Prophylaxis Against Infective Endocarditis

5 Appendices

Glossary

Case–control study

Comparative observational study in which the investigator selects individuals who have experienced an event (for example, developed a disease), known as the 'case' and others who have not (controls), and then collects data to determine previous exposure to a possible cause.

Cohort study (also known as follow-up, incidence, longitudinal, or prospective study)

An observational study in which a defined group of people (the cohort) is followed over time. Outcomes are compared in subsets of the cohort who were exposed or not exposed (or exposed at different levels) to an intervention or other factor of interest.

Case series

A group or series of case reports involving patients who were given similar treatment. Reports of case series usually contain detailed information about the individual patients. This includes demographic information and information on diagnosis, treatment, response to treatment, and follow-up after treatment.

Comorbidity

Two or more diseases or conditions occurring at the same time, such as depression and anxiety.

Confidence interval

The range within which the 'true' values (for example, size of effect of an intervention) are expected to lie with a given degree of certainty (for example, 95% or 99%).

Note: confidence intervals represent the probability of random errors, but not systematic errors or bias.

Cost-effectiveness analysis

An economic evaluation that compares alternative options for a specific patient group looking at a single effectiveness dimension measured in a non-monetary (natural) unit. It expresses the result in the form of an incremental (or average or marginal) cost-effectiveness ratio.

Economic evaluation

Technique developed to assess both costs and consequences of alternative health strategies and to provide a decision-making framework.

Generalisability

The degree to which the results of a study or systematic review can be extrapolated to other circumstances, particularly routine healthcare situations in the NHS in England and Wales.

Guideline Development Group

An independent group set up on behalf of NICE to develop a guideline. It includes academic experts, healthcare professionals and patient and carer representatives.

Heterogeneity

A term used to illustrate the variability or differences between studies in the estimates of effects.

Odds ratio

A measure of treatment effectiveness. The odds of an event happening in the intervention group, divided by the odds of it happening in the control group. The 'odds' is the ratio of non-events to events.

Quality-adjusted life year (QALY)

A measure of health outcome that assigns to each period of time a weight, ranging from 0 to 1, corresponding to the health-related quality of life during that period, where a weight of 1 corresponds to optimal health, and a weight of 0 corresponds to a health state judged equivalent to death; these are then aggregated across time periods.

Randomised controlled trial (also called a randomised clinical trial)

An experiment in which investigators randomly allocate eligible people into groups to receive or not to receive one or more interventions that are being compared. The results are assessed by comparing outcomes in the different groups. The groups should be similar in all aspects apart from the treatment they receive during the study.

Relative risk (also known as risk ratio)

The ratio of risk in the intervention group to the risk in the control group. The risk (proportion, probability or rate) is the ratio of people with an event in a group to the total in the group. A relative risk (RR) of 1 indicates no difference between comparison groups. For undesirable outcomes, an RR that is less than 1 indicates that the intervention was effective in reducing the risk of that outcome.

Systematic review

Research that summarises the evidence on a clearly formulated question according to a pre-defined protocol using systematic and explicit methods to identify, select and appraise relevant studies, and to extract, collate and report their findings. It may or may not use statistical meta-analysis.

Abbreviations

AHA American Heart Association
ASD Atrial septal defect
BCS British Cardiac Society
BE Bacterial endocarditis
BSAC British Society for Antimicrobial Chemotherapy
CHD Congenital heart disease
CHF Congestive heart failure
CFU Colony forming units
CI Confidence interval
ENT Ear, nose and throat
ERCP Endoscopic retrograde cholangiopancreatography
ESC European Society of Cardiology
FNA Fine needle aspiration
GA General anaesthetic
GI Gastrointestinal
GU Genitourinary
GUCH Grown-up congenital heart
ICU Intensive care unit
IE Infective endocarditis
MVP Mitral valve prolapse
NVE Native valve endocarditis
NCC National Collaborating Centre
NS Non significant
OR Odds ratio
PICO Population, intervention, comparison, outcome
QALY Quality-adjusted life year
PVE Prosthetic valve endocarditis
RCP Royal College of Physicians
RCT Randomised controlled trial
RR Relative risk
SD Standard deviation
TOE Transoesophageal echocardiography
UTI Urinary tract infection
VSD Ventricular Septal Defect

5.1 Appendix 1 – Scope

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

SHORT CLINICAL GUIDELINE

SCOPE

1 Guideline title

Antimicrobial prophylaxis against infective endocarditis in adults and children undergoing interventional procedures

1.1 Short title

Prophylaxis against infective endocarditis

2 Background

a) The Department of Health has asked the National Institute for Health and Clinical Excellence ('NICE' or 'the Institute') to prepare guidance on 'antimicrobial prophylaxis against endocarditis for adults and children undergoing an interventional procedure (including dentistry)'. The guideline will provide recommendations for good practice that are based on the best available evidence of clinical and cost effectiveness.

b) The Institute's clinical guidelines will support the implementation of National Service Frameworks (NSFs) in those aspects of care where a Framework has been published. The statements in each NSF reflect the evidence that was used at the time the Framework was prepared. The clinical guidelines and technology appraisal guidance published by the Institute after an NSF has been issued will have the effect of updating the Framework.

c) NICE clinical guidelines support the role of healthcare professionals in providing care in partnership with patients, taking account of their individual needs and preferences, and ensuring that patients (and their carers and families, where appropriate) can make informed decisions about their care and treatment.

3 Clinical need for the guideline

a) Infective endocarditis (IE) is an inflammation of the inner lining of the heart, particularly affecting the heart valves, caused by bacterial or other infections. It is a rare condition, with an annual incidence of less than 10 per 100,000 population. It is, however, a life-threatening disease with significant mortality (approximately 20%) and morbidity. IE predominantly affects people with underlying structural cardiac defects, both congenital and acquired, who develop bacteraemia (presence of bacteria in the blood) with organisms likely to cause IE. People with underlying structural cardiac defects constitute an important patient group ‘at risk’ of developing IE.

b) The prevention of IE has focused on the need to reduce bacteraemia in people at risk. This approach has three components: promotion of good oral health, timely treatment of sepsis and giving antimicrobial prophylaxis to at-risk people undergoing an interventional procedure that is considered likely to cause bacteraemia. The frequency of bacteraemia after healthcare procedures varies depending on type and site of the procedure. There is, however, controversy about whether procedure-based bacteraemia causes IE. There is a view that cumulative bacteraemia, caused by everyday activities like eating and tooth brushing, is more likely to cause IE, particularly in the case of dental procedures (including dentogingival manipulation).

c) It is considered biologically plausible that antimicrobial prophylaxis can reduce the risk of developing IE in people at risk. There is

support for this position from laboratory animal models, although there is controversy about whether laboratory animal models can explain the pathophysiology of spontaneous IE in humans. The rarity of IE means that it is difficult to undertake controlled clinical trials, so evidence about the effectiveness of antimicrobial prophylaxis in reducing the risk of developing IE is likely to come from well conducted observational studies. Potential risks of inappropriate use of antibiotics include serious adverse events (such as anaphylaxis) and development of antimicrobial resistance.

d) There is currently conflicting UK guidance relating to prophylaxis for IE. The chief area of controversy relates to the need for antibiotic prophylaxis for dental procedures, where there is concern that the likelihood of preventing IE by using antibiotics is less than the risk of the antibiotics causing serious adverse events.

4 The guideline

a) This document is the scope. It defines exactly what this guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health.

b) The areas that will be addressed by the guideline are described in the following sections.

4.1 Population

4.1.1 Groups that will be covered

a) Adults and children with known underlying structural cardiac defects, including those who have previously had IE.

b) Adults and children who have previously had IE (irrespective of whether they have a known underlying cardiac defect).

c) There are no additional subgroups of patients who may need specific consideration in their treatment or care.

4.1.2 Groups that will not be covered

a) People at increased risk of IE who do not have structural cardiac defects (such as intravenous drug users).

4.2 Healthcare setting

a) Primary dental care, primary medical care and community settings.

b) Secondary care.

4.3 Clinical management

a) Definition of people with structural heart lesions at risk of developing IE. This will include classifying structural heart lesions into those at risk and those not at risk of IE.

b) Definition of interventional procedures considered to need antimicrobial prophylaxis for IE for specific at-risk groups. This will include:

- Dental procedures.
- Other interventional procedures if there is considered to be an increased risk of IE in at-risk people. The following sites will be covered.
  - Upper and lower gastrointestinal (GI) tract.
  - Genitourinary tract. This includes urological, gynaecological and obstetric procedures (including childbirth).
  - Upper and lower respiratory tract. This includes ear nose and throat and bronchoscopy procedures.

c) Antimicrobial regimen to be used. This will include:

- specifying antibiotics that may be used
- the role of chlorhexidine mouthwash.

d) The guideline will not offer detailed recommendations on the route of administration, timing and duration of antibiotic and antimicrobial regimen(s). It is anticipated that the GDG and technical team will liaise with the 'British National Formulary' to ensure that the March 2008 'British National Formulary' publication will provide advice for clinicians that complements this guideline.

e) The information needs of patients regarding the benefits and risks of antimicrobial prophylaxis for IE. This will specifically include advice regarding body piercing and tattooing that involves damage to mucosal tissue.

f) The guideline defines IE as bacterial endocarditis. Non-infective, fungal and atypical bacterial causes of IE will not be considered.

g) The Guideline Development Group will take reasonable steps to identify ineffective interventions and approaches to care. If robust and credible recommendations for re-positioning the intervention for optimal use, including the identification of appropriate patient subgroups, or changing the approach to care to make more efficient use of resources, can be made, they will be clearly stated. If the resources released are substantial, consideration will be given to listing such recommendations in the 'Key priorities for implementation' section of the guideline.

4.4 Key outcome measures

Key outcomes that will be considered when reviewing the evidence include:

- risk of dental and other interventional procedures causing IE
- risk of antibiotics prescribed for prophylaxis causing serious adverse events, for example anaphylaxis, in 'at risk' population
- mortality and/or morbidity (for example congestive cardiac failure)
- health-related quality of life
- resource use and costs.

4.5 Economic aspects

The developers will take into account the cost-effectiveness of antimicrobial (principally antibiotic) prophylaxis against infective bacterial endocarditis in people undergoing the interventional procedures described in section 4.3b. .

4.6 Status

4.6.1 Scope

This is the final version of the scope.

4.6.2 Guideline

The development of the guideline recommendations will begin in July 2007.

5 Further information

Information on the guideline development process is provided in:

- 'The guideline development process: an overview for stakeholders, the public and the NHS'
- 'The guidelines manual'.

These booklets are available as PDF files from the NICE website (www.nice.org.uk/guidelinesmanual). Information on the progress of the guideline will also be available from the website.

The Guideline Development Group will work in accordance with the methods set out in the documents above. The short clinical guidelines programme is in development and will be consulted on.

