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Expert consensus recommendations for the provision of infective endocarditis services: updated guidance from the Joint British Societies

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ABSTRACT

Infective endocarditis (IE) remains a difficult condition to diagnose and treat and is an infection of high consequence for patients, causing long hospital stays, life-changing complications and high mortality. A new multidisciplinary, multiprofessional, British Society for Antimicrobial Chemotherapy (BSAC)-ledWorking Party was convened to undertake a focused systematical review of the literature and to update the previous BSAC guidelines relating delivery of services for patients with IE. A scoping exercise identified new questions concerning optimal delivery of care, and the systematic review identified 16 231 papers of which 20 met the inclusion criteria. Recommendations relating to endocarditis teams, infrastructure and support, endocarditis referral processes, patient follow-up and patient information, and governance are made as well as research recommendations. This is a report of a joint Working Party of the BSAC, British Cardiovascular Society, British Heart Valve Society, British Society of Echocardiography, Society of Cardiothoracic Surgeons of Great Britain and Ireland, British Congenital Cardiac Association and British Infection Association.

INTRODUCTION

In 2012, the Endocarditis Working Party of the British Society for Antimicrobial Chemotherapy (BSAC) published updated guidelines for the treatment of endocarditis.[1] Given the significant progress in the field, a new multidisciplinary and multiprofessional BSAC Working Party was convened to systematically review the literature and update the previous guideline where appropriate. This statement includes native valve endocarditis (NVE) and prosthetic valve endocarditis (PVE). For the purposes of this guideline 'PVE' includes prosthetic valves of all types, annuloplasty rings, intracardiac patches, aortic root grafts and patches, and shunts. There is some overlap with management of implantable cardiac electronic device infections, but many issues have been previously addressed elsewhere.[2]

Infective endocarditis (IE) remains a difficult condition to diagnose with a high mortality. Patients with IE can present with a wide variety of symptoms, signs and complications and are consequently managed by teams from a wide variety of specialties. In the UK, patients with IE may present acutely to district general hospitals or to a heart centre (hospital with a cardiac surgical unit). Only patients living in the immediate catchment of a heart centre are likely be admitted directly to a heart centre. Detailed data on place of presentation are lacking, but a recent study from a heart centre in London found the vast majority of patients were transferred from district general hospitals.[3] Clinicians with primary responsibility for a patient with IE may have relatively little experience of management of the condition, regardless of whether the patient is based in a heart centre or district general hospital. There are consultant cardiologists and microbiologists working in most district general hospitals in the UK. In this update, the Working Party initially aimed to provide recommendations concerning service provision for patients with suspected or confirmed IE to promote a standardised approach to this important clinical condition, improve networking and patient outcomes. The need for this statement and specific recommendations comes from opinion leaders and colleagues working in the UK National Health Service (NHS) with the specific challenges found in the NHS. There are clear differences in the epidemiology of IE between continents and countries.[4] While this statement is intended for the NHS, the findings of the literature review and UK approach are likely to be of interest to an international audience.

Updates on antibiotic treatment and imaging in IE will be covered in separate documents. Antibiotic prophylaxis against IE is covered by National Institute for Health and Care Excellence guideline CG64.

METHODS

The starting point for this review was the previous 2012 guideline, and we sought evidence that warranted a change from previous recommendations.[1] The Working Party was recruited from the BSAC membership and specialist cardiology societies that might wish to be involved in the preparation of the guideline, each society nominating a participant following approval from their respective governance structures. Other members were invited to ensure diverse expert and non-expert representation, including infection specialists, cardiologists, cardiac surgeons, pharmacists, laboratory scientists, and a patient and public representative. The joint Working Party comprised members of the BSAC,

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the British Cardiovascular Society, the British Heart Valve Society, the British Society of Echocardiography, the Society of Cardiothoracic Surgeons of Great Britain and Ireland, and the British Infection Association. The British Congenital Cardiac Association joined later in the processes and contributed to the final guideline. During a face-to-face meeting, an initial scoping exercise was undertaken by Working Party members to identify key clinical questions concerning the delivery of specialist IE services to patients in the UK NHS, followed by round-table discussion to determine and prioritise principal guideline topics. A systematic review of the literature was undertaken (see online supplemental file for search strategy and methods for screening and selection of papers for inclusion), followed by development of initial recommendations from the literature review and identification of important areas where published data were lacking. Draft recommendations were then proposed to the wider Working Party and iterated until consensus was achieved. As per previous guidelines,[1] evidence levels to support recommendations were graded as follows: A, based on high-quality evidence from systematic reviews of randomised controlled trials; B, based on observational studies; and C, based on expert consensus. After consensus was reached within the Working Party, the guideline was circulated to stakeholder organisations, as well as the Department of Health Advisory Committee for Antimicrobial Prescribing, Resistance and Healthcare Associated Infections, for comment.Each comment was addressed by the Working Party and the guideline was amended accordingly. Once recommendations had been agreed, an audit tool was developed, based on the recommendations.

