Supplementary Table 1 Characteristics of patients without final infective endocarditis diagnosis

No infective endocarditis (n=1031)

	endocardii	tis (n=1031)
Final diagnosis		
Other type of infection, n (%)	855	(83)
Stroke, n (%)	25	(2)
Malignancy-related fever, n (%)	21	(2)
Fever of unknown origin, n (%)	36	(4)
Autoimmune disease, n (%)	23	(2)
Non-infective endocarditis, n (%)	12	(1)
Other diagnoses, n (%)	59	(6)

Supplementary Table 2. Misclassification of non-infective endocarditis cases as definite infective endocarditis by clinical criteria (by any version of Duke criteria)

	Microbiologic criterion (positive bcs)	Imaging criterion	Predisposition	Fever	Vascular phenomena	Immunologic phenomena	Valve surgery	Pathological exclusion criterion	Final diagnosis
1	Bacteremia S. aureus (2 bcs)	Significant new valvular regurgitation		Y			N	N	Catheter-related bacteremia
2	Bacteremia S. mitis (2 bcs)	Significant new valvular regurgitation	Moderate valve stenosis	Y			Y	Y	Oral abscess
3	Bacteremia <i>C.</i> hominis (1 bcs)	Significant new valvular regurgitation	Prosthetic valve, prior IE	Y			N	N	Auto-immune diseases (translocation)
4	Bacteremia S. anginosus (2 bcs)		Prosthetic valve	Y	Pulmonary septic emboli	Roth's spot	N	N	Catheter-related bacteremia with septic thrombophlebitis
5		Vegetation, significant new valvular regurgitation	Prosthetic valve	Y	Cerebral emboli		Y	Y	Marantic IE
6	Bacteremia S. aureus (2 bcs)		IV drug use, prosthetic valve	Y	Peripheral mycotic aneurysm		N	N	Contiguous mycotic aneurysm (IV drug use)
7		Significant new valvular regurgitation	Prosthetic valve	Y	Cerebral emboli		Y	Y	Marantic IE
8		Significant new valvular regurgitation		Y	Cerebral emboli	Positive rheumatoid factor	N	N	Pneumonia
9	Bacteremia <i>S.</i> pneumoniae (2 bcs)	Significant new valvular regurgitation	Bicuspid aortic valve	Y	Cerebral emboli		N	N	Pneumonia
10	B. henselae IgG titer ≥1:800	Significant new valvular regurgitation		N			N	N	Paradoxal reaction to tuberculosis treatment

11	Bacteremia (nosocomial) <i>E. faecalis</i> (2 bcs)	Abnormal metabolic activity (¹⁸ F-FDG PET/CT) of native valve		N			N	N	Catheter-related bacteremia
12	Bacteremia <i>S. epidermidis</i> (2 bcs)		Moderate valve regurgitation, CIED	N	Pulmonary septic emboli		N	N	Catheter-related bacteremia with septic thrombophlebitis
13	Bacteremia <i>L.</i> garvieae (3 bcs)		Prosthetic valve	Y	Cerebral emboli		N	N	Spondylodiscitis (cerebral emboli due to atrial fibrillation)
14	Bacteremia <i>S. epidermidis</i> (3 bcs)		Prior IE	Y		Roth's spot	N	N	Catheter-related bacteremia with septic thrombophlebitis
15	Bacteremia S. aureus (2 bcs)		IV drug use	Y	Pulmonary septic emboli		N	N	Cellulitis with septic thrombophlebitis
16	Bacteremia S. aureus (2 bcs)		CIED	Y	Pulmonary septic emboli		N	N	Catheter-related bacteremia with septic thrombophlebitis
17	Candidemia C. tropicalis (3 bcs)			Y	Ocular emboli	Roth's spot	N	N	Catheter-related urinary tract infection

¹⁸F-FDG PET/CT: ¹⁸F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography; bcs: blood culture set; CIED: cardiac implantable electronic device; IE: infective endocarditis; N: no; Y: yes

Supplementary table 3. Misclassification of infective endocarditis cases as rejected by clinical criteria (by any version of Duke criteria)