5.2 Appendix 2 – Key Clinical Questions

Topic Areas and Structured Clinical Questions

Topic Area 1: Risk of developing infective endocarditis

Clinical questions:
SCQ 1a) What pre-existing cardiac conditions, in adults and children increase the risk of developing IE?

SCQ 1b) What pre-existing cardiac conditions are not associated with increased risk of developing IE?

SCQ 2) Which pre-existing cardiac conditions are associated with relatively poorer outcomes from IE?

Topic Area 2: Interventional procedures:

- *which increase the risk of those at risk developing IE*
- *which cause significant bacteraemia*

Clinical questions:

SCQ 3) Which dental and other interventional procedures are associated with increased incidence of IE in those considered at risk of IE?
SCQ 4) What levels of bacteraemia are associated with interventional procedures, both pre and post-procedure (including consideration of what is considered significant bacteraemia?)

SCQ 5) What levels of bacteraemia are associated with everyday activities (toothbrushing/chewing/urination/defecation)?

Topic Area 3: Prophylaxis regimen to be used

Clinical questions:
SCQ 6a) Does antibiotic prophylaxis in those at risk of developing IE reduce the incidence of IE when given before a defined Interventional Procedure?

SCQ 6b) Does oral chlorhexidine prophylaxis in those at risk of developing IE reduce the risk of developing IE when given before a defined Interventional Procedure?

SCQ 7a) Does antibiotic prophylaxis given to those undergoing Interventional Procedures reduce the level and duration of bacteraemia?

SCQ 7b) Does oral chlorhexidine prophylaxis given to those undergoing Interventional Procedures reduce the level and duration of bacteraemia?

SCQ 8) What rates of adverse events (in particular, anaphylaxis) have been found in those taking antibiotic prophylaxis?

Topic Area 4: Patient perspectives

Clinical question:

SCQ 9) What are the issues that individuals, who are considered at risk of IE regarding prophylaxis against infective endocarditis, report as important?

5.3 Appendix 3 – Search Strategy

Medline search strategies for PIE guideline

X.X Search strategies

X.X.X Scoping searches

Scoping searches were undertaken on the following websites and databases in January 2007 to provide information for scope development and project planning. Browsing or simple search strategies were employed.

Guidance/guidelines	Systematic reviews/economic evaluations
• British Cardiovascular Society • British Dental Association • British Society for Antimicrobial Chemotherapy • British Society of Gastroenterology • British Thoracic Society • Canadian Medical Association Infobase • Department of Health • Guidelines International Network (GIN) • National Guideline Clearing House (US) • National Health and Medical Research Council (Australia) • National Institute for Health and Clinical Excellence (NICE) - published & in development • National Institute for Health and Clinical Excellence (NICE) - Topic Selection • National Library for Health (NLH) Guidelines Finder • National Library for Health (NLH) Protocols and Care Pathways Database • National Library for Health (NLH) Specialist Libraries • New Zealand Guidelines Group • Prodigy • Royal College of General Practitioners • Royal College of Radiologists • Royal College of Surgeons • Scottish Intercollegiate Guidelines Network (SIGN)	• Cochrane Database of Systematic Reviews (CDSR) • Database of Abstracts of Reviews of Effects (DARE) • Health Economic Evaluations Database (HEED) • Health Technology Assessment (HTA) Database • National Coordinating Centre for • NHS Economic Evaluation Database (NHS EED) • Health Technology Assessment (NCCHTA) • TRIP Database

Simple, exploratory scoping searches were also undertaken on primary literature bibliographic databases and clinical trials sources to provide information for scope development and project planning.

Primary literature	Clinical Trials
• CINAHL • EMBASE • MEDLINE • MEDLINE IN PROCESS	• Cochrane Central Register of Controlled Trials (CENTRAL) • ClinicalTrials.gov • Current Controlled Trials (mRCT) • National Research Register (NRR) • Research Findings Electronic Register (ReFeR)

X.X.X Main searches

X.X.X.X The following sources were searched for the topics presented in sections X.X.X.X–X.X.X.X below.

- Cochrane Database of Systematic Reviews – CDSR (Wiley)
- Cochrane Central Register of Controlled Trials – CENTRAL (Wiley)
- Database of Abstracts of Reviews of Effects – DARE (Wiley)
- Health Technology Assessment Database – HTA (Wiley)
- CINAHL (Ovid)
- EMBASE (Ovid)
- MEDLINE (Ovid)
- MEDLINE In-Process (Ovid)
- PsycINFO (Ovid)
- Science Citation Index (Dialog DataStar)

X.X.X.X Identification of evidence on infective endocarditis

The searches were conducted on May 29th 2007. The aim of the searches was to identify papers on infective endocarditis to provide evidence on risk factors associated with the condition and evidence on the effectiveness of antibiotic prophylaxis in preventing the condition. Search filters for systematic reviews, randomised controlled trials and observational studies were appended to the search strategies to retrieve high quality papers (see x.x.x.x -

Identification of systematic reviews, randomised controlled trials and observational studies).

The MEDLINE search strategy is presented below. It was translated for use in all of the other databases.

Ovid MEDLINE(R) <1950 to May Week 3 2007>

1. exp Endocarditis/
2. endocardit$.tw.
3. 1 or 2

X.X.X.X Identification of evidence on bacteraemia levels associated with defined interventional procedures

The searches were conducted on August 31st 2007. Search filters for systematic reviews, randomised controlled trials and observational studies were appended to the search strategies to retrieve high quality papers (see x.x.x.x - **Identification of systematic reviews, randomised controlled trials and observational studies**).

The MEDLINE search strategy is presented below. It was translated for use in all of the other databases.

Ovid MEDLINE(R) <1950 to July Week 3 2007>

---

1 exp Dentistry, Operative/

2 exp Dental Prophylaxis/

3 ((dent$ or tooth$ or teeth or peridont$ or orthodont$) adj prophyla$).tw.

4 (crown adj3 length$).tw.

5 exp Endodontics/

6 endodontic$.tw.

7 Apicoectom$.tw.

8 (pulp$ adj3 cap$).tw.

9 Pulpectom$.tw.

10 Pulpotom$.tw.

11 exp Oral Surgical Procedures/

12 Gingivectom$.tw.

13 Gingivoplast$.tw.

14 Glossectom$.tw.

15 mucoperio$ flap$.tw.

16 (tartar adj3 remov$).tw.

17 Sialography/

18 sialograph$.tw.

19 (root adj2 canal adj3 (therap$ or treat$)).tw.

20 ((dent$ or oral$ or tooth$ or teeth or peridont$ or orthodont$ or root$) adj3 (restorat$ or implant$ or replant$ or reimplant$ or re-implant$ or extract$ or remov$ or scal$ or polish$ or fill$ or irrigat$ or separat$ or expos$ or bond$ or band$ or prob$ or investigat$ or rubber dam$ or wedg$ or lining$ or liner$ or planing$)).tw

21 ((dent$ or oral$ or tooth$ or teeth$ or peridont$ or orthodont$ or root$ canal$) adj3 (surg$ or procedure$ or endoscop$ or operat$ or incis$ or excis$ or intervention$ or invasiv$ or biops$ or inject$)).tw.

22 or/1-21

23 exp Digestive System Surgical Procedures/

24 roux-en-y.tw.

25 Appendectom$.tw.

26 (Bili$ adj3 (bypas$ or divers$)).tw.

27 Cholecystectom$.tw.

28 (gallbladder adj3 remov$).tw.

29 Cholecystostom$.tw.

30 portoenterostom$.tw.

31 Sphincterotom$.tw.

32 papillotom$.tw.

33 Colectom$.tw.

34 Proctocolectom$.tw.

35 coloproctectom$.tw.

36 laparotom$.tw.

37 endoscop$.tw.

38 Colonoscop$.tw.

39 Duodenoscop$.tw.

40 Gastroscop$.tw.

41 Proctoscop$.tw.

42 Cholangiopancreatograph$.tw.

43 ercp.tw.

44 Esophagoscop$.tw.

45 esophagogastroduodenoscop$.tw.

46 oesophagoscop$.tw.

47 oesophagogastroduodenoscop$.tw.

48 (oesophag$ adj3 dilat$).tw.

49 (esophag$ adj3 dilat$).tw.

50 Echocardiography, Transesophageal/

51 Echocardiography/

52 (transesophag$ adj3 echo$).tw.

53 (trans-esophag$ adj3 echo$).tw.

54 (esophag$ adj3 echo$).tw.

55 (transoesophag$ adj3 echo$).tw.

56 (trans-oesophag$ adj3 echo$).tw.

57 (oesophag$ adj3 echo$).tw.

58 tee.tw.

59 toe.tw.

60 exp Lithotripsy/

61 lithotrip$.tw.

62 litholapax$.tw.

63 Enterostom$.tw.

64 Cecostom$.tw.

65 Colostom$.tw.

66 Duodenostom$.tw.

67 Ileostom$.tw.

68 Jejunostom$.tw.

69 Esophagectom$.tw.

70 oesophagectom$.tw.

71 Esophagoplast$.tw.

72 oesophagoplast$.tw.

73 Esophagostom$.tw.

74 oesophagostom$.tw.

75 Fundoplicat$.tw.

76 nissen.tw.

77 Gastrectom$.tw.

78 Gastroenterostom$.tw.

79 billroth.tw.

80 gastrojejunostom$.tw.

81 (Gast$ adj3 Bypass).tw.

82 Gastroplast$.tw.

83 Gastrostom$.tw.

84 Hepatectom$.tw.

85 (Jejunoileal adj3 Bypass).tw.

86 (ileojejunal adj3 bypass).tw.

87 (intestin$ adj3 bypass).tw.

88 ((liver or hepat$) adj3 (transplant$ or graft$)).tw.

89 (pancrea$ adj3 (transplant$ or graft$)).tw.

90 Pancreatectom$.tw.

91 (pancrea$ adj3 remov$).tw.

92 Pancreaticoduodenectom$.tw.

93 duodenopancreatectom$.tw.

94 pancreatoduodenectom$.tw.

95 Pancreaticojejunostom$.tw.

96 (Periton$ adj3 Shunt$).tw.

97 (leveen adj3 shunt$).tw.

98 ((digest$ or gastr$ or intestin$ or gi or oesophag$ or esophag$ or stomach or bowel$ or colon$ or liver or hepat$ or bili$ or duoden$ or gall$ or pancrea$ or append$ or abdom$ or anal or anus or sphinct$) adj3 (surg$ or procedure$ or operat$ or incis$ or excis$ or intervention$ or invasiv$ or biops$ or endoscop$ or sclerotherap$)).tw.

99 or/23-98

100 exp Urogenital Surgical Procedures/

101 Colposcop$.tw.

102 Colpotom$.tw.

103 Culdoscop$.tw.

104 (Dilatation adj3 Curettage).tw.

105 (Vacuum adj3 Curettage).tw.

106 Hysterectom$.tw.

107 Hysteroscop$.tw.

108 (uter$ adj3 endoscop$).tw.