RESULTS

The scoping exercise for this guideline revision identified new questions concerning optimal delivery of care for patients with IE. The first questions were (1) how should IE services be delivered? (2) what outpatient follow-up should be provided? and (3) what information should be given to patients? After excluding duplicates, 16 231 papers relating to IE were identified, of which 20 were related to delivery of IE services and met the inclusion criteria. The findings of these papers were categorised into broad themes: endocarditis teams, infrastructure and support, referral processes, patient follow-up and information, and governance. Eight studies involved adults only and 12 did not state age inclusion or exclusion criteria. No study explicitly included children. The audit tool is shown in table 1. Results of the risk of bias assessment are shown in online supplemental file 2.

RECOMMENDATIONS

Endocarditis teams

Recommendation 4.1.1

All hospitals involved in the care of patients with confirmed or suspected IE should have an IE team. (C)

Recommendation 4.1.2

The IE team should include as a minimum, an infection specialist and a cardiologist who is an accredited specialist in echocardiography (or a cardiologist and an additional accredited specialist in echocardiography who can be a cardiologist or clinical physiologist/scientist). (C)

Recommendation 4.1.3

At heart centres (hospitals with cardiac surgical units), there should also be access to cardiac surgeons and cardiologists with

Table 1 Audit tool to assess compliance with current infective endocarditis service delivery guidelines

Audit tool	Compliant
4.1 Endocarditis teams	
Hospital is involved in the care of patients with confirmed or suspected IE and has an IE team.	y/n/na
IE team includes an infection specialist.	y/n
IE team includes a cardiologist.	y/n
IE team includes an accredited specialist in echocardiography.	y/n/na
At heart centres, the IE team includes a cardiac surgeon.	y/n
At heart centres, the IE team includes a cardiologist with expertise in adult congenital heart disease.	y/n/na
At heart centres, the IE team includes cardiologists with expertise in the removal of infected implantable cardiac electronic devices.	y/n
Local guidelines for the diagnosis, investigation, and the empirical and directed antibiotic therapy of suspected/confirmed IE	y/n
Weekly IE team review of patients with confirmed or suspected IE (MDT meeting and/or bedside patient review, over and above daily clinical review)	y/n
4.2 Endocarditis service infrastructure and support	
IE team in referring centres can transfer patients to a heart centre 24 hours a day 7 days a week	y/n/na
Operating schedules allow for urgent or emergency surgery in patients with IE	y/n/na
IE team at the heart centre has access to specialist advice: ► Spinal surgery. ► Neurology. ► Neurosurgery. ► Renal medicine. ► Radiology (with specialist interest in cardiac imaging). ► Antimicrobial pharmacist.	y/n y/n y/n y/n y/n y/n
IE team has access to on-site ► Transthoracic echocardiography. ► Transoesophageal echocardiography. IE team has timely access (within a week) to ► MRI. ► CT scanning. ► FDG-PET/CT scanning.	y/n y/n y/n y/n y/n y/n
Substance misuse teams are available to support people who inject drugs and have IE	y/n
4.3 Endocarditis referral processes	
All patients with IE at a referring hospital discussed with the IE team at a heart centre to allow decisions regarding treatment and transfer	% compliance/na
Cardiac imaging from all patients included in discussions with IE team at heart centre	% compliance/na
All patients with IE at referring hospitals with 'red flags' (box 2) transferred to a heart centre	% compliance/na
Clear point of contact for the IE team (including a dedicated phone line or email address)	y/n
System of alerts based on clinical, microbiological or echocardiographic findings that trigger referral to the IE team	y/n
Communication system for referral of new patients to/between IE teams in place	y/n
Patients with IE transferred between hospitals accompanied by records detailing their	
Clinical presentation	% compliance
Medical/cardiac history	% compliance
Medications	% compliance
Allergies	% compliance
Microbiological findings	% compliance
Imaging findings	% compliance

Continued

Table 1 Continued

Audit tool	Compliant
Details of all recent antibiotic therapy (including start/stop dates, doses, frequency and route of administration)	% compliance
Vascular access device(s) details (presence and insertion date)	% compliance
4.4 Patient follow-up and patient information	
All patients being treated for IE offered written information about the condition.	% compliance
All patients who are discharged following treatment for IE advised of the risk of relapse and recurrence, and how to recognise the symptoms of IE.	% compliance
All patients advised to inform their GP that they have had IE and discuss the need for blood cultures if they have a persistent non-specific feverish illness.	% compliance
All patients with IE offered follow-up in a valve or general cardiology clinic.	% compliance

GP, general practitioner; IE, infective endocarditis; n, no; na, not applicable; y, yes.

expertise in the removal of infected implantable cardiac electronic devices. (C)

Recommendation 4.1.4
At heart centres, where patients with adult congenital heart disease (ACHD) are managed, there should also be access to a cardiologist with ACHD expertise. (C)

Recommendation 4.1.5
The IE team should have access to paediatric infection specialists and paediatric cardiologists (unless there is a paediatric IE team). (C)