<u></u>	Microbiologic criterion (positive bcs)	Imaging criterion		Fever	Vascular phenomena	Immunologic phenomena	Valve surgery	Surgical criterion	Pathological criterion	Other information
1	Bacteremia S. epidermidis (2 bcs)	Abnormal metabolic activity (¹⁸ F-FDG PET/CT) of native valve	Prior IE (S.epidermidis)	N			N	N	N	
2	On antibiotic treatment	CIED-lead lesion (degenerative)	CIED	N			N	N	N	Positive CIED- lead culture
3	On antibiotic treatment	CIED-lead lesion (degenerative)	CIED	N			N	N	N	Positive CIED- lead culture
4	On antibiotic treatment	CIED-lead lesion (degenerative)	CIED	N			N	N	N	Positive CIED- lead culture
5	On antibiotic treatment	CIED-lead lesion (degenerative)	CIED	N			N	N	N	Positive CIED- lead culture
6	Bacteremia S. epidermidis (2 bcs)	Abnormal metabolic activity (18F-FDG PET/CT) of CIED cable	CIED	Y			N	N	N	Positive CIED- lead culture
7	Bacteremia S. agalactiae (2 bcs)	Abnormal metabolic activity (¹⁸ F-FDG PET/CT) of native valve		Y			N	N	N	
8	Bacteremia B. pumilus (2 bcs)	Abnormal metabolic activity (¹⁸ F-FDG PET/CT) of TAVI	TAVI	Y			N	N	N	
9	Bacteremia (persistent) <i>S. epidermidis</i> (2 bcs)	*	TAVI	Y			N	N	N	
10	Bacteremia (persistent) S. epidermidis (2		TAVI	Y			N	N	N	

	bcs)							
11	Bacteremia S. agalactiae (2	Small mobile element	TAVI	Y	N	N	N	
	bcs)	(degenerative)						
12	Bacteremia		Prosthetic valve,	Y	Y	Y	Y	Positive CIED-
	(persistent) S.		CIED, prior IE (S.					lead culture
	epidermidis (2 bcs)		epidermidis)					
13	Bacteremia <i>S</i> .	Small mobile		Y	N	N	N	
10	dysgalactiae (2	element		-	11	11	11	
	bcs)	(degenerative)						
14	Bacteremia S.	Significant new		Y	N	N	N	
	agalactiae (3	valvular						
15	bcs) On antibiotic	regurgitation	Bicuspid aortic	N	Y	Y	Y	
13	treatment		valve	11	1	1	1	
16	Bacteremia C.	Small mobile		N	N	N	N	
	fetus (2	element						
	bcs)	(degenerative), abnormal						
		metabolic activity						
		(18F-FDG						
		PET/CT) of native						
		valve						
17	On antibiotic	CIED-cable lesion	Prosthetic valve, CIED	N	N	N	N	Positive CIED-
18	treatment On antibiotic	(degenerative) CIED-lead	CIED	N	N	N	N	lead culture
10	treatment	vegetation	CILD	1	11	11	11	
19	On antibiotic	CIED-lead	CIED	N	N	N	N	Positive CIED-
	treatment	vegetation, valve						lead culture
20	Bacteremia S.	vegetation	CIED	N	N	N	N	Positive CIED-
20	aureus (2		CIED	1N	IN	1N	1N	lead culture
	bcs)							ioud cuitare
21	Bacteremia S.	CIED-lead	CIED	N	N	N	N	Positive CIED-
	epidermidis (2	vegetation						lead culture
	bcs)							

22	Bacteremia (community-acquired) <i>E</i> .	CIED-lead vegetation, abnormal	CIED	N	N	N	N	Positive CIED- lead culture
	faecium (1 bcs)	metabolic activity (¹⁸ F-FDG PET/CT) of CIED cable						
23	On antibiotic treatment	Significant new valvular regurgitation		Y	Y	Y	Y	
24	On antibiotic treatment	CIED-lead vegetation	CIED	N	N	N	N	Positive CIED- lead culture
25	On antibiotic treatment	Valve vegetation	Prior IE	N	N	N	N	
26	Bacteremia (community-acquired) <i>E. faecalis</i> (2 bcs)	Significant new valvular regurgitation	Severe valve stenosis	N	N	N	N	
27	Bacteremia S. lugdunensis (2 bcs)	Abnormal metabolic activity (¹⁸ F-FDG PET/CT) of prosthetic valve	Prosthetic valve	Y	Y	Y	N	
28	Candidemia <i>C.</i> glabrata (3 bcs)	Abnormal metabolic activity (18F-FDG PET/CT) of prosthetic valve	Prosthetic valve	Y	N	N	N	
29	B. henselae IgG titer ≥1:800	Abnormal metabolic activity (18F-FDG PET/CT) of prosthetic valve	Prosthetic valve	Y	N	N	N	
30	Bacteremia P. aeruginosa (2 bcs)	Thickening valve leaflet, abnormal metabolic activity (18F-FDG	Moderate valve stenosis	Y	N	N	N	