109 Ovariectom$.tw.

110 oophorectom$.tw.

111 Salpingostom$.tw.

112 (reproduct$ adj3 sterili$).tw.

113 (tub$ adj3 Sterili$).tw.

114 (tub$ adj3 ligat$).tw.

115 aldridge.tw.

116 (tub$ adj3 occlu$).tw.

117 cooke.tw.

118 (cornual adj3 coagulat$).tw.

119 fimbriectom$.tw.

120 irving.tw.

121 kroener.tw.

122 madlener.tw.

123 pomeroy.tw.

124 (tub$ adj3 excis$).tw.

125 (tub$ adj3 ring$).tw.

126 uchida.tw.

127 Vasectom$.tw.

128 Cystectom$.tw.

129 Cystoscop$.tw.

130 Cystostom$.tw.

131 Cystotom$.tw.

132 (Kidney$ adj3 Transplant$).tw.

133 (kidney$ adj3 graft$).tw.

134 Nephrectom$.tw.

135 vesicotom$.tw.

136 Ureteroscop$.tw.

137 (Urin$ adj3 Diver$).tw.

138 Nephrostom$.tw.

139 nephroli$.tw.

140 Ureterostom$.tw.

141 Orchiectom$.tw.

142 (Pen$ adj3 Implant$).tw.

143 Prostatectom$.tw.

144 Trans?uret$.tw.

145 Trans?rect$.tw.

146 Vasovasostom$.tw.

147 castrat$.tw.

148 circumci$.tw.

149 (Uret$ adj3 catheter$).tw.

150 (Uret$ adj3 dilatat$).tw.

151 exp Obstetric Surgical Procedures/

152 Abortion$.tw.

153 embryotom$.tw.

154 Cerclage.tw.

155 (obstetr$ adj3 deliver$).tw.

156 (abdom$ adj3 deliver$).tw.

157 Cesarean.tw.

158 Caesarean.tw.

159 Episiotom$.tw.

160 (Obstetr$ adj3 extract$).tw.

161 (Induc$ adj3 (labor$ or labour$)).tw.

162 Parturition/

163 parturit$.tw.

164 childbirth$.tw.

165 birth$.tw.

166 (vagina$ adj3 deliver$).tw.

167 ((fet$ or cepha$) adj3 version$).tw.

168 Fetoscop$.tw.

169 Intrauterine Devices/

170 (Intra?uterine adj3 device$).tw.

171 iud.tw.

172 Vaginal Smears/

173 ((vagina$ or cervi$ or papanicolaou) adj3 smear$).tw.

174 ((genit$ or urin$ or uro$ or uret$ or endometr$ or ovar$ or ooph$ or uter$ or bladder or vagina$ or cervi$ or gyn$ or obstet$ or prostat$ or reproduct$) adj3 (surg$ or procedure$ or operat$ or incis$ or excis$ or intervention$ or invasiv$ or biops$ or endoscop$)).tw.

175 or/100-174

176 exp Pulmonary Surgical Procedures/

177 (Collapse adj3 Therap$).tw.

178 Pneumonolys$.tw.

179 Pneumothora$.tw.

180 Bronchoscopy/

181 bronchoscop$.tw.

182 thyroidectomy/ or adenoidectomy/ or laryngectomy/ or laryngoscopy/ or neck dissection/ or pharyngectomy/ or pharyngostomy/ or rhinoplasty/ or tonsillectomy/ or tracheostomy/ or tracheotomy/

183 thyroidectom$.tw.

184 adenoidectom$.tw.

185 laryngectom$.tw.

186 laryngoscop$.tw.

187 neck dissect$.tw.

188 pharyngectom$.tw.

189 pharyngostom$.tw.

190 rhinoplast$.tw.

191 tonsillectom$.tw.

192 tracheostom$.tw.

193 tracheotom$.tw.

194 (nasal adj3 pack$).tw.

195 Pneumonectomy/

196 Pneumonectom$.tw.

197 (lung$ adj3 transplant$).tw.

198 (lung$ adj3 graft$).tw.

199 ((nasal or sinus$ or rhino$ or rhina$ or pharyn$ or laryn$ or trache$ or bronch$ or lung$ or pulmonar$ or respirat$) adj3 (surg$ or procedure$ or endoscop$ or operat$ or incis$ or excis$ or intervention$ or invasiv$ or biops$)).tw.

200 or/176-199

201 22 or 99 or 175 or 200

202 (bacter$ adj5 (level$ or rate$ or incidence$ or prevalence$ or duration$ or cumulat$ or transient or translocat$ or trans-locat$ or transfer$)).tw.

203 (streptococ$ adj5 (level$ or rate$ or incidence$ or prevalence$ or duration$ or cumulat$ or transient or translocat$ or trans-locat$ or transfer$)).tw.

204 (staphylococ$ adj5 (level$ or rate$ or incidence$ or prevalence$ or duration$ or cumulat$ or transient or translocat$ or trans-locat$ or transfer$)).tw.

205 (enterococ$ adj5 (level$ or rate$ or incidence$ or prevalence$ or duration$ or cumulat$ or transient or translocat$ or trans-locat$ or transfer$)).tw.

206 or/202-205

207 201 and 206

X.X.X.X Identification of evidence on bacteraemia levels associated with defined activities of daily living

The searches were conducted on August 9th 2007. Search filters for systematic reviews, randomised controlled trials and observational studies were appended to the search strategies to retrieve high quality papers (see x.x.x.x - **Identification of systematic reviews, randomised controlled trials and observational studies**).

The MEDLINE search strategy is presented below. It was translated for use in all of the other databases.

Database: Ovid MEDLINE(R) <1950 to July Week 3 2007>

---

1. Oral Hygiene/
2. ((oral$ or dent$ or mouth$) adj3 hyg$).tw.
3. Toothbrushing/
4. toothbrush$.tw.
5. tooth-brush$.tw.
6. ((tooth$ or teeth) adj3 brush$).tw.
7. ((tooth$ or teeth) adj3 clean$).tw.
8. (tongue$ adj3 (brush$ or scrap$ or clean$)).tw.
9. Dental Devices, Home Care/
10. floss$.tw.
11. ((tooth$ or teeth) adj3 pick$).tw.
12. Mastication/

13. masticat$.tw.
14. chew$.tw.
15. or/1-14
16. Exercise/
17. exercise.tw.
18. exercising.tw.
19. physical$ activit$.tw.
20. exp Sports/
21. sport$.tw.
22. (workout$ or work$ out$).tw.
23. Exertion/
24. exertion$.tw.
25. physical effort$.tw.
26. Physical Fitness/
27. fit$.tw.
28. or/16-27
29. Defecation/
30. defecat$.tw.
31. defaecat$.tw.
32. ((void$ or pass$ or excret$ or evac$ or discharg$ or empt$ or mov$ or motion$ or open$) adj3 bowel$).tw.
33. laxation.tw.

34. ((void$ or pass$ or discharg$ or excret$) adj3 (excreta or stool$ or feces or fecal or faec$)).tw.

35. or/29-34

36. Urination/

37. (urinat$ or micturit$).tw.

38. ((void$ or pass$ or excret$ or evac$ or discharg$ or empt$) adj3 (bladder or urin$)).tw.

39. ((pass$ or mak$) adj2 water$).tw.

40. or/36-39

41. 15 or 28 or 35 or 40

42. (bacter$ adj5 (level$ or rate$ or incidence$ or prevalence$ or duration$ or cumulat$ or transient or translocat$ or trans-locat$ or transfer$)).tw.

43. (streptococ$ adj5 (level$ or rate$ or incidence$ or prevalence$ or duration$ or cumulat$ or transient or translocat$ or trans-locat$ or transfer$)).tw.

44. (staphylococ$ adj5 (level$ or rate$ or incidence$ or prevalence$ or duration$ or cumulat$ or transient or translocat$ or trans-locat$ or transfer$)).tw.

45. (enterococ$ adj5 (level$ or rate$ or incidence$ or prevalence$ or duration$ or cumulat$ or transient or translocat$ or trans-locat$ or transfer$)).tw.

46. or/42-45

47. 41 and 46

X.X.X.X Identification of evidence on the effectiveness of antibiotic prophylaxis in reducing bacteraemia levels associated with defined interventional procedures

The searches were conducted on September 7th 2007. Search filters for systematic reviews, randomised controlled trials and observational studies were appended to the search strategies to retrieve high quality papers (see x.x.x.x- **Identification of systematic reviews, randomised controlled trials and observational studies**).

The MEDLINE search strategy is presented below. It was translated for use in all of the other databases.

Ovid MEDLINE(R) <1950 to August Week 5 2007>

1 exp Dentistry, Operative/

2 exp Dental Prophylaxis/

3 ((dent$ or tooth$ or teeth$ or peridont$ or orthodont$) adj prophyla$).tw.

4 (crown adj3 length$).tw.

5 exp Endodontics/

6 endodontic$.tw.

7 Apicoectom$.tw.

8 (pulp$ adj3 cap$).tw.

9 Pulpectom$.tw.

10 Pulpotom$.tw.

11 exp Oral Surgical Procedures/

12 Gingivectom$.tw.

13 Gingivoplast$.tw.

14 Glossectom$.tw.

15 mucoperio$ flap$.tw.

16 (tartar adj3 remov$).tw.

17 Sialography/

18 sialograph$.tw.

19 (root adj2 canal adj3 (therap$ or treat$)).tw.

20 ((dent$ or oral$ or tooth$ or teeth or peridont$ or orthodont$ or root$) adj3 (restorat$ or implant$ or replant$ or reimplant$ or re-implant$ or extract$ or remov$ or scal$ or polish$ or fill$ or irrigat$ or separat$ or expos$ or bond$ or band$ or prob$ or investigat$ or rubber dam$ or wedg$ or lining$ or liner$ or planing$)).tw.

21 ((dent$ or oral$ or tooth$ or teeth$ or peridont$ or orthodont$ or root$ canal$) adj3 (surg$ or procedure$ or endoscop$ or operat$ or incis$ or excis$ or intervention$ or invasiv$ or biops$ or inject$)).tw.

22 or/1-21

23 exp Digestive System Surgical Procedures/

24 roux-en-y.tw.

25 Appendectom$.tw.

26 (Bili$ adj3 (bypas$ or divers$)).tw.

27 Cholecystectom$.tw.

28 (gallbladder adj3 remov$).tw.

29 Cholecystostom$.tw.

30 portoenterostom$.tw.

31 Sphincterotom$.tw.

32 papillotom$.tw.

33 Colectom$.tw.

34 Proctocolectom$.tw.

35 coloproctectom$.tw.

36 laparotom$.tw.

37 endoscop$.tw.

38 Colonoscop$.tw.

39 Duodenoscop$.tw.

40 Gastroscop$.tw.

41 Proctoscop$.tw.

42 Cholangiopancreatograph$.tw.

43 ercp.tw.