Recommendation 4.1.6
Local guidelines should be in place to guide diagnosis, investigation, and the empirical and directed antibiotic therapy of suspected/confirmed IE. (B)

Recommendation 4.1.7
In addition to routine daily clinical care, there should be regular (at least weekly) IE team review of patients with confirmed or suspected IE (in the form of a multidisciplinary team (MDT) meeting and/or bedside patient review). Additional ad hoc MDT meetings may be needed to manage emergencies (C)

Recommendation 4.1.8
All IE teams should have access to advice from an antimicrobial or infection specialist pharmacist. (C)

Infrastructure and support

Recommendation 4.2.1
Hospitals managing patients with confirmed or suspected IE should have rapid access to cardiac surgical services, that is, the ability to transfer patients to a heart centre 24 hours a day, 7 days a week—these heart centres should provide same-day (within 24 hours) surgery if needed. (C)

Recommendation 4.2.2
Operating schedules should allow for emergency (within 24 hours) or urgent (within 2 days) surgery in patients with IE. (C)

Recommendation 4.2.3
Surgery/interventions for ACHD-related IE should be performed in ACHD level 1 units—as per National Health Service England(NHSE) National Standards—unless agreed otherwise by the ACHD MDT. (C)

Recommendation 4.2.4
Heart centres should have access to advice from specialists in the following areas: spinal surgery, neurology, neurosurgery, renal medicine, radiology (with specialist interest in cardiac imaging) and antimicrobial pharmacy. (C)

Recommendation 4.2.5
All hospitals managing patients with suspected or confirmed IE should have on site access to transthoracic and transoesophageal echocardiography. (C)

Recommendation 4.2.6
All IE teams should have timely (within 1 week) access to MRI, CT scanning, and fluorodeoxyglucose positron emission tomography (FDG-PET)/CT scanning [C]

Recommendation 4.2.7
Substance misuse teams should be available to support people who inject drugs (PWID) and have IE. (C)

Recommendation 4.2.8
IE teams should have administrative support to help with documentation of referrals/MDT outcomes and MDT organisation. (C)

Referral processes

Recommendation 4.3.1
All patients with IE presenting to referring hospitals should be discussed with the IE team at the heart centre to allow decisions regarding clinical management and inter-hospital transfer. Discussions should involve a clinician responsible for the patient. (C)

Recommendation 4.3.2
Results of relevant imaging should be shared with the heart centre and reviewed as part of clinical decision making. (C)

Recommendation 4.3.3
All patients with IE managed at referring hospitals who have (or develop) IE 'red flags' should be transferred urgently to a heart centre. This transfer should be immediate if the threat is high (eg, heart failure) or within 2 days if the threat is moderate (eg, *Staphylococcus aureus* infection on a mechanical valve with no dysfunction). (C)

Recommendation 4.3.4
There should be a clear point of contact at each hospital for IE teams to communicate about patients with IE/suspected IE, for example, a dedicated phone line or email address (the latter requiring regular review and response). (C)

Recommendation 4.3.5
There should be a system of alerts in each hospital (based on clinical, microbiological or echocardiographic findings) that triggers referral to the IE team. (B)

Recommendation 4.3.6
An auditable electronic communication system should be in place for the referral of new patients to (and between) IE teams. (C)

Recommendation 4.3.7
Patients with IE who are transferred between hospitals should be accompanied by a standardised form detailing their clinical presentation, medical/cardiac history, medications, allergies, presence of vascular access devices, biochemistry, microbiology (eg, blood culture and susceptibility results) and imaging results, and all recent antibiotic therapy (including start/stop dates, doses, frequency and route of administration). (C)

Patient follow-up and information

Recommendation 4.4.1
Patients being treated for IE should be offered written information about IE. (C)

Recommendation 4.4.2
Patients who are discharged following treatment for an episode of IE should be advised of the risk of relapse and recurrence, how these can be reduced and how to recognise the symptoms of IE. (C)

Recommendation 4.4.3
In addition to usual discharge letters, patients with IE should be advised to inform their general practitioner if they have a persistent non-specific feverish illness, in order to trigger appropriate collection of blood cultures and onward referral. (C)

Recommendation 4.4.4
All patients with IE should be offered follow-up in a valve or general cardiology clinic; patients with ACHD should be followed up in ACHD services. (C)

Governance

Recommendation 4.5.1
Endocarditis teams should have a regular (eg, yearly) review of quality (patient outcomes). (C)

Recommendation 4.5.2
Cases of healthcare-associated endocarditis should be investigated by root cause analysis and linked to existing systems for organisational learning and patient safety. (C)

