tchou P, Niebauer M, Saliba W, Schweikert R, Wilkoff BL. The role of swab and tissue culture in the diagnosis of implantable cardiac device infection. *Pacing Clin Electrophysiol* 2005;**28**:1276–1281.
67. Forward KR. An evaluation of extended incubation time with blind subculture of blood cultures in patients with suspected endocarditis. *Can J Infect Dis Med Microbiol* 2006;**17**:186–188.
68. Mason PK, Dimarco JP, Ferguson JD, Mahapatra S, Mangrum JM, Bilchick KC, Moorman JR, Lake DE, Bergin JD. Sonication of explanted cardiac rhythm management devices for the diagnosis of pocket infections and asymptomatic bacterial colonization. *Pacing Clin Electrophysiol* 2011;**34**:143–149.
69. Oliva A, Nguyen BL, Mascellino MT, D'Abramo A, Iannetta M, Ciccaglioni A, Vullo V, Mastroianni CM. Sonication of explanted cardiac implants improves microbial detection in cardiac device infections. *J Clin Microbiol* 2013;**51**:496–502.
70. Viola GM, Mansouri MD, Nasir N, Darouiche RO. Incubation alone is adequate as a culturing technique for cardiac rhythm management devices. *J Clin Microbiol* 2009;**47**:4168–4170.
71. Harrison JL, Prendergast BD, Sandoe JA. Guidelines for the diagnosis, management and prevention of implantable cardiac electronic device infection. *Heart* 2015;**101**:250–252.
72. Viola GM, Awan LL, Darouiche RO. Nonstaphylococcal infections of cardiac implantable electronic devices. *Circulation* 2010;**121**:2085–2091.
73. Nagpal A, Baddour LM, Sohail MR. Microbiology and pathogenesis of cardiovascular implantable electronic device infections. *Circ Arrhythm Electrophysiol* 2012;**5**:433–441.
74. Vilacosta I, Sarriá C, San Román JA, Jiménez J, Castillo JA, Iturralde E, Rollán MJ, Martínez Elbal L. Usefulness of transesophageal echocardiography for diagnosis of infected transvenous permanent pacemakers. *Circulation* 1994;**89**:2684–2687.

75. Golzio PG, Errigo D, Peyracchia M, Gallo E, Frea S, Castagno D, Budano C, Giustetto C, Rinaldi M. Prevalence and prognosis of lead masses in patients with cardiac implantable electronic devices without infection. *J Cardiovasc Med* 2019;**20**:372–378.
76. Downey BC, Juselius WE, Pandian NG, Estes NA, Link MS. Incidence and significance of pacemaker and implantable cardioverter-defibrillator lead masses discovered during transesophageal echocardiography. *Pacing Clin Electrophysiol* 2011;**34**:679–683.
77. Bongiorno MG, Di Cori A, Soldati E, Zucchelli G, Arena G, Segreti L, De Lucia R, Marzilli M. Intracardiac echocardiography in patients with pacing and defibrillating leads: a feasibility study. *Echocardiography* 2008;**25**:632–638.
78. Narducci ML, Pelargonio G, Russo E, Marinaccio L, Di Monaco A, Perna F, Bencardino G, Casella M, Di Biase L, Santangeli P, Palmieri R, Lauria C, Al Mohani G, Di Clemente F, Tondo C, Pennestri F, Ierardi C, Rebuzzi AG, Crea F, Bellocci F, Natale A, Russo AD. Usefulness of intracardiac echocardiography for the diagnosis of cardiovascular implantable electronic device-related endocarditis. *J Am Coll Cardiol* 2013;**61**:1398–1405.
79. Chang D, Gabriels J, Laighold S, Williamson AK, Ismail H, Epstein LM. A novel diagnostic approach to a mass on a device lead. *HeartRhythm Case Rep* 2019;**5**:306–309.
80. Diemberger I, Biffi M, Lorenzetti S, Martignani C, Raffaelli E, Ziacchi M, Rapezzi C, Pacini D, Boriani G. Predictors of long-term survival free from relapses after extraction of infected CIED. *Europace* 2018;**20**:1018–1027.
81. Kusumoto FM, Schoenfeld MH, Wilkoff BL, Berul CI, Birgersdotter-Green UM, Carrillo R, Cha YM, Clancy J, Deharo JC, Ellenbogen KA, Exner D, Hussein AA, Kennergren C, Krahn A, Lee R, Love CJ, Madden RA, Mazzetti HA, Moore JC, Parsonnet J, Patton KK, Rozner MA, Selzman KA, Shoda M, Srivathsan K, Strathmore NF, Swerdlow CD, Tompkins C, Wazni O. 2017 HRS expert consensus statement on cardiovascular implantable electronic device lead management and extraction. *Heart Rhythm* 2017;**14**:e503–e551.
82. Incani A, Hair C, Purnell P, O'Brien DP, Cheng AC, Appelbe A, Athan E. *Staphylococcus aureus* bacteraemia: evaluation of the role of transoesophageal echocardiography in identifying clinically unsuspected endocarditis. *Eur J Clin Microbiol Infect Dis* 2013;**32**:1003–1008.
83. Rasmussen RV, Høst U, Arpi M, Hassager C, Johansen HK, Korup E, Schønheyder HC, Berning J, Gill S, Rosenvinge FS, Fowler VG Jr, Møller JE, Skov RL, Larsen CT, Hansen TF, Mard S, Smit J, Andersen PS, Bruun NE. Prevalence of infective endocarditis in patients with *Staphylococcus aureus* bacteraemia: the value of screening with echocardiography. *Eur J Echocardiogr* 2011;**12**:414–420.