44 Esophagoscop$.tw.

45 esophagogastroduodenoscop$.tw.

46 oesophagoscop$.tw.

47 oesophagogastroduodenoscop$.tw.

48 Echocardiography, Transesophageal/

49 Echocardiography/

50 (transesophag$ adj3 echo$).tw.

51 (trans-esophag$ adj3 echo$).tw.

52 (esophag$ adj3 echo$).tw.

53 (transoesophag$ adj3 echo$).tw.

54 (trans-oesophag$ adj3 echo$).tw.

55 (oesophag$ adj3 echo$).tw.

56 tee.tw.

57 toe.tw.

58 (oesophag$ adj3 dilat$).tw.

59 (esophag$ adj3 dilat$).tw.

60 exp Lithotripsy/

61 lithotrip$.tw.

62 litholapax$.tw.

63 Enterostom$.tw.

64 Cecostom$.tw.

65 Colostom$.tw.

66 Duodenostom$.tw.

67 Ileostom$.tw.

68 Jejunostom$.tw.

69 Esophagectom$.tw.

70 oesophagectom$.tw.

71 Esophagoplast$.tw.

72 oesophagoplast$.tw.

73 Esophagostom$.tw.

74 oesophagostom$.tw.

75 Fundoplicat$.tw.

76 nissen.tw.

77 Gastrectom$.tw.

78 Gastroenterostom$.tw.

79 billroth.tw.

80 gastrojejunostom$.tw.

81 (Gast$ adj3 Bypass).tw.

82 Gastroplast$.tw.

83 Gastrostom$.tw.

84 Hepatectom$.tw.

85 (Jejunoileal adj3 Bypass).tw.

86 (ileojejunal adj3 bypass).tw.

87 (intestin$ adj3 bypass).tw.

88 ((liver or hepat$) adj3 (transplant$ or graft$)).tw.

89 (pancrea$ adj3 (transplant$ or graft$)).tw.

90 Pancreatectom$.tw.

91 (pancrea$ adj3 remov$).tw.

92 Pancreaticoduodenectom$.tw.

93 duodenopancreatectom$.tw.

94 pancreatoduodenectom$.tw.

95 Pancreaticojejunostom$.tw.

96 (Periton$ adj3 Shunt$).tw.

97 (leveen adj3 shunt$).tw.

98 ((digest$ or gastr$ or intestin$ or gi or oesophag$ or esophag$ or stomach or bowel$ or colon$ or liver or hepat$ or bili$ or duoden$ or gall$ or pancrea$ or append$ or abdom$ or anal or anus or sphinct$) adj3 (surg$ or procedure$ or operat$ or incis$ or excis$ or intervention$ or invasiv$ or biops$ or endoscop$ or sclerotherap$)).tw.

99 or/23-98

100 exp Urogenital Surgical Procedures/

101 Colposcop$.tw.

102 Colpotom$.tw.

103 Culdoscop$.tw.

104 (Dilatation adj3 Curettage).tw.

105 (Vacuum adj3 Curettage).tw.

106 Hysterectom$.tw.

107 Hysteroscop$.tw.

108 (uter$ adj3 endoscop$).tw.

109 Ovariectom$.tw.

110 oophorectom$.tw.

111 Salpingostom$.tw.

112 (reproduct$ adj3 sterili$).tw.

113 (tub$ adj3 Sterili$).tw.

114 (tub$ adj3 ligat$).tw.

115 aldridge.tw.

116 (tub$ adj3 occlu$).tw.

117 cooke.tw.

118 (cornual adj3 coagulat$).tw.

119 fimbriectom$.tw.

120 irving.tw.

121 kroener.tw.

122 madlener.tw.

123 pomeroy.tw.

124 (tub$ adj3 excis$).tw.

125 (tub$ adj3 ring$).tw.

126 uchida.tw.

127 Vasectom$.tw.

128 Cystectom$.tw.

129 Cystoscop$.tw.

130 Cystostom$.tw.

131 Cystotom$.tw.

132 (Kidney$ adj3 Transplant$).tw.

133 (kidney$ adj3 graft$).tw.

134 Nephrectom$.tw.

135 vesicotom$.tw.

136 Ureteroscop$.tw.

137 (Urin$ adj3 Diver$).tw.

138 Nephrostom$.tw.

139 nephroli$.tw.

140 Ureterostom$.tw.

141 Orchiectom$.tw.

142 (Pen$ adj3 Implant$).tw.

143 Prostatectom$.tw.

144 Trans?uret$.tw.

145 Trans?rect$.tw.

146 Vasovasostom$.tw.

147 castrat$.tw.

148 circumci$.tw.

149 (Uret$ adj3 catheter$).tw.

150 (Uret$ adj3 dilatat$).tw.

151 exp Obstetric Surgical Procedures/

152 Abortion$.tw.

153 embryotom$.tw.

154 Cerclage.tw.

155 (obstetr$ adj3 deliver$).tw.

156 (abdom$ adj3 deliver$).tw.

157 Cesarean.tw.

158 Caesarean.tw.

159 Episiotom$.tw.

160 (Obstetr$ adj3 extract$).tw.

161 (Induc$ adj3 (labor$ or labour$)).tw.

162 Parturition/

163 parturit$.tw.

164 childbirth$.tw.

165 birth$.tw.

166 (vagina$ adj3 deliver$).tw.

167 ((fet$ or cepha$) adj3 version$).tw.

168 Fetoscop$.tw.

169 Intrauterine Devices/

170 (Intra?uterine adj3 device$).tw.

171 iud.tw.

172 Vaginal Smears/

173 ((vagina$ or cervi$ or papanicolaou) adj3 smear$).tw.

174 ((genit$ or urin$ or uro$ or uret$ or endometr$ or ovar$ or ooph$ or uter$ or bladder or vagina$ or cervi$ or gyn$ or obstet$ or prostat$ or

reproduct$) adj3 (surg$ or procedure$ or operat$ or incis$ or excis$ or intervention$ or invasiv$ or biops$ or endoscop$)).tw.

175 or/100-174

176 exp Pulmonary Surgical Procedures/

177 (Collapse adj3 Therap$).tw.

178 Pneumonolys$.tw.

179 Pneumothora$.tw.

180 Bronchoscopy/

181 bronchoscop$.tw.

182 thyroidectomy/ or adenoidectomy/ or laryngectomy/ or laryngoscopy/ or neck dissection/ or pharyngectomy/ or pharyngostomy/ or rhinoplasty/ or tonsillectomy/ or tracheostomy/ or tracheotomy/

183 thyroidectom$.tw.

184 adenoidectom$.tw.

185 laryngectom$.tw.

186 laryngoscop$.tw.

187 neck dissect$.tw.

188 pharyngectom$.tw.

189 pharyngostom$.tw.

190 rhinoplast$.tw.

191 tonsillectom$.tw.

192 tracheostom$.tw.

193 tracheotom$.tw.

194 (nasal adj3 pack$).tw.

195 Pneumonectomy/

196 Pneumonectom$.tw.

197 (lung$ adj3 transplant$).tw.

198 (lung$ adj3 graft$).tw.

199 ((nasal or sinus$ or rhino$ or rhina$ or pharyn$ or laryn$ or trache$ or bronch$ or lung$ or pulmonar$ or respirat$) adj3 (surg$ or procedure$ or endoscop$ or operat$ or incis$ or excis$ or intervention$ or invasiv$ or biops$)).tw.

200 or/176-199

201 22 or 99 or 175 or 200

202 exp Chemoprevention/

203 chemoprevent$.tw.

204 chemo-prevent$.tw.

205 prophyla$.tw.

206 chemoprophyla$.tw.

207 chemo-prophyla$.tw.

208 exp anti-infective agents/

209 exp Penicillins/

210 penicillin$.tw.

211 "pen v".tw.

212 "pen g".tw.

213 antibiot$.tw.

214 anti-biot$.tw.

215 antibacter$.tw.

216 anti-bacter$.tw.

217 antimycobacter$.tw.

218 anti-mycobacter$.tw.

219 bacteriocid$.tw.

220 microbicid$.tw.

221 antimicrob$.tw.

222 anti-microb$.tw.

223 anti-infect$.tw.

224 antiinfect$.tw.

225 gentamicin$.tw.

226 gentamycin$.tw.

227 cidomycin$.tw.

228 garamycin$.tw.

229 garamicin$.tw.

230 gentacycol.tw.

231 gentavet.tw.

232 genticin$.tw.

233 Glycopeptides/

234 Teicoplanin$.tw.

235 teichomycin$.tw.

236 teichomicin$.tw.

237 targocid$.tw.

238 clindamycin$.tw.

239 clindamicin$.tw.

240 dalacin c.tw.

241 deoxylincomycin$.tw.

242 chlolincocin$.tw.

243 chlorlincocin$.tw.

244 cleocin.tw.

245 ceftriaxon$.tw.

246 rocephin.tw.

247 cefatriaxon$.tw.

248 cephalexin$.tw.

249 cefalexin$.tw.

250 ceporex.tw.

251 keflex.tw.

252 azithromycin$.tw.

253 azithromicin$.tw.

254 azythromycin$.tw.

255 azythromicin$.tw.

256 zithromax.tw.

257 clarithromycin$.tw.

258 clarithromicin$.tw.

259 clarothromycin$.tw.

260 clarothromicin$.tw.

261 clarosip.tw.

262 klaricid.tw.

263 vancomycin$.tw.

264 vancomicin$.tw.

265 vancocin$.tw.

266 cefuroxime.tw.

267 cephuroxime.tw.

268 zinacef.tw.

269 zinnat.tw.

270 ampicillin$.tw.

271 penbritin.tw.

272 amcill.tw.

273 aminobenzylpenicillin$.tw.

274 aminobenzyl-penicillin$.tw.

275 benzylpenicillin$.tw.

276 benzyl-penicillin$.tw.

277 omnipen.tw.

278 pentrexyl.tw.

279 polycillin$.tw.

280 ukapen.tw.

281 augmentin$.tw.

282 amoxicillin$.tw.

283 amoxycillin$.tw.

284 co-amox$.tw.

285 coamox$.tw.

286 hydroxyampicillin$.tw.

287 actimoxi.tw.

288 amoxil$.tw.

289 amoyl$.tw.

290 clamoxyl.tw.

291 penamox.tw.

292 polymox.tw.

293 trimox.tw.

294 wymox.tw.

295 Flucloxacillin$.tw.

296 fluorochloroxacillin$.tw.

297 floxapen.tw.

298 cefazolin$.tw.

299 cephazolin$.tw.

300 cefamedin$.tw.

301 cefamezine$.tw.

302 gramaxin$.tw.

303 or/202-302

304 ((bacter$ or staphylococ$ or streptococ$ or enterococ$) adj5 (eliminat$ or prevent$ or reduc$ or decreas$ or lower$)).tw.

305 201 and 303 and 304

306 chemoprevent$.ti.

307 chemo-prevent$.ti.