EVIDENCE REVIEW AND DISCUSSION

IE MDT meeting

Three studies evaluated the impact of introducing an IE MDT meeting using a before-and-after design; all were single centre and at moderate or severe risk of bias, reflecting the challenges of adequately controlling such evaluations.[5–7] A further five before-and-after studies (also at serious risk of bias) used multivariable logistic regression, propensity score matching and/or Cox proportional hazard modelling to attempt to account for confounding variables in assessing the effect of an IE MDT on outcomes.[8–12] In multivariable analyses, MDT assessment of NVE and PVE was associated with significantly reduced 3-year mortality (NVE: OR 0.71, 95% CI 0.08 to 0.91; and PVE: OR 0.55, 95% CI 0.22 to 0.98)[8 10] and reduced in-hospital mortality[12] and had no effect on 30-day mortality.[11] Three single-centre cohort studies, with serious/critical risk of bias, used multivariable analysis to assess the effect of an MDT on outcomes.[11 13 14] One study described a cohort of patients managed by an IE MDT but did not evaluate the service.[15] IE MDT meetings occurred ad hoc,[11] weekly/biweekly and discussed patients remotely (using video conferencing at one centre).[15] Details of the format, structure and mechanisms for implementing and documenting decisions were generally not included, but one study described creation of an information sheet with clinical, microbiological and imaging data for patients with suspected IE in their computerised record, which was then presented at the MDT by the treating physician.[15] IE MDTs usually occurred weekly and included infection specialists (microbiology or infectious disease (ID) consultants), cardiologists and cardiac surgeons, and one team also included an IE specialist nurse coordinator.[5–7 15] In the before-and-after studies, introduction of IE MDT meetings was associated with significant reduction in the duration of antibiotic therapy,[6] inpatient stay,[6 7] number of antibiotics prescribed,[5] time to targeted antibiotic therapy,[7] time to surgery,[6] time to first transthoracic[7 11] and transoesophageal echocardiogram,[11] in-hospital/30-day mortality,[5 9 11 16] higher rates of removal of implantable cardiac electronic devices,[11] and the incidence of cardiac and extracardiac complications (eg, reduced postoperative stroke and less postoperative haemodialysis).[5 9] One study found an increase in the rate of blood culture positivity after introduction of the MDT,[5] while others found no difference,[6 7] and one analysis showed an increase in the duration of inpatient stay.[5] One cohort study found a significant effect of MDT review on mortality using univariate analysis (that did not persist on multivariable analysis),[13] and another reported reduced complications, mortality and improved antimicrobial stewardship following introduction of an IE team.[5] Finally, the vast majority of respondents in a survey study of medical and surgical specialities agreed that an IE MDT improved diagnostic evaluation, reduced management errors, increased access to surgery and reduced in-hospital mortality.[17]

One study used a before-and-after design to investigate the impact of a regional IE service involving a telephone consultation service for referring hospitals, criteria for referral and meetings to raise awareness of IE.[9] Although there were methodological issues with this study, time between the onset of symptoms to referral or to surgery, and rates of both preoperative stroke and congestive heart failure were significantly lower in the period following introduction of the service.[9]

We agreed that individuals regularly involved in the care of patients with IE build up valuable clinical experience which impacts positively on patient care, although we found no direct evidence to support this view. There is evidence of clinical experience improving outcomes in other areas. Conversely, inexperience is potentially detrimental to care. Suboptimal care is far more likely to happen when an inexperienced clinician works in isolation to manage a complex clinical problem, and it is this scenario we aim to avoid. There is wide international consensus that MDTs are the right way to deliver care, that is, the best way to ensure patients are appropriately assessed, investigated, managed and referred. A guidance document for the format of cardiac MDTs has been recently published.[18]

Bedside patient review

One IE team reviewed patients on the wards two times a week with the purpose of establishing or excluding the diagnosis

Box 1 Functions of the multidisciplinary IE team

All hospitals.

Diagnosis.
⇒ Use a system of alerts to allow notification of possible IE cases from microbiology and echocardiography laboratories.
⇒ Receive requests for review of all patients admitted with possible IE.
⇒ Confirm or reject diagnosis of IE (applying Duke criteria[26] as appropriate) to reach a working diagnosis.
⇒ Investigate for extracardiac secondary infections.

Antibiotic treatment.
⇒ Formulate an antimicrobial management plan, including antimicrobial agents, dose, frequency, route of administration and duration of therapy (including therapeutic drug monitoring).
⇒ Monitor for adverse drug reactions and modify therapy as required.
⇒ Determine suitability for outpatient parenteral antibiotic therapy.

Collaboration.
⇒ Discuss each case with the appropriate heart centre within 12 hours of diagnosis.
⇒ Communicate progress with the heart centre at least weekly (or more frequently depending on clinical urgency).
⇒ Arrange transfer to the heart centre if indicated to improve patient care.
⇒ Consider investigation of portals of entry (eg, teeth, gut, etc).
⇒ Discuss treatment of extracardiac infection (eg, splenic or spinal abscess).

Monitor.
⇒ Ensure that clinical progress is monitored at least daily.
⇒ Monitor CRP and renal function.
⇒ Arrange echocardiography if any change in clinical condition (or predischarge if transfer for surgery is not required).
⇒ Arrange outpatient follow-up after discharge (initially at 1 and 3 months).