84. Pizzi MN, Roque A, Fernández-Hidalgo N, Cuéllar-Calabria H, Ferreira-González I, González-Alujas MT, Oristrell G, Gracia-Sánchez L, González JJ, Rodríguez-Palomares J, Galánés M, Maisterra-Santos O, Garcia-Dorado D, Castell-Conesa J, Almirante B, Aguadé-Bruix S, Tornos P. Improving the diagnosis of infective endocarditis in prosthetic valves and intracardiac devices with <sup>18</sup>F-fluorodeoxyglucose positron emission tomography/computed tomography angiography: initial results at an infective endocarditis referral center. *Circulation* 2015;**132**:1113–1126.
85. Erba PA, Lancellotti P, Vilacosta I, Gaemperli O, Rouzet F, Hacker M, Signore A, Slart R, Habib G. Recommendations on nuclear and multimodality imaging in IE and CIED infections. *Eur J Nucl Med Mol Imaging* 2018;**45**:1795–1815.
86. Vos FJ, Bleeker-Rovers CP, Kullberg BJ, Adang EMM, Oyen WJG. Cost-effectiveness of routine <sup>18</sup>F-FDG PET/CT in high-risk patients with Gram-positive bacteremia. *J Nucl Med* 2011;**52**:1673–1678.
87. Berrevoets MAH, Kouijzer IJE, Aarntzen EHJG, Janssen MJR, De Geus-Oei L-F, Wertheim HFL, Kullberg B-J, Oever JT, Oyen WJG, Bleeker-Rovers CP. <sup>18</sup>F-FDG PET/CT optimizes treatment in *Staphylococcus aureus* bacteremia and is associated with reduced mortality. *J Nucl Med* 2017;**58**:1504–1510.
88. Amraoui S, Tlili G, Sohal M, Berte B, Hindié E, Ritter P, Ploux S, Denis A, Derval N, Rinaldi CA, Cazanave C, Jais P, Haissaguerre M, Bordenave L, Bordachar P. Contribution of PET imaging to the diagnosis of septic embolism in patients with pacing lead endocarditis. *JACC Cardiovasc Imaging* 2016;**9**:283–290.
89. Erba PA, Sollini M, Conti U, Bandera F, Tascini C, De Tommasi SM, Zucchelli G, Doria R, Menichetti F, Bongiorno MG, Lazzeri E, Mariani G. Radiolabeled WBC scintigraphy in the diagnostic workup of patients with suspected device-related infections. *JACC Cardiovasc Imaging* 2013;**6**:1075–1086.
90. Sollini M, Berchiolli R, Delgado Bolton RC, Rossi A, Kirienco M, Boni R, Lazzeri E, Slart R, Erba PA. The “3M” approach to cardiovascular infections: multimodality, multitracers, and multidisciplinary. *Semin Nucl Med* 2018;**48**:199–224.
91. Paparoupa M, Spinelli L, Framke T, Ho H, Schuppert F, Gillissen A. Pulmonary embolism in pneumonia: still a diagnostic challenge? Results of a case-control study in 100 patients. *Dis Markers* 2016;**2016**:1–8.
92. Narducci ML, Di Monaco A, Pelargonio G, Leoncini E, Boccia S, Mollo R, Perna F, Bencardino G, Pennestri F, Scoppettuolo G, Rebuzzi AG, Santangeli P, Di Biase L, Natale A, Crea F. Presence of ‘ghosts’ and mortality after transvenous lead extraction. *Europace* 2017;**19**:432–440.
93. Park S-J, Gentry JL, Varma N, Wazni O, Tarakji KG, Mehta A, Mick S, Grimm R, Wilkoff BL. Transvenous extraction of pacemaker and defibrillator leads and the risk of tricuspid valve regurgitation. *JACC Clin Electrophysiol* 2018;**4**:1421–1428.
94. Pijl JP, Glaudemans AWJM, Slart RHJA, Yakar D, Wouthuyzen-Bakker M, Kwee TC. FDG-PET/CT for detecting an infection focus in patients with bloodstream infection: factors affecting diagnostic yield. *Clin Nucl Med* 2019;**44**:99–106.
95. Berrevoets MAH, Kouijzer IJE, Sliker K, Aarntzen EHJG, Kullberg BJ, Oever JT, Bleeker-Rovers CP. <sup>18</sup>F-FDG PET/CT-guided treatment duration in patients with high-risk *Staphylococcus aureus* bacteremia: a proof of principle. *J Nucl Med* 2019;**60**:998–1002.
96. Mandry D, Tatopoulos A, Chevalier-Mathias E, Lemarié J, Bollaert P-E, Roch V, Olivier P, Marie P-Y, Gibot S. <sup>18</sup>F-fluorodeoxyglucose positron emission tomography combined with whole-body computed tomographic angiography in critically ill patients with suspected severe sepsis with no definite diagnosis. *Eur J Nucl Med Mol Imaging* 2014;**41**:1924–1930.
97. Vos FJ, Kullberg BJ, Sturm PD, Krabbe PFM, van Dijk APJ, Wanten GJA, Oyen WJG, Bleeker-Rovers CP. Metastatic infectious disease and clinical outcome in *Staphylococcus aureus* and *Streptococcus* species bacteremia. *Medicine* 2012;**91**:86–94.
98. Botelho-Nevers E, Thuny F, Casalta JP, Richet H, Gouriet F, Collart F, Riberi A, Habib G, Raoult D. Dramatic reduction in infective endocarditis-related mortality with a management-based approach. *Arch Intern Med* 2009;**169**:1290–1298.