		PET/CT) of native							
		valve							
31	On antibiotic	Abnormal	Prosthetic valve	Y		N	N	N	
	treatment	metabolic activity							
		(¹⁸ F-FDG							
		PET/CT) of							
		prosthetic valve							
32	On antibiotic	Small mobile		Y	Arterial	N	N	N	
32	treatment	element		1	emboli,	11	11	11	
	treatment				cerebral				
		(degenerative), abnormal			emboli				
					embon				
		metabolic activity							
		(¹⁸ F-FDG							
		PET/CT) of native							
		valve, abscess on							
		cardiac CT							
33	On antibiotic		Prosthetic valve	N		Y	Y	N	
	treatment								
34	Bacteremia	Small mobile	Prosthetic valve	Y		N	N	N	
	(persistent) S.	element							
	epidermidis (2	(degenerative)							
	bcs)								
35	Bacteremia	Thickening valve	TAVI, CIED	Y		N	N	N	
	(nosocomial) E.	leaflet							
	faecalis (2								
	bcs)								
36	Bacteremia S.	Abnormal		Y	Pulmonary	N	N	N	
	enteritidis (2	metabolic activity			septic				
	bcs)	(¹⁸ F-FDG			emboli				
	,	PET/CT) of native							
		valve							
37	On antibiotic		Prior IE	Y	Cerebral	N	N	N	
-	treatment				emboli				
38	Bacteremia <i>S</i> .		Severe valve	Y	Pulmonary	N	N	N	
-	epidermidis (2		regurgitation	-	septic	-,	- 1	-,	
	bcs)		04-0-44		emboli,				
	223)				mycotic				
					aneurysm				
					ancary on				

39	Bacteremia S. pneumoniae (2 bcs)	CIED-lead lesion (degenerative)	CIED	Y		N	N	N	Multiple septic arthritis
40	On antibiotic treatment	Thickening valve leaflet		Y		N	N	N	Multiple septic arthritis
41	Bacteremia <i>S. epidermidis</i> (2 bcs)	Thickening valve leaflet		N	Cerebral emboli	N	N	N	
42	Bacteremia S. agalactiae (2 bcs)		Bicuspid aortic valve	Y		Y	Y	Y	
43	Bacteremia (community-acquired) <i>E. faecalis</i> (2 bcs)	Small mobile element (degenerative)	Prosthetic valve	Y		N	N	N	
44	On antibiotic treatment	Thickening valve leaflet		Y	Mycotic aneurysm	N	N	N	Septic arthritis
45	Bacteremia S. aureus (1 bcs)	Thickening valve leaflet		Y		N	N	N	
46	Bacteremia (community-acquired) <i>E. faecalis</i> (1 bcs)	Thickening valve leaflet		N		N	N	N	Septic arthritis
47	Bacteremia A. defectiva (2 bcs)	Thickening valve leaflet	Prolapsus of mitral valve	Y		Y	Y	Y	
48	Bacteremia S. mitis (2 bcs)	Thickening valve leaflet	Severe valve regurgitation	N		N	N	N	
49	On antibiotics	Small mobile element (degenerative)	Prosthetic valve, CIED	N		N	N	N	
50	Bacteremia <i>S. epidermidis</i> (3 bcs)	Small mobile element (degenerative)		N		N	N	N	