Documentation.
⇒ Document findings from each ward review or MDT meeting in the clinical notes.
⇒ Provide a comprehensive summary of management for transferred patients.

Patient perspective.
⇒ Explain the diagnosis of IE to patients, and how it will be managed, and answer their questions.
⇒ Provide written information for patients about IE and how to reduce the risk of future episodes.
⇒ Refer to the local drug addiction team (if appropriate).

Heart centre.

MDT.
⇒ Hold a meeting at least once each week.
⇒ Provide advice/support/training for IE teams in centres without cardiac surgical facilities.

Further management.
⇒ Arrange further imaging (including TOE, FDG-PET/CT) if indicated and unavailable at DGH.
⇒ Discuss with relevant cardiac specialists (eg, cardiologist specialising in lead extraction).
⇒ Discuss with relevant non-cardiac specialists (eg, neurosurgeon or renal physician).

Cardiac surgery
⇒ Discuss transfer from referring centre.
⇒ Monitor clinical progress (including potential indications for cardiac surgery).
⇒ For patients requiring surgery, determine the most appropriate intervention (and its timing).
⇒ Assign surgeon with appropriate subspecialist expertise (eg, mitral valve repair, adult congenital heart disease).
⇒ Monitor progress after surgery.
⇒ Arrange outpatient follow-up after discharge.

CRP, C reactive protein; DGH, district general hospital; FDG-PET, fluorodeoxyglucose positron emission tomography; IE, infective endocarditis; MDT, multidisciplinary team; TOE, transoesophageal echocardiography.

of IE, agreeing on antibiotic therapy, making decisions about surgery and evaluating clinical progress.[7] There was significant reduction in both the time to commencing IE-specific antibiotic therapy (4.0±4.0 days vs 2.5±3.2 days, p=0.004) and the time from suspected IE to surgery (7.8±7.3 days vs 5.3±4.2 days, p=0.004). In multivariable analysis, IE team review was associated with reduced risk of mortality (HR 0.24, 95% CI 0.07 to 0.87), but this IE team also carried out MDT meetings in addition to ward review.

IE 'alerts'

A 'multidisciplinary alert for endocarditis' has been described in which comprehensive patient assessment was triggered by physicians appointed to monitor for clinical, microbiological and echocardiographic suspicions of IE.[16] This process was associated with a significant reduction in mortality (OR 0.27, 95%CI 0.10 to 0.71), but the study compared outcomes to historical controls, was at high risk of bias and failed to describe the nature of comprehensive patient assessment. Analysis of a period of ID review of all bacteraemic patients compared with a prior period without consultation was associated with increased diagnosis of IE, although this study was at high risk of bias.[19] In single-centre cohort studies of patients with *S. aureus* bacteraemia, ID consultation was associated with higher rates of echocardiography in two studies[20 21] and lower mortality rates in one.[20] Similarly, in a retrospective cohort study of patients with at least one blood culture positive for *Enterococcus* spp., patients with an ID consultation were more likely to undergo repeat cultures to ensure clearance (99% vs 74%, p<0.001), echocardiography (79% vs 45%, p<0.001), surgical intervention (20% vs 7%, p=0.01) and receive antibiotics for an appropriate duration (90% vs 46%, p<0.001).[22]

IE guidelines and protocols

One study evaluated the introduction of a local consensus IE 'protocol' that included recommendations for microbiological investigation, antibiotic treatment and surgical intervention.[23] In multivariable analysis, mortality was reduced in the period using the protocol when compared with a prior control period (HR 0.26, 95%CI 0.09 to 0.76). Introduction of a hospital-wide protocol for the management of *S. aureus* bacteraemia was associated with increased rates of echocardiography and IE diagnosis (with no impact on survival), although this study was at serious risk of bias.[24]

Aim of IE services

In the absence of high-quality evidence, all new recommendations in this section represent Working Party consensus. IE is

Box 2 Infective endocarditis service: indications for emergency transfer to (or discussion with) a heart centre.

⇒ Indications for emergency transfer to a heart centre (ie, 'red flags').
Prosthetic valve dehiscence.
Valve regurgitation (moderate or severe) and heart failure or haemodynamic instability.
Large/highly mobile vegetations.
Cardiac abscess, fistula and pseudoaneurysm.
⇒ Indications for non-emergency transfer to a heart centre.
Prosthetic valve endocarditis.
Failure to respond to antibiotics (persistently positive blood cultures or fever after 7 days days of appropriate therapy).
Moderate/severe valve regurgitation (without heart failure or haemodynamic instability).
Stroke (or other embolism) and large residual vegetation.
⇒ Indications for discussion with a heart centre.
All other cases.

an uncommon and challenging condition, and management by experienced MDTs is widely considered to be the standard of care. In our opinion, the primary aim of the IE team is to improve patient outcomes with a secondary aim to improve efficiency of care. The need for IE teams in all hospitals is axiomatic, since patients with IE or suspected IE can present to any acute hospital; however, this has not been sufficiently emphasised. The functions and composition of an IE team will vary in different settings (box 1) and may need to be dynamic, allowing individuals to rotate into the role, depending on resources and local staffing arrangements.