99. Juneau D, Golfam M, Hazra S, Zuckier LS, Garas S, Redpath C, Bernick J, Leung E, Chih S, Wells G, Beanlands RS, Chow BJ. Positron emission tomography and single-photon emission computed tomography imaging in the diagnosis of cardiac implantable electronic device infection: a systematic review and meta-analysis. *Circ Cardiovasc Imaging* 2017;**10**:e005772.
100. Mahmood M, Kendi AT, Farid S, Ajmal S, Johnson GB, Baddour LM, Chareonthaitawee P, Friedman PA, Sohail MR. Role of <sup>18</sup>F-FDG PET/CT in the diagnosis of cardiovascular implantable electronic device infections: a meta-analysis. *J Nucl Cardiol* 2019;**26**:958–970.
101. Diemberger I, Bonfiglioli R, Martignani C, Graziosi M, Biffi M, Lorenzetti S, Ziacchi M, Nanni C, Fanti S, Boriani G. Contribution of PET imaging to mortality risk stratification in candidates to lead extraction for pacemaker or defibrillator infection: a prospective single center study. *Eur J Nucl Med Mol Imaging* 2019;**46**:194–205.
102. Lebeaux D, Fernández-Hidalgo N, Chauhan A, Lee S, Ghigo J-M, Almirante B, Beloin C. Management of infections related to totally implantable venous-access ports: challenges and perspectives. *Lancet Infect Dis* 2014;**14**:146–159.
103. Peacock JE, Stafford JM, Le K, Sohail MR, Baddour LM, Prutkin JM, Danik SB, Vikram HR, Hernandez-Meneses M, Miró JM, Blank E, Saba S, Carrillo RG, Greenspon AJ, Tseng CH, Uslan DZ. Attempted salvage of infected cardiovascular implantable electronic devices: are there clinical factors that predict success? *Pacing Clin Electrophysiol* 2018;**41**:524–531.
104. Le KY, Sohail MR, Friedman PA, Uslan DZ, Cha SS, Hayes DL, Wilson WR, Steckelberg JM, Baddour LM; Mayo Cardiovascular Infections Study Group. Impact of timing of device removal on mortality in patients with cardiovascular implantable electronic device infections. *Heart Rhythm* 2011;**8**:1678–1685.
105. Patel D, Khan F, Shah H, Bhattacharya S, Adelstein E, Saba S. Cardiac implantable electronic device lead extraction in patients with underlying infection using open thoracotomy or percutaneous techniques. *Cardiol J* 2015;**22**:68–74.
106. Schaerf RHM, Najibi S, Conrad J. Percutaneous vacuum-assisted thrombectomy device used for removal of large vegetations on infected pacemaker and defibrillator leads as an adjunct to lead extraction. *J Atr Fibrillation* 2016;**9**:1455.
107. Starck CT, Eulert-Grehn J, Kukucka M, Eggert-Doktor D, Dreizler T, Haupt B, Falk V. Managing large lead vegetations in transvenous lead extractions using a percutaneous aspiration technique. *Expert Rev Med Devices* 2018;**15**:757–761.
108. Lakshmanadoss U, Nunez B, Kutinsky I, Khalid R, Haines DE, Wong WS. Incidence of pocket infection postcardiac device implantation using antibiotic versus saline solution for pocket irrigation. *Pacing Clin Electrophysiol* 2016;**39**:978–984.
109. Le KY, Sohail MR, Friedman PA, Uslan DZ, Cha SS, Hayes DL, Wilson WR, Steckelberg JM, Baddour LM. Clinical features and outcomes of cardiovascular implantable electronic device infections due to staphylococcal species. *Am J Cardiol* 2012;**110**:1143–1149.
110. Madhavan M, Sohail MR, Friedman PA, Hayes DL, Steckelberg JM, Wilson WR, Baddour LM; Mayo Cardiovascular Infections Study Group. Outcomes in patients with cardiovascular implantable electronic devices and bacteremia caused by Gram-positive cocci other than *Staphylococcus aureus*. *Circ Arrhythm Electrophysiol* 2010;**3**:639–645.
111. Maskarinec SA, Thaden JT, Cyr DD, Ruffin F, Souli M, Fowler VG. The risk of cardiac device-related infection in bacteremic patients is species specific: results of a 12-year prospective cohort. *Open Forum Infect Dis* 2017;**4**:ofx132.
112. Uslan DZ, Sohail MR, Friedman PA, Hayes DL, Wilson WR, Steckelberg JM, Baddour LM. Frequency of permanent pacemaker or implantable cardioverter-

- defibrillator infection in patients with Gram-negative bacteremia. *Clin Infect Dis* 2006;**43**:731–736.
113. Huang X-M, Fu H-X, Zhong L, Cao J, Asirvatham SJ, Baddour LM, Sohail MR, Nkomo VT, Nishimura RA, Greason KL, Suri RM, Friedman PA, Cha Y-M. Outcomes of transvenous lead extraction for cardiovascular implantable electronic device infections in patients with prosthetic heart valves. *Circ Arrhythm Electrophysiol* 2016;**9**:e004188.
  114. Viganego F, O'Donoghue S, Eldadah Z, Shah MH, Rastogi M, Mazel JA, Platia EV. Effect of early diagnosis and treatment with percutaneous lead extraction on survival in patients with cardiac device infections. *Am J Cardiol* 2012;**109**:1466–1471.
  115. Rusanov A, Spotnitz HM. A 15-year experience with permanent pacemaker and defibrillator lead and patch extractions. *Ann Thorac Surg* 2010;**89**:44–50.