308 chemoprophyla$.ti.

309 chemo-prophyla$.ti.

310 (antibiot$ and prophyla$).ti.

311 (anti-biot$ and prophyla$).ti.

312 (antimicrob$ and prophyla$).ti.

313 (anti-microb$ and prophyla$).ti.

314 (antibacter$ and prophyla$).ti.

315 (anti-bacter$ and prophyla$).ti.

316 (antibiot$ and premedi$).ti.

317 (anti-biot$ and premedi$).ti.

318 (antimicrob$ and premedi$).ti.

319 (anti-microb$ and premedi$).ti.

320 (antibacter$ and premedi$).ti.

321 (anti-bacter$ and premedi$).ti.

322 (antibiot$ and prevent$).ti.

323 (anti-biot$ and prevent$).ti.

324 (antimicrob$ and prevent$).ti.

325 (anti-microb$ and prevent$).ti.

326 (antibacter$ and prevent$).ti.

327 (anti-bacter$ and prevent$).ti.

328 or/306-327

329 201 and 328

330 305 or 329

X.X.X.X Identification of evidence on the effectiveness of oral chlorhexidine prophylaxis in reducing bacteraemia levels associated with dental interventional procedures

The searches were conducted on September 4th 2007. Search filters for systematic reviews, randomised controlled trials and observational studies were appended to the search strategies to retrieve high quality papers (see x.x.x.x - **Identification of systematic reviews, randomised controlled trials and observational studies**).

The MEDLINE search strategy is presented below. It was translated for use in all of the other databases.

Ovid MEDLINE(R) <1950 to August Week 4 2007>

1 exp Dentistry, Operative/

2 exp Dental Prophylaxis/

3 ((dent$ or tooth$ or teeth or peridont$ or orthodont$) adj prophyla$).tw.

4 (crown adj3 length$).tw.

5 exp Endodontics/

6 endodontic$.tw.

7 Apicoectom$.tw.

8 (pulp$ adj3 cap$).tw.

9 Pulpectom$.tw.

10 Pulpotom$.tw.

11 exp Oral Surgical Procedures/

12 Gingivectom$.tw.

13 Gingivoplast$.tw.

14 Glossectom$.tw.

15 mucoperio$ flap$.tw.

16 (tartar adj3 remov$).tw.

17 Sialography/

18 sialograph$.tw.

19 (root adj2 canal adj3 (therap$ or treat$)).tw.

20 ((dent$ or oral$ or tooth$ or teeth or peridont$ or orthodont$ or root$) adj3 (restorat$ or implant$ or replant$ or reimplant$ or re-implant$ or extract$ or remov$ or scal$ or polish$ or fill$ or irrigat$ or separat$ or expos$ or bond$ or band$ or prob$ or investigat$ or rubber dam$ or wedg$ or lining$ or liner$ or planing$)).tw.

21 ((dent$ or oral$ or tooth$ or teeth$ or peridont$ or orthodont$ or root$ canal$) adj3 (surg$ or procedure$ or endoscop$ or operat$ or incis$ or excis$ or intervention$ or invasiv$ or biops$ or inject$)).tw.

22 or/1-21

23 Mouthwashes/

24 mouthwash$.tw.

25 mouth wash$.tw.

26 Chlorobenzenes/

27 Biguanides/

28 Chlorhexidine/

29 chlorhex$.tw.

30 chlorohex$.tw.

31 corsodyl.tw.

32 eludril.tw.

33 tubulicid.tw.

34 ((cavit$ or oral or dent$ or mouth$ or endodontic$ or orthodontic$ or peridont$) adj3 (antibiot$ or anti-biot$ or antimicrob$ or anti-microb$ or anti-bacter$ or antibacter$ or anti-mycobacter$ or antimycobacter$ or bacteriocid$ or microbicid$ or anti-infect$ or antiinfect$ or anti-sept$ or antisept$ or disinfect$ or dis-infect$ or prophyla$ or chemoprophyla$ or chemo-prophyla$ or irrigant$)).tw.

35 or/23-34

36 exp Bacteria/

37 Bacterial Infections/

38 exp Bacteremia/

39 bacter$.tw.

40 enterococ$.tw.

41 streptococ$.tw.

42 staphylococ$.tw.

43 or/36-42

44 22 and 35 and 43

X.X.X.X Identification of systematic reviews, randomised controlled trials and observational studies

Search filters for systematic reviews, randomised controlled trials and observational studies were appended to the search strategies above to retrieve high quality evidence.

The MEDLINE search filters are presented below. They were translated for use in all of the other databases.

Systematic Reviews

1. meta-analysis.pt.
2. review.pt.
3. exp review literature/
4. meta-analysis/
5. (metaanaly$ or metanaly$ or (meta adj2 analy$)).tw.
6. (review$ or overview$).ti.
7. (systematic$ adj4 (review$ or overview$)).tw.
8. ((quantitative$ or qualitative$) adj4 (review$ or overview$)).tw.
9. ((studies or trial$) adj1 (review$ or overview$)).tw.
10. (integrat$ adj2 (research or review$ or literature)).tw.
11. (pool$ adj1 (analy$ or data)).tw.
12. (handsearch$ or (hand adj2 search$)).tw.
13. (manual$ adj2 search$).tw.
14. or/1-13

Randomised Controlled Trials

1. randomized controlled trial.pt.
2. controlled clinical trial.pt.
3. clinical trial.pt.
4. exp clinical trials/
5. placebos/
6. random allocation/
7. double-blind method/
8. single-blind method/
9. cross-over studies/
10. ((random$ or control$ or clinical$) adj2 (trial$ or stud$)).tw.
11. (random$ adj2 allocat$).tw.
12. placebo$.tw.
13. ((singl$ or doubl$ or trebl$ or tripl$) adj (blind$ or mask$)).tw.
14. (crossover$ or (cross adj over$)).tw.
15. or/1-14

Observational Studies

1. Epidemiologic Studies/
2. exp Case-Control Studies/

3. exp Cohort Studies/
4. Cross-Sectional Studies/
5. Comparative Study.pt.
6. case control$.tw.
7. case series.tw.
8. (cohort adj (study or studies)).tw.
9. cohort analy$.tw.
10. (follow up adj (study or studies)).tw.
11. (observational adj (study or studies)).tw.
12. longitudinal.tw.
13. prospective.tw.
14. retrospective.tw.
15. cross sectional.tw.
16. or/1-15

X.X.X.X Identification of evidence on patient views about antibiotic prophylaxis for infective endocarditis

The searches were conducted on September 21st 2007.

The MEDLINE search strategy is presented below. It was translated for use in all of the other databases.

Ovid MEDLINE(R) <1950 to September Week 2 2007>

---

1 Qualitative Research/

2 Nursing Methodology Research/

3 exp Interviews/

4 Questionnaires/

5 Narration/

6 Health Care Surveys/

7 (qualitative$ or interview$ or focus group$ or questionnaire$ or narrative$ or narration$ or survey$).tw.

8 (ethno$ or emic or etic or phenomenolog$ or grounded theory or constant compar$ or (thematic$ adj3 analys$) or theoretical sampl$ or purposive sampl$).tw.

9 (hermeneutic$ or heidegger$ or husser$ or colaizzi$ or van kaam$ or van manen$ or giorgi$ or glaser$ or strauss$ or ricoeur$ or spiegelberg$ or merleau$).tw.

10 (metasynthes$ or meta-synthes$ or metasummar$ or meta-summar$ or metastud$ or meta-stud$).tw.

11 or/1-10

12 exp Patients/px

13 exp Parents/px

14 exp Family/px

15 Caregivers/px

16 Stress, Psychological/

17 Emotions/

18 Anxiety/

19 Fear/

20 exp Consumer Satisfaction/

21 ((patient$ or parent$ or famil$ or carer$ or caregiver$ or care-giver$ or inpatient$ or in-patient$) adj2 (experience$ or belief$ or stress$ or emotion$ or anx$ or fear$ or concern$ or uncertain$ or unsure or thought$ or feeling$ or felt$ or view$ or opinion$ or perception$ or perspective$ or attitud$ or satisfact$ or know$ or understand$ or aware$)).tw.

22 or/12-21

23 11 or 22

24 exp Endocarditis/

25 endocardit$.tw.

26 24 or 25

27 exp Chemoprevention/

28 chemoprevent$.tw.

29 chemo-prevent$.tw.

30 prophyla$.tw.

31 chemoprophyla$.tw.

32 chemo-prophyla$.tw.

33 exp anti-infective agents/

34 exp Penicillins/

35 penicillin$.tw.

36 "pen v".tw.

37 "pen g".tw.

38 antibiot$.tw.

39 anti-biot$.tw.

40 antibacter$.tw.

41 anti-bacter$.tw.

42 antimycobacter$.tw.

43 anti-mycobacter$.tw.

44 bacteriocid$.tw.

45 microbicid$.tw.

46 antimicrob$.tw.

47 anti-microb$.tw.

48 antiinfect$.tw.

49 anti-infect$.tw.

50 or/27-49

51 26 and 50

52 23 and 51

X.X.X Health economics

X.X.X.X Sources

The following sources were searched to identify economic evaluations:

- NHS Economic Evaluation Database – NHS EED (via Cochrane Library, Wiley)
- Health Economic Evaluations Database – HEED (OHE interface)
- MEDLINE (Ovid)
- MEDLINE In-Process (Ovid)

X.X.X.X Strategies

The searches were undertaken on September 21st 2007. The MEDLINE search strategy presented in X.X.X.X **[Identification of evidence on infective endocarditis]** was used and translated for use in NHS EED and HEED. Filters to retrieve economic evaluations and quality of life papers were appended to the MEDLINE search to identify relevant evidence.

The MEDLINE economic evaluations and quality of life search filters are presented below. They were translated for use in the MEDLINE In-Process database.

Ovid MEDLINE(R) <1950 to September Week 2 2007>

Economic Evaluations

1 Economics/

2 exp "Costs and Cost Analysis"/

3 Economics, Dental/

4 exp Economics, Hospital/

5 exp Economics, Medical/

6 Economics, Nursing/

7 Economics, Pharmaceutical/

8 Budgets/

9 "Quality of Life"/

10 "Value of Life"/

11 quality-adjusted life years/

12 exp models, economic/

13 markov chains/

14 monte carlo method/

15 Decision Trees/

16 economic$.tw.

17 quality of life.tw.

18 qol?.tw.

19 hrqol?.tw.

20 quality adjusted life year?.tw.

21 qaly?.tw.

22 cba.tw.

23 cea.tw.

24 cua.tw.

25 markov$.tw.

26 (monte adj carlo).tw.

27 (decision adj2 (tree? or analys$)).tw.

28 utilit$.tw.

29 pathway?.tw.

30 ((critical or clinical or patient) adj (path? or protocol?)).tw.

31 (cost? or costing? or costly or costed).tw.

32 (price? or pricing?).tw.

33 fiscal$.tw.