We believe that early diagnosis of IE leads to improved outcomes, but this is likely to be dependent on early initiation of optimal antibiotic therapy and the optimal timing of surgery. Reduction in time to targeted antibiotic therapy and first transthoracic echocardiogram was observed in one MDT evaluation.[7] Educational packages to raise awareness of the risk of IE in patients with *S. aureus* bacteraemia may also help to speed diagnosis.[24] One of the factors that is likely to affect outcome positively for many patients is prompt access to cardiac surgery; since this is best assessed in a heart centre, there is a need for clear pathways for consultation and referral between non-surgical and surgical centres, and objective criteria to guide referral or transfer (box 2). Hospitalisation with IE has also been identified as an opportunity to engage PWID[25] with drug addiction services and the IE team should support this process.

Information for patients

No studies were identified that evaluated the information required by patients; our recommendations have therefore been developed in consultation with a patient representative.

Training

No studies were identified that addressed postgraduate medical training in IE. Until objective evidence is available to identify a better approach, established IE teams should help to train junior doctors and support the development of new IE teams through collaborative, cross-centre case discussions and regular regional/national educational events including trainees in cardiology, cardiac surgery and infection specialties.

Outpatient follow-up

No studies were identified that assessed requirements for and/or the value of outpatient follow-up after treatment for IE. By consensus, it was agreed that outpatient follow-up was indicated to monitor for relapse or deterioration in valve function and plan surgery for residual valve disease.

IE in children

Children did not explicitly feature in the literature reviewed, and no primary research studies were identified that investigated service delivery for children with IE. Pending more specific data, we feel the principles outlined in these recommendations would apply as much to children as adults.

The Working Party supported setting up of a formal paediatric cardiac IE team and noted that there are already well-established regional networks of local hospitals for paediatric congenital cardiac services led by level 1 or 2 centres that host weekly (at least) paediatric congenital multidisciplinary meetings. Paediatric IE cases are usually discussed in that forum with invited experts such as microbiologists, ID specialists and local paediatricians. Rather than developing a separate structure, it may be preferable to embed the paediatric IE team within that existing structure.

CONCLUSIONS

There is clear consensus that MDTs should drive the care of patients with IE, despite a paucity of high-quality evidence to guide these recommendations (with most studies at serious or critical risk of bias). The infrequent nature of IE means that clinical decision making should be guided by clinicians who gain and share their experience of the care of these patients. More evidence is needed to guide the development of optimal models of care delivery, clinical training, patient information and follow-up.

RESEARCH RECOMMENDATIONS

The lack of high-quality evidence to inform practice around delivery of care for patients with suspected or confirmed IE was striking. The following research questions arise in the wake of this guideline development process.

IE team

What are the clinical and cost benefits of an IE team?

What is the most clinically and cost-effective model of service delivery?

Infrastructure and location of care of the patients with IE

What are the relative benefits and risks of patients with IE being cared for in a local hospital without the facilities of a heart centre on site (eg, availability of transoesophageal echocardiography or cardiac surgical support)?

Patient follow-up

What is the most clinically and cost-effective timing, nature and frequency of follow-up after an episode of IE?

Patient information

What information would patients prefer and how is this best provided?

People who inject drugs

What are the clinical and cost-effective benefits of substance misuse teams to support PWID who also have IE?

IE registry

Would an IE registry improve benchmarking and research?

Can local data be linked to central NHS Digital or other relevant databases to report on patient outcomes?

Children

How are IE services best delivered for children?

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Contributors JAS lead the project, systematic review, risk of bias assessment, evidence synthesis and drafted the manuscript. FA, PA, AG, BDP, RS, RS, RW, OW, and JBC: systematic review and risk of bias assessment. All authors contributed to the scoping exercise, final analysis and writing of the final manuscript.

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Supplemental information
Infective endocarditis guideline update -delivery of services

Systematic review method
The working party agreed key questions during face to face discussion (pre-COVID-19)

1.0 Types of studies
We considered randomised controlled trials (RCTs), controlled clinical trials (CCTs), interrupted time series with at least three data points before and after implementation of the intervention (ITS), controlled before and after studies (CBA), systematic reviews and meta-analyses, case-controlled studies, case series comprising >10 patients, qualitative studies and journal supplements were considered. Articles in English language were included, and full journal publication was required.

2.0 Types of participants
Patients with definite or possible infective endocarditis according to Duke or modified Duke criteria (or clearly defined clinical coding data).