  116. Meier-Ewert HK, Gray M-E, John RM. Endocardial pacemaker or defibrillator leads with infected vegetations: a single-center experience and consequences of transvenous extraction. *Am Heart J* 2003;**146**:339–344.
  117. Pérez Bazarrica G, Gariglio L, Salvaggio F, Reolón E, Blanco N, Mazzetti H, Villecco S, Botbol A, Porcile R. Transvenous extraction of pacemaker leads in infective endocarditis with vegetations  $\geq 20$  mm: our experience. *Clin Cardiol* 2012;**35**:244–249.
  118. Tan EM, DeSimone DC, Sohail MR, Baddour LM, Wilson WR, Steckelberg JM, Virk A. Outcomes in patients with cardiovascular implantable electronic device infection managed with chronic antibiotic suppression. *Clin Infect Dis* 2017;**64**:1516–1521.
  119. Sohail MR, Palraj BR, Khalid S, Uslan DZ, Al-Saffar F, Friedman PA, Hayes DL, Lohse CM, Wilson WR, Steckelberg JM, Baddour LM. Predicting risk of endovascular device infection in patients with *Staphylococcus aureus* bacteremia (PREDICT-SAB). *Circ Arrhythm Electrophysiol* 2015;**8**:137–144.
  120. Thwaites GE, Scarborough M, Szubert A, Nsutebu E, Tilley R, Greig J, Wyllie SA, Wilson P, Auckland C, Cairns J, Ward D, Lal P, Guleri A, Jenkins N, Sutton J, Wiselka M, Armando GR, Graham C, Chadwick PR, Barlow G, Gordon NC, Young B, Meisner S, McWhinney P, Price DA, Harvey D, Nayar D, Jeyaratnam D, Planche T, Minton J, Hudson F, Hopkins S, Williams J, Török ME, Llewelyn MJ, Edgeworth JD, Walker AS; United Kingdom Clinical Infection Research Group (UKCIRG). Adjunctive rifampicin for *Staphylococcus aureus* bacteraemia (ARREST): a multicentre, randomised, double-blind, placebo-controlled trial. *Lancet* 2018;**391**:668–678.
  121. Bongiorni MG, Marinakis G, Lip GY, Svendsen JH, Dobreaun D, Blomström-Lundqvist C; Scientific Initiative Committee, European Heart Rhythm Association. How European centres diagnose, treat, and prevent CIED infections: results of an European Heart Rhythm Association survey. *Europace* 2012;**14**:1666–1669.
  122. Grammes JA, Schulze CM, Al-Bataineh M, Yesenosky GA, Saari CS, Vrabel MJ, Horrow J, Chowdhury M, Fontaine JM, Kutalek SP. Percutaneous pacemaker and implantable cardioverter-defibrillator lead extraction in 100 patients with intracardiac vegetations defined by transesophageal echocardiogram. *J Am Coll Cardiol* 2010;**55**:886–894.
  123. Tarakji KG, Chan EJ, Cantillon DJ, Doonan AL, Hu T, Schmitt S, Fraser TG, Kim A, Gordon SM, Wilkoff BL. Cardiac implantable electronic device infections: presentation, management, and patient outcomes. *Heart Rhythm* 2010;**7**:1043–1047.
  124. Braun MU, Rauwolf T, Bock M, Kappert UTZ, Boscheri A, Schnabel A, Strasser RH. Percutaneous lead implantation connected to an external device in stimulation-dependent patients with systemic infection—a prospective and controlled study. *Pacing Clin Electrophysiol* 2006;**29**:875–879.
  125. Kornberger A, Schmid E, Kalender G, Stock UA, Doernberger V, Khalil M, Lisy M. Bridge to recovery or permanent system implantation: an eight-year single-center experience in transvenous semipermanent pacing. *Pacing Clin Electrophysiol* 2013;**36**:1096–1103.
  126. Kawata H, Pretorius V, Phan H, Mulpuru S, Gadiyaram V, Patel J, Steltzner D, Krummen D, Feld G, Birgersdotter-Green U. Utility and safety of temporary pacing using active fixation leads and externalized re-usable permanent pacemakers after lead extraction. *Europace* 2013;**15**:1287–1291.
  127. Pecha S, Aydin MA, Yildirim Y, Sill B, Reiter B, Wilke I, Reichenspurner H, Treede H. Transcutaneous lead implantation connected to an externalized pacemaker in patients with implantable cardiac defibrillator/pacemaker infection and pacemaker dependency. *Europace* 2013;**15**:1205–1209.
  128. Zucchelli G, Bongiorni MG, Di Cori A, Soldati E, Solarino G, Fabiani I, Segreti L, De Lucia R, Viani S, Coluccia G, Paperini L. Cardiac resynchronization therapy after coronary sinus lead extraction: feasibility and mid-term outcome of transvenous reimplantation in a tertiary referral centre. *Europace* 2012;**14**:515–521.
  129. Bongiorni MG, Della Tommasina V, Barletta V, Di Cori A, Rogani S, Viani S, Segreti L, Paperini L, Soldati E, De Lucia R, Zucchelli G. Feasibility and long-term effectiveness of a non-apical Micra pacemaker implantation in a referral centre for lead extraction. *Europace* 2019;**21**:114–120.
  130. Beurskens NEG, Tjong FVY, Dasselaar KJ, Kuijt WJ, Wilde AAM, Knops RE. Leadless pacemaker implantation after explantation of infected conventional pacemaker systems: a viable solution? *Heart Rhythm* 2019;**16**:66–71.