34 (fund? or funding or funded).tw.

35 financ$.tw.

36 budget$.tw.

37 expenditure?.tw.

38 (fee or fees).tw.

39 saving?.tw.

40 (value adj2 (money or monetary)).tw.

41 (pharmacoeconomic? or (pharmaco adj economic?)).tw.

42 ration$.tw.

43 (resource? adj2 allocat$).tw.

44 or/1-43

Ovid MEDLINE(R) <1950 to September Week 2 2007>

Quality of Life

1 value of life/

2 quality adjusted life year/

3 quality adjusted life.tw.

4 (qaly$ or qald$ or qale$ or qtime$).tw.

5 disability adjusted life.tw.

6 daly$.tw.

7 health status indicators/

8 (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw.

9 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw.

10 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw.

11 (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw.

12 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw.

13 (euroqol or euro qol or eq5d or eq 5d).tw.

14 (hql or hqol or h qol or hrqol or hr qol).tw.

15 (hye or hyes).tw.

16 health$ year$ equivalent$.tw.

17 health utilit$.tw.

18 (hui or hui1 or hui2 or hui3).tw.

19 disutili$.tw.

20 rosser.tw.

21 quality of wellbeing.tw.

22 quality of well-being.tw.

23 qwb.tw.

24 willingness to pay.tw.

25 standard gamble$.tw.

26 time trade off.tw.

27 time tradeoff.tw.

28 tto.tw.

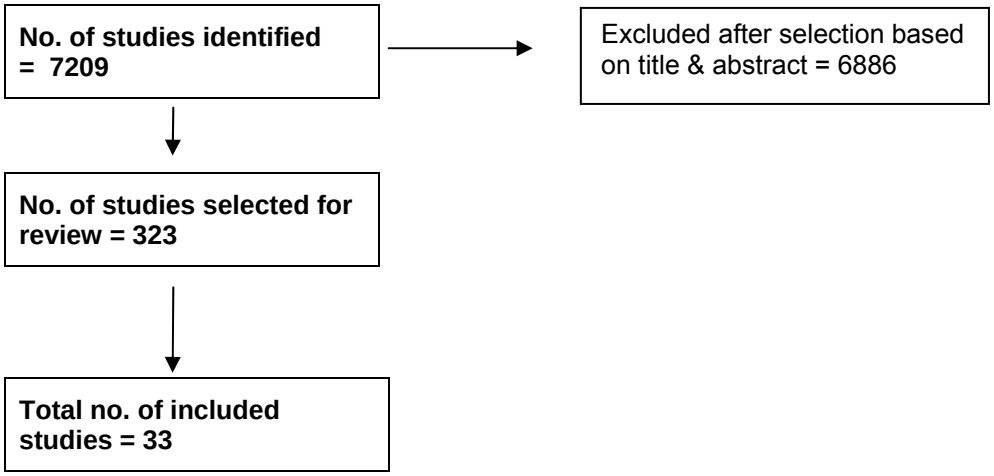
29 or/1-28

5.4 Appendix 4 – Evidence Flow Charts and Evidence Tables

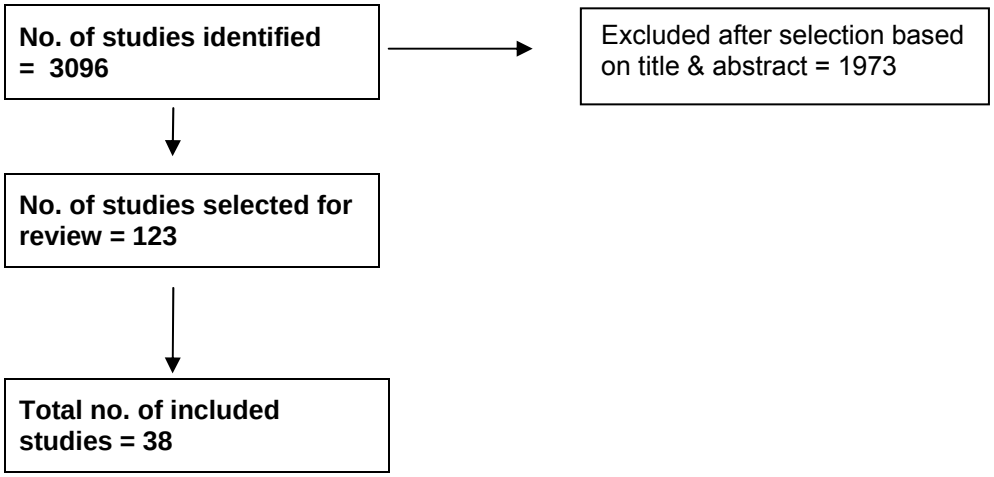
Flowchart figures

This initial search was a very broad search which used infective endocarditis as the main search term. The consideration of the titles and abstracts from this search yielded a large number of papers which included those which would be relevant to the consideration of the risk/outcomes of developing IE with cardiac conditions but also included papers which it was identified would be appropriate for other sections under consideration in this guideline.

Initial search – infective endocarditis search and including risk and outcomes

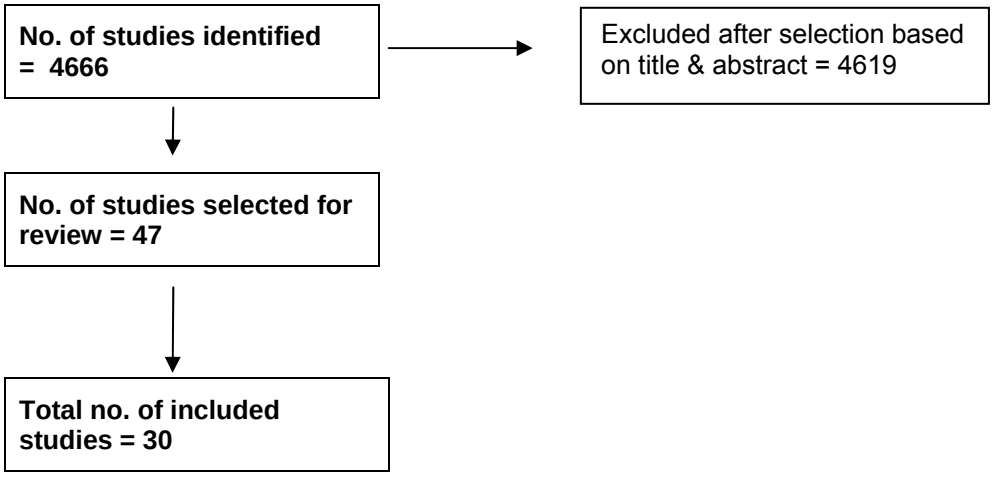


Bacteraemia and interventional procedures.



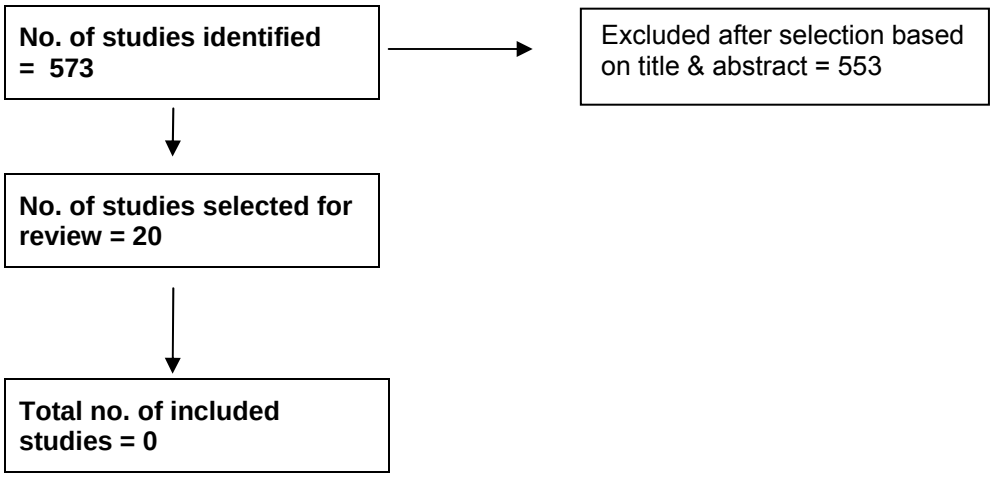
The third search was devised in consideration of antibiotic prophylaxis against IE.

Antibiotic prophylaxis



The final search was devised to consider patient perspectives on prophylaxis against IE.

Patient perspectives



Evidence Tables

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Al Karaawi ZM, Lucas VS, Gelbier M, Roberts GJ. Dental procedures in children with severe congenital heart disease: A theoretical analysis of prophylaxis and non-prophylaxis procedures. *Heart* 2001;**85**:66-8. Ref ID: 3435	retrospective theoretical analysis	Between June 1993 to June 1998 at GOSH and from January to June 1998 at Eastman Dental Hospital N=136 (N=133 GOSH and N=3 EDH) UK	Records of children with severe congenital disease and from the case records of a dento-gingival manipulative procedure	Prophylaxis procedures[1]	Non-prophylaxis procedures[2]	5yrs from GSOH and 6mths at EDH	Cumulative exposure derived from the equation: intensity x tally x prevalence x duration = cumulative exposure in cfu/ml/procedure/yr Intensity is the number of colony forming units (cfu)/ml blood[3] Tally is the average number of a given dento-gingival manipulative procedure performed annually[4]	Not stated

[1] According to the guidelines of the endocarditis working party of the British Society of Antimicrobial Chemotherapy (1993) and the American Heart Association (1997)
[2] According to the guidelines of the endocarditis working party of the British Society of Antimicrobial Chemotherapy (1993) and the American Heart Association (1997)
[3] Derived from several sources
[4] Derived solely from this study

							Prevalence is the number of positive cultures expressed as a proportion[5], for purposes of calculation, a percentage prevalence is converted to a proportion (e.g. 38% = 0.38) Duration is the length of bacteraemia, which is 15mins	

[5] Derived from several sources

Effect size:

Cumulative exposure
The theoretical cumulative exposure was expressed as the number of colony forming units/ml blood/minute in the standardised year[6]
The greatest cumulative exposure was for the placement of a rubber dam and the smallest was from a single primary tooth extraction

Prophylaxis procedures		***Non-prophylaxis procedures***	
Scaling	1.685	Dental examination	1.999
Single extraction primary tooth	0.059	Polishing teeth	16.410
Single extraction permanent tooth	0.685	Local anaesthetic infiltration	4.925
Multiple extractions – primary & permanent	51.775	Rubber dam placement with clamps	8210.970
Mucoperiosteal surgery	18.428	Slow drill	0.993
		Fast drill	1.904
		Matrix band placement	2.7648

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Allan WR, Kumar A (1985) Prophylactic mezlocillin for transurethral prostatectomy. British Journal of Urology 57:	RCT [7]	N=100 UK	Inclusion: undergoing transurethral prostatectomy Exclusion: allergy to penicillin, known UTI, had received antibiotics in the week before surgery There was NS difference between the groups	N=50 mezlocillin Blood samples: immediately after the operation, first post-operative day, at removal of urethral catheter	N=50 placebo Blood samples: immediately after the operation, first post-operative day, at removal of urethral catheter		Bacteraemia	Bayer Company

[6] As some individual's records covered less than a year or several years the number of times a dento-gingival manipulative procedure was carried out was standardised on a year

46-9.								