3.0 Inclusion criteria
All studies that were relevant to the specific questions listed in Methods Section 2 were included (i.e related to delivery of IE services)

4.0 Exclusion criteria
References with no named author, case reports (defined as ≤10 patients), animal studies, abstract and conference proceedings, correspondence and articles in a language other than English were excluded. Studies of the infection of implantable cardiac electronic devices were excluded, as were studies considering the prevention of IE

5.0 Electronic databases searches.
The search was performed on the following electronic databases:

- MEDLINE (1 January 2009 to date)
- EMBASE (1 January 2009 to date)
- WEB OF SCIENCE (Science Citation Index Expanded – 1 January 2009 to present)
- Cochrane Library (including CENTRAL Register of Controlled Trials – Issue 1 2004 to Issue 2 2009)

2009 was chosen as the start date to include some overlap with the end of previous guideline development period.

6.0 Search terms
A “catch-all literature” search strategy was undertaken to identify all new endocarditis publications, from which relevant papers were identified. Literature searches were completed by Vittoria Lutje a literature review consultant.

1. Endocarditis ti, ab, MeSH.
2. Endocarditis, bacterial [MeSH]
3. 1 or 2

To include native valve endocarditis, prosthetic valve endocarditis, heart valve prosthesis, prosthesis related infection.

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To exclude: 1. cardiac implantable electronic device (CIED) infection and related endocarditis (including infection of: permanent pacemakers, implantable cardioverter-defibrillators, cardiac resynchronization therapy devices).
To exclude 2. implantable cardiac electronic device infection and related endocarditis (including infection of: permanent pacemakers, implantable cardioverter-defibrillators, cardiac resynchronization therapy devices).
Search terms were limited to humans.

1. Delivery of healthcare [Mesh]
2. Service delivery ti, ab
3. Service structure ti ab
4. Ward round ti ab
5. Multidisciplinary ti ab

7.0 Search diaries.

Search diary October 2018

Search No.	Date	Database (platform) searched	Time limits	Hits (before duplicate removal)
1	28/10/2018	Medline (OVID)	1 January 2009-18 October 2018	7645
2	28/10/2018	Cochrane Library Issue 10, 2018 (Cochrane Reviews and CENTRAL register of controlled trials)	Issue 1 2009-Issue 10 2018	503
3	28/10/2189	EMBASE (OVID) (Exclude Medline journals)	1 January 2009 – 18 October 2018	2621
4	28/10/2018	Web of Science (Science Citation Index Expanded)	1 January 2004-18 October 2018	2905
Final number of records in Endnote after de-duplication = 9669				

Duplicates were deleted from the Endnote database after import of results following the order above (default is Medline format). The final databases were re-checked for duplicates using several criteria (title only, author name+publication date).

Search diary February 2020

Search No.	Date	Database (platform) searched	Time limits	Hits (before duplicate removal)
1	19 February 2020	Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed	1 January 2018-19 February 2020	1569

		Citations, Daily and Versions(R) <1946 to February 18, 2020>		
2		Cochrane Library Issue 2, 2020 (Cochrane Reviews and CENTRAL register of controlled trials)	Issue 1 2018-Issue 2 2020	77
3		EMBASE (OVID) (Exclude Medline journals)	1 January 2018-19 February 2020	1014
4		Web of Science (Science Citation Index Expanded)	1 January 2018-19 February 2020	1015
			TOTAL NUMBER OF RESULTS	3675
			Final number of records in Endnote after removing duplicates	2425

Duplicates were deleted from the Endnote database after import of results following the order above (default is Medline format). The final databases were re-checked for duplicates using several criteria (title only, author name+publication date).

Search diary November 2020

Search No.	**Date**	**Database (platform) searched**	**Time limits**	**Hits (before duplicate removal)**
1	4th November 2020	Ovid MEDLINE® and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions® <1946 to November 4, 18, 2020>	1 January 2020-19 February 2020 Human, English language	311
2		Cochrane Library Issue 11, 2020 (Cochrane Reviews and CENTRAL register of controlled trials)	Issue 1 2020-Issue 2 2020	31
3		EMBASE (OVID) (Exclude Medline journals)	1 January 2020-5 November 2020	405
4		Web of Science (Science Citation Index Expanded)	1 January 2020-5 November 2020	578

			TOTAL NUMBER OF RESULTS	1325
			Final number of records in Endnote after removing duplicates	1015

Duplicates were deleted from the Endnote database after import of results following the order above (default is Medline format). The final databases were re-checked for duplicates using several criteria (title only, author name+publication date).

Search diary March 2022

Search No.	**Date**	**Database (platform) searched**	**Time limits**	**Hits (before duplicate removal)**
1	2 March 2022	Ovid MEDLINE® and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions® <1946 to March 1, 2022>	1 January 2020-2 March 2022	2165
2		Cochrane Library Issue 2, 2022 (Cochrane Reviews and CENTRAL register of controlled trials)	Issue 1 2020-Issue 2 2022	121
3		EMBASE (OVID) (Exclude Medline journals)	1 January 2020-2 March 2022	1545
4		Web of Science (Science Citation Index Expanded)	1 January 2208-2 March 2022	1030
			TOTAL NUMBER OF RESULTS	4861
			Final number of records in Endnote after removing 1770 duplicates	3091

Duplicates were deleted from the Endnote database after import of results following the order above (default is Medline format). The final databases were re-checked for duplicates using several criteria (title only, author name+publication date).