  131. Kypta A, Blessberger H, Kammler J, Lambert T, Lichtenauer M, Brandstaetter W, Gabriel M, Steinwender C. Leadless cardiac pacemaker implantation after lead extraction in patients with severe device infection. *J Cardiovasc Electrophysiol* 2016;**27**:1067–1071.
  132. Viani S, Migliore F, Tola G, Pisanò ECL, Russo AD, Luzzi G, Sartori P, Piro A, Rordorf R, Forleo GB, Rago A, Segreti L, Bertaglia E, Biffi M, Lovecchio M, Valsecchi S, Diemberger I, Bongiorni MG. Use and outcomes of subcutaneous implantable cardioverter-defibrillator (ICD) after transvenous ICD extraction: an analysis of current clinical practice and a comparison with transvenous ICD reimplantation. *Heart Rhythm* 2019;**16**:564–571.
  133. Boersma L, Burke MC, Neuzil P, Lambiase P, Friehling T, Theuns DA, Garcia F, Carter N, Stivland T, Weiss R, Investigators E, Study I. Infection and mortality after implantation of a subcutaneous ICD after transvenous ICD extraction. *Heart Rhythm* 2016;**13**:157–164.
  134. Darouiche R, Mosier M, Voigt J. Antibiotics and antiseptics to prevent infection in cardiac rhythm management device implantation surgery. *Pacing Clin Electrophysiol* 2012;**35**:1348–1360.
  135. Deharo JC, Bongiorni MG, Rozkovec A, Bracke F, Defaye P, Fernandez-Lozano I, Golzio PG, Hansky B, Kennergren C, Manolis AS, Mitkowski P, Platou ES; European Heart Rhythm Association. Pathways for training and accreditation for transvenous lead extraction: a European Heart Rhythm Association position paper. *Europace* 2012;**14**:124–134.
  136. El-Chami MF, Johansen JB, Zaidi A, Faerstrand S, Reynolds D, Garcia-Seara J, Mansourati J, Pasquie J-L, McElderry HT, Roberts PR, Soejima K, Stromberg K, Piccini JP. Leadless pacemaker implant in patients with pre-existing infections: results from the Micra postapproval registry. *J Cardiovasc Electrophysiol* 2019;**30**:569–574.
  137. Reynolds D, Duray GZ, Omar R, Soejima K, Neuzil P, Zhang S, Narasimhan C, Steinwender C, Brugada J, Lloyd M, Roberts PR, Sagi V, Hummel J, Bongiorni MG, Knops RE, Ellis CR, Gornick CC, Bernabei MA, Laager V, Stromberg K, Williams ER, Hudnall JH, Ritter P; Micra Transcatheter Pacing Study Group. A leadless intracardiac transcatheter pacing system. *N Engl J Med* 2016;**374**:533–541.
  138. Brouwer TF, Yilmaz D, Lindeboom R, Buiten MS, Olde Nordkamp LRA, Schalijs MJ, Wilde AA, van Erven L, Knops RE. Long-term clinical outcomes of subcutaneous versus transvenous implantable defibrillator therapy. *J Am Coll Cardiol* 2016;**68**:2047–2055.
  139. Boersma L, Barr C, Knops R, Theuns D, Eckardt L, Neuzil P, Scholten M, Hood M, Kuschyk J, Jones P, Duffy E, Husby M, Stein K, Lambiase PD, Group EI. Implant and midterm outcomes of the subcutaneous implantable cardioverter-defibrillator registry: the EFFORTLESS study. *J Am Coll Cardiol* 2017;**70**:830–841.
  140. Rizwan Sohail M, Henrikson CA, Jo Braid-Forbes M, Forbes KF, Lerner DJ. Increased long-term mortality in patients with cardiovascular implantable electronic device infections. *Pacing Clin Electrophysiol* 2015;**38**:231–239.
  141. Sohail MR, Henrikson CA, Braid-Forbes MJ, Forbes KF, Lerner DJ. Mortality and cost associated with cardiovascular implantable electronic device infections. *Arch Intern Med* 2011;**171**:1821–1828.
  142. Greenspon AJ, Eby EL, Petrilla AA, Sohail MR. Treatment patterns, costs, and mortality among Medicare beneficiaries with CIED infection. *Pacing Clin Electrophysiol* 2018;**41**:495–503.
  143. Maytin M, Jones SO, Epstein LM. Long-term mortality after transvenous lead extraction. *Circ Arrhythm Electrophysiol* 2012;**5**:252–257.
  144. Lee DH, Gracely EJ, Aleem SY, Kutalek SP, Vielmeyer O. Differences of mortality rates between pocket and nonpocket cardiovascular implantable electronic device infections. *Pacing Clin Electrophysiol* 2015;**38**:1456–1463.
  145. Tarakji KG, Wazni OM, Harb S, Hsu A, Saliba W, Wilkoff BL. Risk factors for 1-year mortality among patients with cardiac implantable electronic device infection undergoing transvenous lead extraction: the impact of the infection type and the presence of vegetation on survival. *Europace* 2014;**16**:1490–1495.
  146. Sohail MR, Henrikson CA, Braid-Forbes MJ, Forbes KF, Lerner DJ. Comparison of mortality in women versus men with infections involving cardiovascular implantable electronic device. *Am J Cardiol* 2013;**112**:1403–1409.
  147. Guha A, Maddox WR, Colombo R, Nahman NS Jr, Kintziger KW, Waller JL, Diamond M, Murphy M, Kheda M, Litwin SE, Sorrentino RA. Cardiac implantable electronic device infection in patients with end-stage renal disease. *Heart Rhythm* 2015;**12**:2395–2401.