Effect size:

Bacteraemia
After completion of operation N=2, 4% mezlocillin, N=16, 36% control, p<0.001
First day post-op and after removal of catheter NS difference between the groups
Progressed to septicaemia in N=4 patients, but in no cases where prophylactic cover was given

Catheter
N=8 mezlocillin and N=15 control had a pre-op catheter, 12% (N=1/8) mezlocillin and 33% (N=5/15) control had a positive blood culture

If there was a pre-op infected urine bacteraemia was likely to follow the operation, in N=7/8 in the control group and N=1/2 in the mezlocillin group
Of those who developed bacteraemia 94% also developed infection in the urine

Organisms isolated
Mezlocillin group; blood (E. coli, Bacteroides fragilis), urine (E. coli, Proteus, Enterococci, Staphylococcus aureus, Sthapylococcus albus)
Control group; blood (E. coli, Proteus, Enterococci, Staphylococcus aureus, Sthapylococcus albus, Streptococcus faecalis), urine (E. coli, Proteus, Pseudomonas, Enterococci, Staphylococcus aureus, Sthapylococcus albus, Streptococcus faecalis)

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Anderson DJ, Olaison L, Mcdonald J et al.	Case series	N=159	Inclusion: data collected by the International Collaboration on Endocarditis-Merged Endocarditis Database (ICE-MD)[8], a large	N=45 prosthetic valve endocarditis	N=114 native valve endocarditis		Patient characteristics, complications of IE, outcomes of	Not stated

[7] Allocated by coded sealed letter from Bayer Co, opened by the anaesthetist when the patient came to the theatre
[8] Databases originated in locations in the USA (2 locations) and Europe (Spain, France, Sweden, UK)

(2005) Enterococcal prosthetic valve infective endocarditis: report of 45 episodes from the International Collaboration on Endocarditis-merged database. Eur J Clin Microbiol Infect Dis. 24: 665-70			multinational study of IE; IE was defined according to the Duke Criteria				IE due to enterococci	

Effect size:

Characteristics
N=159 (7.2%) cases with definite enterococcal IE occurred among the N=2212 patients with definite IE in the merged database , Enterococcus faecalis accounted for 94%
N=45 involved a prosthetic valve; N=114 involved native valves

Outcomes
Those with enterococcal PVE were more likely to have intracardiac abscesses vs. NVE, p=0.009
Those with enterococcal NVE were more likely to have detectable vegetations vs. PVE, p<0.001
There was NS difference between the groups with respect to valvular location of infection

Rates of complications/outcomes were NS different between the groups:
- heart failure; PVE N=17/45 (38%); NVE N=54/114 (47%)
- all embolisation; PVE N=9/45 (20%); NVE N=31/114 (27%)

- central nervous system; PVE N=5/42 (12%); NVE N=12/100 (12%)
- stroke; PVE N=3/41 (7%); NVE N=9/102 (9%)
- valvular surgery this episode; PVE N=14/45 (31%); NVE N=35/114 (31%)
- death (during hospitalisation); PVE N=6/43 (14%); NVE N=14/114 (12%)

N=46/296 (16%) cases of PVE were definite nonenterococcal
Those with enterococcal PVE were similar to those with nonenterococcal PVE for clinical characteristics, rates of complications and echocardiographic characteristics
Mortality was NS higher in those with nonenterococcal PVE

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding

Barawi M, Gottlieb K, Cunha B, Portis M, Gress F. A prospective evaluation of the incidence of bacteremia associated with EUS-guided fine-needle aspiration. *Gastrointestinal Endoscopy* 2001;**53**:189-92. Ref ID: 411	Pilot study, case series	N=100 (N=108 sites aspirated) USA	Inclusion: those undergoing endoscopic ultrasound (EUS)- guided fine needle aspiration (FNA), mean age 65.5yrs (range 34 to 94yrs), most common reason was for evaluation of pancreatic mass Exclusion: conditions for which the American Society for Gastrointestinal Endoscopy or AHA guidelines recommend antibiotic prophylaxis , antibiotic use within 1 week before procedure, a requirement for dilation of a stricture or stenosis of the GI tract within 24 to 48hrs or immediately before EUS-guided FNA, the presence of a cystic lesion, advanced liver disease or HIV/AIDS	EUS-guided FNA 200 sets of blood cultures Blood samples: 30 and 60mins after the last EUS-guided FNA		1wk	Blood cultures Microbiological techniques: 10ml of blood drawn at each sample time point and were injected into commercially available aerobic/anaerobic blood culture bottles, cultures were incubated for 7days and 37.5˚C	Not stated
Effect size: **Blood cultures** In the 200 sets of blood cultures, in these incubated blood cultures there was no significant bacterial growth except in N=6 patients in whom coagulase negative Staphylococcus grew in 1 of 2 bottles (these 6 positive blood cultures were considered due to contaminants) There was no infectious complication reported by any subjects or the referring physicians at 1 week after the procedure								

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding

Barragan Casas JM, Hernandez Hernandez JM, Garcinuno Jimenez MA, Gonzalo Molina MA, Carbonero DP, Ibanez R *et al*. Bacteremia cased by digestive system endoscopy. *Revista Espanola de Enfermedades Digestivas* 1999;**91**:111-6. Ref ID: 1680	Randomised, prospective study	N=102 Single hospital site, Spain	Inclusion: random selection from all patients scheduled for endoscopic examination (gastroscopy, sigmoidoscopy or colonoscopy, or ERCP) in a hospital in Spain, regardless of reason for admission, N=55 male, N=47 female, mean age 59.6±16yrs (range 16 to 87yrs) Exclusion: febrile syndrome before the endoscope, prior treatment with antibiotics, bacterial growth in the blood sample obtained before the examination, incomplete blood sampling, emergency endoscopic examination	N=44 gastroscopy N=30 colonscopy N=28 ERCP	Blood samples: baseline and 5 and 30min after the start of the procedure, in most cases this meant that blood samples were obtained while the examination was still in progress	16mths	Blood cultures Microbiology: Blood samples were incubated in aerobic (ESP 80A) and anaerobic blood culture bottles (ESP 80N, Difco) and processed with habitually used techniques, cultures were considered negative with no signs of growth at 6days	Not stated
Effect size: **Gastroscopy** Blood cultures were positive in N=11/44 (25%) with Staphylococcus spp and Streptococcus spp isolated, in N=8 (72.7%) the 5min sample was positive, N=6 (54.5%) the 30min was positive, N=2 (18.1%) both cultures were positive, N=1 patient had polymicrobial growth in one sample The most frequent endoscopic findings were hiatus hernia with varying degrees of oesophagitis (N=4) and peptic ulcer (N=4) **Lower digestive tract endoscopy**								

Blood cultures were positive in N=3/30 (10%) all in the 5min samples, N=1 was also positive in the 30min sample

ERCP
Blood cultures were positive in N=11/28 (39.2%) with Escherichia coli, Morganella morganii, Staphylococcus spp and Streptococcus spp were isolated, in N=4 (36.3%) the 5min sample was positive, N=9 (81.8%) the 30min was positive, N=2 (18.1%) both cultures were positive, N=1 culture was positive for more than one microorganism
The most frequent endoscopic finding was biliary-pancreatic tree disease (N=8)

(endoscopic examination frequently causes bacteraemia, generally due to saprophytic gram-positive microorganisms of the skin and mucosa)

Antimicrobial sensitivity
The microorganisms found most frequently were Staphylococcus spp and Streptococcus spp, antimicrobial sensitivity of these pathogens was; vancomycin 100%, rifampicin and amikacin 96.5%, gentamicin 93.1%, cefotaxime 89.6%, etercyclines 79.3%, ciprofloxacin, erythromycin, clindamycin and trimethoprim 75.8%, amoxicillin-clavulanic acid 68.9%, ampicillin 55.1%
Enterobacteria and Gram-negative microorganisms were sensitive to amikacin, gentamicin and ciprofloxacin in all N=3 patients

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding

Benn M, Hagelskjer LH, Tvede M. Infective Endocarditis, 1984 through 1993: A clinical and microbiologi cal survey. *Journal of Internal Medicine* 1997;**242**:15-22	Retrospe ctive review	N=59 patients N=62 episodes of IE Denmark	Patients were identified from hospital discharge statistics, the study used von Reyn's diagnostic criteria Mean age 55.4yrs, median age 60.7yrs (range 14.5-82.9) The mean age was 50.8yrs for males and 65.9yrs for females Male/female ratio was 1:4			10yr review, between 1st January 1984 to 31st December 1993	Incidence, predisposing factors, complications	Not stated

Effect size:

Incidence
62 episodes in N=59 patients (40 definite, 16 probable, 6 possible)
The overall incidence was 27 episodes per million per year, for native valve IE was 23.5 episodes per million per year.
The overall incidence increased from 17.4 to 36.5 episodes per million per year from the first part to the second part of the decade ($p<0.001$)
(The authors identified concerns about the quality of the data with a retrospective study and also noted that the main reason for increased incidence is probably due to the unmasking of more episodes of IE)

Predisposing factors
From N=62 total number of episodes, N=41 (66.1%) had identified predisposing factors, with N=21 episodes without predisposing factors

Congenital heart disease – total	***7***	***Acquired heart disease – total***	***34***
Aortic stenosis	2	Aortic valve prosthesis	6
Aortic, mitral and triscuspid regurgitation	1	Mitral valve prosthesis	2
Floppy mitral valve	1	Pacemaker & mitral valve prosthesis	1
Fistula in septum	1	Aortic regurgitation	5
Ebstein's anomaly	1	Aortic stenosis	6

Transposition of great arteries & VSD	1	Mitral stenosis	8
		Mitral stenosis, rheumatic	3
		Aortic stenosis, rheumatic	3

For N=11 already known portals of entry were found (an intravenous catheter; impetigo; erysipelas; bursitis; two episodes of septic arthritis; UTI; GI tract infection)

N=2 patients had recorded surgical treatment in the 3mths prior to admission

None of the episodes had recorded dental treatment as the portal of entry (The authors noted that there is a high level of dental hygiene and a high focus on prophylaxis in Denmark)

Complications
There was no difference in the relative risk of embolism between the aortic and mitral valve IE and between the native and prosthetic valve IE.
Mortality was N=22/62 episodes, 35.5% overall.