51	Bacteremia A.	Valve vegetation		Y		N	N	N
01	defectiva (2	. arve vegetation		•		11	21	- 1
52	bcs) On antibiotics	Abnormal	CIED	N		N	N	N
32	on antibiotics	metabolic activity	CILID	14		11	11	14
		(¹⁸ F-FDG						
		PET/CT) of CIED-						
		lead						
53	Bacteremia P.	Abnormal	CIED	Y		N	N	N
	aeruginosa (2	metabolic activity						
	bcs)	(¹⁸ F-FDG PET/CT) of CIED-						
		lead						
54	Bacteremia S.	Small mobile	Prosthetic valve,	Y		N	N	N
٠.	agalactiae (1	element	CIED	-		-,	- '	- '
	bcs)	(degenerative)						
55	Bacteremia	Abnormal	CIED	N		N	N	N
	(community-	metabolic activity						
	acquired) E.	(18F-FDG						
	faecium (3 bcs)	PET/CT) of CIED-lead						
56	Bacteremia S.	Small mobile		Y	Pulmonary	N	N	N
30	epidermidis (2	element		1	septic	14	11	14
	bcs)	(degenerative)			emboli			
57	On antibiotics	Small mobile	Severe valve	N		Y	Y	Y
		element	regurgitation					
		(degenerative)						
58	Bacteremia S.	Small mobile	Severe valve	N		N	N	N
	aureus (2	element	regurgitation					
50	bcs) On antibiotics	(degenerative) Abnormal	Dwaathatia valve	Y		N	N	N
59	On antibiotics	metabolic activity	Prosthetic valve, CIED	ĭ		1N	IN	IN
		(18F-FDG	CIED					
		PET/CT) of						
		prosthetic valve						
60	On antibiotics	Abnormal	Prosthetic valve,	N		N	N	N
		metabolic activity	CIED					
		(¹⁸ F-FDG						

		PET/CT) of							
		prosthetic valve							
61	On antibiotics	Abnormal	Prosthetic valve,	N	Cerebral	N	N	N	
		metabolic activity	CIED		emboli,				
		(¹⁸ F-FDG			renal				
		PET/CT) of			emboli				
		prosthetic valve							
62	Bacteremia	Abnormal	Prosthetic valve,	Y		N	N	N	
	Gemella spp. (3	metabolic activity	CIED						
	bcs)	(¹⁸ F-FDG							
	,	PET/CT) of							
		prosthetic valve							
63	Bacteremia S.	CIED-lead lesion	CIED	N		N	N	N	
-	aureus (2	(degenerative)							
	bcs)	()							
64	On antibiotics	CIED-lead lesion	Prior IE, CIED	N		N	N	N	
		(degenerative)	- , -						
65	Bacteremia S.	CIED-lead lesion	Prior IE, CIED	N		N	N	N	
	aureus (2	(degenerative)	,						
	bcs)	(3.18. 3.3.)							
66	On antibiotics	Valve vegetation	Prior IE, CIED	N		N	N	N	
67	On antibiotics	CIED-lead	CIED	N		N	N	N	
		vegetation							
68	On antibiotics	CIED-lead	Prior IE, CIED	N		N	N	N	
		vegetation	- , -						
69	On antibiotics	Valve vegetation		N		N	N	N	
70	On antibiotics	Small mobile	Prosthetic valve,	Y		Y	Y	N	
		element	CIED	-		-	-	·	
		(degenerative)							
71	Bacteremia	Small mobile	Prior IE, CIED	Y		N	N	N	
	(community-	element	,	-		-,	= -		
	acquired) E.	(degenerative)							
	faecalis (3	(======================================							
	bcs)								
72	Bacteremia <i>S</i> .	CIED-lead lesion	CIED	Y		N	N	N	
. –	epidermidis (3	(degenerative)		-		- '	-,	- 1	
	bcs)	(acgonorum vo)							
	000)								

73	Bacteremia S. lugdunensis (3 bcs)	Valve vegetation, abscess	TAVI	N	Y	Y	N
74	Bacteremia S.	CIED-lead vegetation	CIED	N	N	N	N

¹⁸F-FDG PET/CT: ¹⁸F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography; bcs: blood culture set; CIED: cardiac implantable electronic device; IE: infective endocarditis; N: no; TAVI: Transcatheter aortic valve implantation; Y: yes

Supplementary Figure 1. Classifications of episodes by different versions of Duke criteria based on **A**) clinical criteria, **B**) clinical criteria and implementation of the pathological confirmation and rejection criteria and **C**) final infective endocarditis diagnosis.