  148. Deharo JC, Quatre A, Mancini J, Khaïry P, Le Dolley Y, Casalta JP, Peyrouse E, Prevot S, Thuny F, Collart F, Raout D, Habib G, Franceschi F. Long-term outcomes following infection of cardiac implantable electronic devices: a prospective matched cohort study. *Heart* 2012;**98**:724–731.
  149. Rickard J, Tarakji K, Cheng A, Spragg D, Cantillon DJ, Martin DO, Baranowski B, Gordon SM, Tang WH, Kanj M, Wazni O, Wilkoff BL. Survival of patients

- with biventricular devices after device infection, extraction, and reimplantation. *JACC Heart Fail* 2013;**1**:508–513.
150. Armaganjian LV, Toff WD, Nielsen JC, Andersen HR, Connolly SJ, Ellenbogen KA, Healey JS. Are elderly patients at increased risk of complications following pacemaker implantation? A meta-analysis of randomized trials. *Pacing Clin Electrophysiol* 2012;**35**:131–134.
  151. Habib A, Le KY, Baddour LM, Friedman PA, Hayes DL, Lohse CM, Wilson WR, Steckelberg JM, Sohail MR; Mayo Cardiovascular Infections Study Group. Predictors of mortality in patients with cardiovascular implantable electronic device infections. *Am J Cardiol* 2013;**111**:874–879.
  152. Nielsen JC, Gerdes JC, Varma N. Infected cardiac-implantable electronic devices: prevention, diagnosis, and treatment. *Eur Heart J* 2015;**36**:2484–2490.
  153. Voigt A, Shalaby A, Saba S. Continued rise in rates of cardiovascular implantable electronic device infections in the United States: temporal trends and causative insights. *Pacing Clin Electrophysiol* 2010;**33**:414–419.
  154. Afialo J, Alexander KP, Mack MJ, Maurer MS, Green P, Allen LA, Popma JJ, Ferrucci L, Forman DE. Frailty assessment in the cardiovascular care of older adults. *J Am Coll Cardiol* 2014;**63**:747–762.
  155. Green AR, Leff B, Wang Y, Spatz ES, Masoudi FA, Peterson PN, Daugherty SL, Matlock DD. Geriatric conditions in patients undergoing defibrillator implantation for prevention of sudden cardiac death: prevalence and impact on mortality. *Circ Cardiovasc Qual Outcomes* 2016;**9**:23–30.
  156. Kramer DB, Tsai T, Natarajan P, Tewksbury E, Mitchell SL, Trivison TG. Frailty, physical activity, and mobility in patients with cardiac implantable electrical devices. *J Am Heart Assoc* 2017;**6**:e004659.
  157. Farage MA, Miller KW, Elsnor P, Maibach HI. Structural characteristics of the aging skin: a review. *Cutan Ocul Toxicol* 2007;**26**:343–357.
  158. Poole J, Larson L, Olshansky B. *Cardiac Implantable Electronic Device Surgical Implant*. 1st ed. Philadelphia, PA: Elsevier; 2018.
  159. Atallah J, Erickson CC, Cecchin F, Dubin AM, Law IH, Cohen MI, Lapage MJ, Cannon BC, Chun TU, Freedman V, Gierdalski M, Berul CI; Pediatric and Congenital Electrophysiology Study. Multi-institutional study of implantable defibrillator lead performance in children and young adults: results of the Pediatric Lead Extractability and Survival Evaluation (PLEASE) study. *Circulation* 2013;**127**:2393–2402.
  160. Padfield GJ, Steinberg C, Bennett MT, Chakrabarti S, Deyell MW, Bashir J, Krahn AD. Preventing cardiac implantable electronic device infections. *Heart Rhythm* 2015;**12**:2344–2356.
  161. Rohacek M, Weisser M, Kobza R, Schoenenberger AW, Pfyffer GE, Frei R, Erne P, Trampuz A. Bacterial colonization and infection of electrophysiological cardiac devices detected with sonication and swab culture. *Circulation* 2010;**121**:1691–1697.
  162. Poole JE, Gleva MJ, Mela T, Chung MK, Uslan DZ, Borge R, Gottipaty V, Shinn T, Dan D, Feldman LA, Seide H, Winston SA, Gallagher JJ, Langberg JJ, Mitchell K, Holcomb R; for the REPLACE Registry Investigators. Complication rates associated with pacemaker or implantable cardioverter-defibrillator generator replacements and upgrade procedures: results from the REPLACE registry. *Circulation* 2010;**122**:1553–1561.
  163. Fortescue EB, Berul CI, Cecchin F, Walsh EP, Triedman JK, Alexander ME. Patient, procedural, and hardware factors associated with pacemaker lead failures in pediatrics and congenital heart disease. *Heart Rhythm* 2004;**1**:150–159.
  164. Gleva MJ, Wang Y, Curtis JP, Berul CI, Huddleston CB, Poole JE. Complications associated with implantable cardioverter defibrillators in adults with congenital heart disease or left ventricular noncompaction cardiomyopathy (From the NCDR<sup>®</sup> Implantable Cardioverter-Defibrillator Registry). *Am J Cardiol* 2017;**120**:1891–1898.
  165. Berul CI, Van Hare GF, Kertesz NJ, Dubin AM, Cecchin F, Collins KK, Cannon BC, Alexander ME, Triedman JK, Walsh EP, Friedman RA. Results of a multicenter retrospective implantable cardioverter-defibrillator registry of pediatric and congenital heart disease patients. *J Am Coll Cardiol* 2008;**51**:1685–1691.