8.0 Literature search results flow diagram

Sandoe JAT, *et al. Heart* 2023;0:1–7. doi: 10.1136/heartjnl-2022-321791

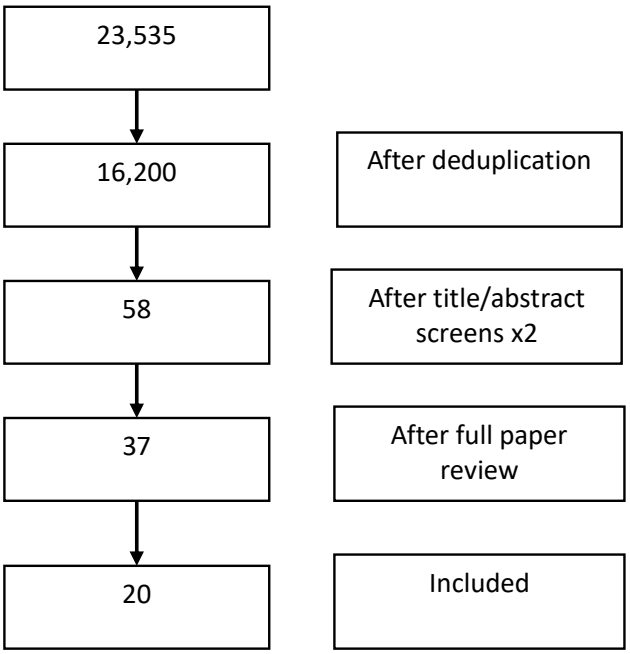

Figure S1 Results of literature search strategy

9.0 Quality assurance (search strategy)
A selection of key papers was used to test the search strategy. In addition, working party members were asked if they are aware of any significant papers that were absent from the output of the literature search.

10.0 Selection of studies
A staged selection process was undertaken. In the first stage, papers that clearly fulfilled exclusion criteria, based on study type, were removed from further consideration by one author (CH), based on titles and abstracts. In order to quality assure this process, a random selection of the references (titles and abstracts) removed was circulated to co-authors to determine if anything of relevance had been excluded (none had). In the second stage of selection, remaining papers, titles and abstracts were screened for inclusion by at least two authors. All reviewers were blinded to the decisions made by their colleagues. If reviewers disagreed whether a reference should be included in the review, the opinion of a third author was sought. In all cases the majority decision for inclusion was taken. For papers deemed eligible for inclusion, full copies were obtained and screened to ensure fulfilment of inclusion criteria. All authors agreed the inclusion of the final papers.

11.0 Data extraction and management
A data extraction record was developed to facilitate the collection of data from each included study. Data extraction included the following information:

- Lead author and date of publication
- Participant details including numbers and age of subjects
- Setting and geographical location

- Study type
- Risk of bias

12.0 Assessment of risk of bias in included studies

Two authors independently assessed the risk of bias for each study. No randomised controlled trials were identified, so a risk of bias tool was not required; the ROBINS-I tool for assessing risk of bias in non-randomised studies of interventions.[24]

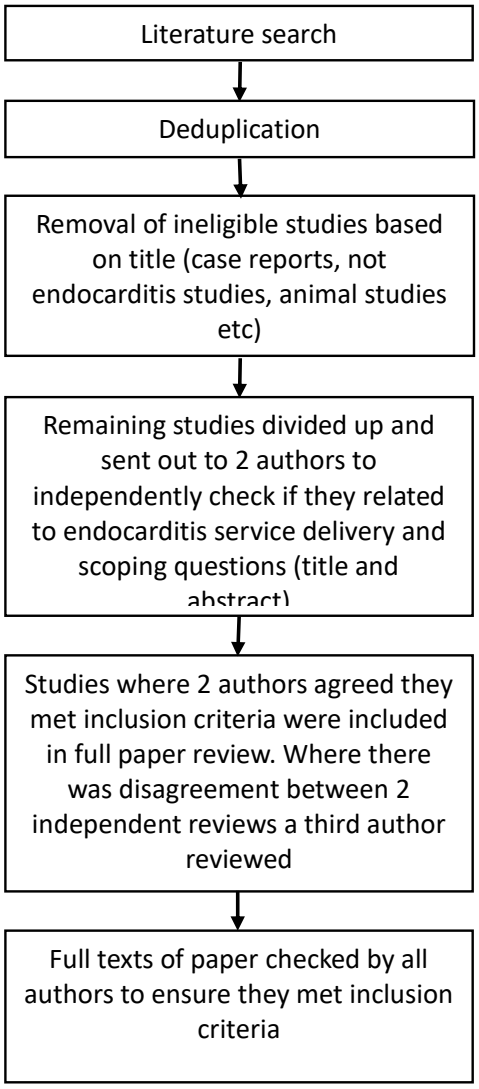

Figure S2 Literature selection strategy summary