  166. Vehmeijer JT, Brouwer TF, Limpens J, Knops RE, Bouma BJ, Mulder BJ, de Groot JR. Implantable cardioverter-defibrillators in adults with congenital heart disease: a systematic review and meta-analysis. *Eur Heart J* 2016;**37**:1439–1448.
  167. McCanta AC, Tanel RE, Gralla J, Runciman DM, Collins KK. The fate of nontargeted endocardial leads during the extraction of one or more targeted leads in pediatrics and congenital heart disease. *Pacing Clin Electrophysiol* 2014;**37**:104–108.
  168. Cannon BC, Friedman RA, Fenrich AL, Fraser CD, McKenzie ED, Kertesz NJ. Innovative techniques for placement of implantable cardioverter-defibrillator leads in patients with limited venous access to the heart. *Pacing Clin Electrophysiol* 2006;**29**:181–187.
  169. Konta L, Chubb MH, Bostock J, Rogers J, Rosenthal E. Twenty-seven years experience with transvenous pacemaker implantation in children weighing <10 kg. *Circ Arrhythm Electrophysiol* 2016;**9**:e003422.
  170. Molina JE. Surgical options for endocardial lead placement when upper veins are obstructed or nonusable. *J Interv Card Electrophysiol* 2004;**11**:149–154.
  171. Silveti MS, Drago F. Upgrade of single chamber pacemakers with transvenous leads to dual chamber pacemakers in pediatric and young adult patients. *Pacing Clin Electrophysiol* 2004;**27**:1094–1098.
  172. Suzuki S, Motohashi S, Matsumoto M. Surgical techniques for implanting implantable cardioverter defibrillators in children and infants. *Surg Today* 2014;**44**:1801–1806.
  173. Gillette PC, Edgerton J, Kratz J, Zeigler V. The subpectoral pocket: the preferred implant site for pediatric pacemakers. *Pacing Clin Electrophysiol* 1991;**14**:1089–1092.
  174. D'Souza BA, Epstein AE, Garcia FC, Kim YY, Agarwal SC, Belott PH, Burke MC, Leon AR, Morgan JM, Patton KK, Shah M. Outcomes in patients with congenital heart disease receiving the subcutaneous implantable-cardioverter defibrillator: results from a pooled analysis from the IDE study and the EFFORTLESS S-ICD registry. *JACC Clin Electrophysiol* 2016;**2**:615–622.
  175. Moore JP, Mondésert B, Lloyd MS, Cook SC, Zaidi AN, Pass RH, John AS, Fish FA, Shannon KM, Aboulhosn JA, Khairy P; Alliance for Adult Research in Congenital Cardiology (AARCC). Clinical experience with the subcutaneous implantable cardioverter-defibrillator in adults with congenital heart disease. *Circ Arrhythm Electrophysiol* 2016;**9**:e004338.
  176. Bordachar P, Marquie C, Pospiech T, Pasquie JL, Jalal Z, Haissaguerre M, Thambo JB. Subcutaneous implantable cardioverter defibrillators in children, young adults and patients with congenital heart disease. *Int J Cardiol* 2016;**203**:251–258.
  177. Celiker A, Olgun H, Karagoz T, Ozer S, Ozkutlu S, Alehan D. Midterm experience with implantable cardioverter-defibrillators in children and young adults. *Europace* 2010;**12**:1732–1738.
  178. Ferrero P, Ali H, Barman P, Foresti S, Lupo P, D'Elia E, Cappato R, Stuart AG. Entirely subcutaneous defibrillator and complex congenital heart disease: data on long-term clinical follow-up. *World J Cardiol* 2017;**9**:547–552.
  179. Chang PM, Saxon LA, Doshi RN. The subcutaneous implantable cardioverter defibrillator as part of dual device therapy in complex congenital heart disease. *J Innov Card Rhythm Manag* 2016;**7**:2395–2399.
  180. Aggarwal RK, Connelly DT, Ray SG, Ball J, Charles RG. Early complications of permanent pacemaker implantation: no difference between dual and single chamber systems. *Br Heart J* 1995;**73**:571–575.
  181. Mounsey JP, Griffith MJ, Tynan M, Gould FK, MacDermott AF, Gold RG, Bexton RS. Antibiotic prophylaxis in permanent pacemaker implantation: a prospective randomised trial. *Br Heart J* 1994;**72**:339–343.
  182. Eberhardt F, Bode F, Bonnemeier H, Boguschewski F, Schlei M, Peters W, Wiegand UK. Long term complications in single and dual chamber pacing are influenced by surgical experience and patient morbidity. *Heart* 2005;**91**:500–506.
  183. Wiegand UK, Lejeune D, Boguschewski F, Bonnemeier H, Eberhardt F, Schunkert H, Bode F. Pocket hematoma after pacemaker or implantable cardioverter defibrillator surgery: influence of patient morbidity, operation strategy, and perioperative antiplatelet/anticoagulation therapy. *Chest* 2004;**126**:1177–1186.
  184. Al-Khatib SM, Lucas FL, Jollis JG, Malenka DJ, Wennberg DE. The relation between patients' outcomes and the volume of cardioverter-defibrillator implantation procedures performed by physicians treating Medicare beneficiaries. *J Am Coll Cardiol* 2005;**46**:1536–1540.
  185. Krahn AD, Lee DS, Birnie D, Healey JS, Crystal E, Dorian P, Simpson CS, Khaykin Y, Cameron D, Janmohamed A, Yee R, Austin PC, Chen Z, Hardy J, Tu JV, Ontario ICDDI. Predictors of short-term complications after implantable cardioverter-defibrillator replacement: results from the Ontario ICD Database. *Circ Arrhythm Electrophysiol* 2011;**4**:136–142.
  186. Tobin K, Stewart J, Westveer D and Frumin H. Acute complications of permanent pacemaker implantation: their financial implication and relation to volume and operator experience. *Am J Cardiol* 2000;**85**:774–776, A9.
  187. Kirkfeldt RE, Johansen JB, Nohr EA, Jorgensen OD, Nielsen JC. Complications after cardiac implantable electronic device implantations: an analysis of a complete, nationwide cohort in Denmark. *Eur Heart J* 2014;**35**:1186–1194.
  188. Udo EO, Zuithoff NP, van Hemel NM, de Cock CC, Hendriks T, Doevendans PA, Moons KG. Incidence and predictors of short- and long-term complications in pacemaker therapy: the FOLLOWPACE study. *Heart Rhythm* 2012;**9**:728–735.
  189. Nowak B, Tasche K, Barnewold L, Heller G, Schmidt B, Bordignon S, Chun KR, Furnkranz A, Mehta RH. Association between hospital procedure volume and early complications after pacemaker implantation: results from a large, unselected, contemporary cohort of the German nationwide obligatory external quality assurance programme. *Europace* 2015;**17**:787–793.
  190. Cabell CH, Heidenreich PA, Chu VH, Moore CM, Stryjewski ME, Corey GR, Fowler VG Jr. Increasing rates of cardiac device infections among Medicare beneficiaries: 1990-1999. *Am Heart J* 2004;**147**:582–586.
  191. Sridhar AR, Lavu M, Yarlagadda V, Reddy M, Gunda S, Afzal R, Atkins D, Gopinathanair R, Dawn B, Lakkireddy DR. Cardiac implantable electronic

- device-related infection and extraction trends in the U.S. *Pacing Clin Electrophysiol* 2017;**40**:286–293.
192. Sohail MR, Eby EL, Ryan MP, Gunnarsson C, Wright LA, Greenspon AJ. Incidence, treatment intensity, and incremental annual expenditures for patients experiencing a cardiac implantable electronic device infection: evidence from a large US payer database 1-year post implantation. *Circ Arrhythm Electrophysiol* 2016;**9**:e003929.
  193. Boriani G, Lane DA, Windecker S, Huber K, Kirchhof P, Lip GY. Difficult decision making in the management of patients with atrial fibrillation and acute coronary syndrome or invasive cardiovascular interventions: new recommendations for daily practice. *Europace* 2015;**17**:1319–1322.
  194. Boriani G, Burri H, Mantovani LG, Maniadakis N, Leyva F, Kautzner J, Lubinski A, Braunschweig F, Jung W, Lozano IF, Fattore G. Device therapy and hospital reimbursement practices across European countries: a heterogeneous scenario. *Europace* 2011;**13**(Suppl 2):ii59–ii65.
  195. Boriani G, Elsner C, Diemberger I. The struggle against infections of cardiac implantable electrical devices: the burden of costs requires new personalized solutions. *Europace* 2018;**20**:1877–1879.
  196. Boriani G, Maniadakis N, Auricchio A, Muller-Riemenschneider F, Fattore G, Leyva F, Mantovani L, Siebert M, Willich SN, Vardas P, Kirchhof P. Health technology assessment in interventional electrophysiology and device therapy: a position paper of the European Heart Rhythm Association. *Eur Heart J* 2013;**34**:1869–1874.
  197. Maniadakis N, Vardas P, Mantovani LG, Fattore G, Boriani G. Economic evaluation in cardiology. *Europace* 2011;**13**(Suppl 2):ii3–ii8.
  198. Baddour LM, Wilson WR, Bayer AS, Fowler VG Jr, Tleyjeh IM, Rybak MJ, Barsic B, Lockhart PB, Gewitz MH, Levison ME, Bolger AF, Steckelberg JM, Baltimore RS, Fink AM, O’Gara P, Taubert KA; American Heart Association Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease of the Council on Cardiovascular Disease in the Young, Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and Stroke Council. Infective endocarditis in adults: diagnosis, antimicrobial therapy, and management of complications: a scientific statement for healthcare professionals from the American Heart Association. *Circulation* 2015;**132**:1435–1486.
  199. da Silva KR, Costa R, Crevelari ES, Lacerda MS, de Moraes Albertini CM, Filho MM, Santana JE, Vissoci JR, Pietrobon R, Barros JV. Global clinical registries: pacemaker registry design and implementation for global and local integration—methodology and case study. *PLoS One* 2013;**8**:e71090.
  200. Weintraub WS, Karlsberg RP, Tcheng JE, Boris JR, Buxton AE, Dove JT, Fonarow GC, Goldberg LR, Heidenreich P, Hendel RC, Jacobs AK, Lewis W, Mirro MJ, Shahian DM, Hendel RC, Bozkurt B, Jacobs JP, Peterson PN, Roger VL, Smith EE, Tcheng JE, Wang T; American College of Cardiology Foundation; American Heart Association Task Force on Clinical Data Standards. ACCF/AHA 2011 key data elements and definitions of a base cardiovascular vocabulary for electronic health records: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Clinical Data Standards. *Circulation* 2011;**124**:103–123.
  201. Gliklich RE, Dreyer NA, Leavy MB. Data Collection and Quality Assurance in Registries for Evaluating Patient Outcomes: A User’s Guide [Internet]. 2014; Report No. 13(14)-EHC111.