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Bhanji S, Williams B, Sheller B, Elwood T, Mancl L, Bhanji S *et al*. Transient bacteremia induced by toothbrushing a comparison of the Sonicare toothbrush with a conventional toothbrush.	RCT Not blinded	N=50 children Children's hospital & regional medical centre, USA	Inclusion: between the ages of 2 and 6yrs, had no medical conditions requiring antibiotic prophylaxis for dental treatment, had not received antibiotic therapy within the past 30days, had no sinus tracts associated with dental abscesses, had no conditions altering alveolar ridge or gingival anatomy Exclusion: positive blood cultures before toothbrushing	N=25 Teeth brushed for a timed one-minute interval manually Blood cultures taken 30 seconds after	N=25 Teeth brushed for a timed one-minute interval with the Sonicare electric toothbrush (high frequency brushing, 31,000 brush strokes per minute) Blood cultures taken 30 seconds after		Gingival health and plaque scores were determined for participants Positive blood cultures Microbiology: 10ml drawn per sample, divided into 3ml into an aerobic vial and 7ml into an anaerobic vial, vials were incubated for	Washington Dental Service Foundation, Phillips Oral Healthcare Corporation

Pediatric dentistry 2002;**24**:295-9. Ref ID: 829				toothbrushing	toothbrushing		5days using BacTec9240, positive vials were gram stained, isolated on agar media and analysed	
Effect size: **Positive blood cultures** Toothbrushing resulted in positive blood cultures in N=11/24 (46%, 26 to 66%, 95% CI) of manual and N=18/23 (78%, 62 to 95%, 95% CI) of Sonicare participants, p=0.022 Gingival score There was no significant difference in gingival health and plaque scores between the 2 groups. Analysis which controlled for plaque and gingival scores indicated that bacteraemia levels were higher in the Sonicare group (OR 6.6, p=0.013) There was NS difference in the rate of bacteraemia in those with normal gingiva and those with mild inflammation and there was no relationship between plaque scores and bacteraemia								

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Bhattacharya S, Parkin DE, Reid TM et al. (1995) A prospective randomised study of the	RCT [9] [10]	N=116 ITT analysis UK	Inclusion: women with menorrhagia undergoing either transcervical resection (TCRE) or laser ablation of the endometrium (ELA)	N=55 1.2g augmentin IV at the induction of anaesthesia Blood samples: immediately	N=61 No antibiotic	Discharged same or following day, given a diary to record events over the next	Blood cultures, infectious morbidity Blood culture bottles incubated in a non-	Chief Scientists Office of the Scottish Office

[9] Randomised by the opening of sealed opaque envelopes
[10] Study had 80% power to detect a difference of 15%, from 1% to 16% at the 5% significance level

effects of prophylactic antibiotics on the incidence of bacteraemia following hysteroscopic surgery. European Journal of Obstetrics, Gynecology, & Reproductive Biology 63: 37-40				after the routine TCRE or ELA		2wks	radiometirc Bactec 860 analyser at 37C for 5days	
Effect size: **Blood cultures** N=6/61 ELA compared with N=5/55 TCRE N=10 (16%) positive blood cultures in the no antibiotic group compared with N=1 (2%) in the antibiotic group, p<0.02 **Infectious morbidity** No antibiotic; pain (N=26, 43%); offensive discharge (N=14, 23%); fever (N=4, 7%); visit to GP (N=11, 18%); antibiotics prescribed by GP (N=7, 11.4%) Antibiotic; pain (N=29, 53%); offensive discharge (N=14, 26%); fever (N=9, 16%); visit to GP (N=11, 20%); antibiotics prescribed by GP (N=5, 9%) None of the participants, regardless of their blood culture status, became seriously ill								

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding

Boggess KA, Watts DH, Hillier SL, Krohn MA, Benedetti TJ, Eschenbach DA *et al*. Bacteremia shortly after placental separation during cesarean delivery. *Obstetrics & Gynecology* 1996;**87**:779-84. Ref ID: 6337	Case series	N=93 USA	Inclusion: women undergoing caesarean delivery, included if they had rupture of membranes and/or labour for at least 4hrs Exclusion: antibiotic use within 7days before delivery, medical conditions requiring antibiotic treatment during labour, temperature greater than 38C	Blood samples: within 15mins of delivery of the placenta in women undergoing caesarean without labour; within 5mins in women undergoing caesarean after labour		30th July 1985 to 31st July 1986 and 1st October 1993 to 30th September 1994	Blood cultures Microbiology: 10ml per sample, stored at room temperature, inoculated into trypticase-soy yeast broths that were incubated aerobically and anaerobically. Cultures were incubated at 37C, blind cultures were performed from the trypticase-soy yeast bottle at 24hrs and 5days and from the anaerobic bottles at 48hrs and 7days	Not stated

Effect size:

Blood cultures
Bacteraemia occurred in N=13/93 (14%) of women after labour or rupture of membranes, N=6/13 also had positive chorioamnionic membrane cultures, N=5 of these were at ≤32 weeks gestation or less, gestational age of 32 weeks or less was strongly associated with a positive chorioamnionic placental culture

A positive blood culture was associated with earlier median gestational age at delivery (<32 weeks, OR 13.9; 3.5 to 54.8, 95%CI); lower median birth weight (less than 2500g, OR 10.5; 2.8 to 39, 95%CI) and positive chorioamnionic membrane culture (OR 6.4; 1.7 to 24.7, 95%CI)

After adjustment for hours of membrane rupture, hours of labour and intrauterine monitoring; median gestational age and positive chorioamnionic membrane culture remained significantly associated with bacteraemia

After adjustment for gestational age, intrauterine monitor use (OR 9.7; 6.5 to 40.8, 95%CI) and positive chorioamnionic membrane culture (OR 4.4; 1.6 to 26.7 95%CI) were significant predictors of bacteraemia

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Bouza E, Menasalvas A, oz P, Vasallo FJ, Del Mar MM, Garcia Fernandez MA. Infective endocarditis - A prospective study at the end of the twentieth century: New predisposing conditions, new etiologic agents, and	Prospectiv e case series	N=101 (N=109 episodes of IE) Spain	All cases followed by an infectious diseases consultant All cases fulfilled 1 or more of criteria of: clinical suspicion; echocardiographic evidence of IE; bloodstream infections caused by specific organisms; histologic findings N=80 (73%) were male, N=29 (27%) female, male:female ratio was 2.76; mean age 50yrs (range, 19-89)			March 1994 to October 1996	Epidemiology	Not stated

still a high mortality. *Medicine* 2001;**80**:298-307								

Effect size:

Epidemiology
The incidence was 6.4 cases per 100,000 inhabitants per year, 0.8 cases per 1,000 admissions and 3.5% of all cases of significant bacteraemia

Underlying conditions
N=109 episodes of IE (N=39, IVDU), all but N=5 had underlying conditions

Native valve endocarditis	**52**	**Prosthetic valve endocarditis**	**18**
Cardiac diseases	18(34.6%)	Cardiac diseases	18(100%)
Rheumatic valves	6(11.4%)	Valvular prosthesis	18(100%)
Arteriosclerotic valves	4(7.7%)	(previous endocarditis)	3(16.6%)
Mitral prolapse	1(2%)		
Other	7(13.4%)		

Outcome
Related mortality was 25.7%, there was 100% mortality with early PVE (N=6), 25% mortality with late PVE (N=3) and 25% with NVE (N=13)
With multivariate analysis early PVE, the presence of congestive heart failure and acute renal impairment were significantly related to mortality

Valve replacement was required in N=25, N=16(30.7%) of NVE, N=2(33%) with early PVE and N=6(50%) with late PVE.

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Brewster SFM (1995) Antimicrobial prophylaxis for transrectal	RCT	N=111 UK	Inclusion: men undergoing ultrasonically transrectal prostatic biopsy to diagnose or stage carcinoma of the prostate Exclusion: history of penicillin hypersensitivity, prosthetic heart valve,	N=56 1.5g cefuroxime IV over 1-2 mins, 20mins before TPB	N=55 4.5g piperacillin/tazobactam IV over 1-2mins, 20 mins	8hrlt temperature for 4days	Blood cultures, temperature	Not stated

prostatic biopsy: A prospective randomized trial of cefuroxime versus piperacillin/tazobactam. British Journal of Urology : 351-4			heart murmur, rectal stenosis, concurrent antimicrobial therapy, bleeding diathesis, anticoagulant therapy	Blood samples; baseline, 48hr after TRP	before TPB			
Effect size: N=109 evaluable **Clinically unsuccessful outcome** Defined as the presence of symptoms to indicate urinary or systemic sepsis, or pyrexia ≥37.5C after TRB was observed in N=3/56 with cefuroxime and N=5/55 piperacillin/tazobactam **Blood culture positive** N=1 with cefuroxime considered to be septic, urine and blood both grew E coli **Adverse events** N=61/111, N=48 (45%) considered to be drug related, GI events the most common (N=2 cefuroxime and =16 piperacillin/tazobactam mild transient diarrhoea; N=8 piperacillin/tazobactam nausea/vomited once)								

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding

Brown AR, Papasian CJ, Shultz P, Theisen FC, Shultz RE. Bacteremia and intraoral suture removal: can an antimicrobial rinse help? *Journal of the American Dental Association* 1998;**129**:1455-61.	RCT [11]	N=71 (N=10 lost to follow-up) USA	Inclusion: requiring the removal of a third molar which would require at least 8 sutures, N=37 female, aged 15 to 35yrs Exclusion: systemic disease, taking steroids, had used antibiotics or oral rinses within the previous 4wks, moderate-to-severe peridontitis or residual pericoronitis, required preoperative prophylactic antibiotics All used similar flap designs and 3-0 black silk suture placement, used no medication in the sockets, nor did they use preoperative irrigation or rinses, subjects returned for suture removal seven days after the extraction and were randomly assigned to one of two groups	Group I N=31 30 cubic centimetres of 0.12% chlorhexidine preprocedural rinse for 1min Blood samples: baseline, 90sec after suture removal	Group II N=24 no-treatment control		oral hygiene All plates were examined for 7days before negative results were reported, colony counts were performed on media showing growth and organisms identified using morphological criteria and routine bacteriologic methods	Not stated
Effect size: **Bacteraemia** Pre-treatment blood samples were all negative Post-treatment N=4/31 chlorhexidine and N=2/24 control group had positive cultures, total incidence 10.9% (organisms identified: Staphylococcus coagulase negative, Propionibacterium, Staphylococcus aureus, Corynebacterium, Streptococcus sanguis, Bifidobacterium, S. viridans, Micrococcus, S. mitis, Prevotella sp, Peptostreptococcus) There was NS difference in the proportion of bacteraemia with experimental vs. control groups Bleeding on suture removal occurred in N=47/55 patients, none of those in whom bleeding did not occur developed bacteraemia, there was NS relationship between the presence of bleeding after suture removal and the incidence of bacteraemia								

[11] the doctor performing suture removal was unaware of whether or nor a patient had used a rinse; power calculation completed

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Calderwood SB, Swinski LA, Karchmer AW et al. (1986) Prosthetic valve endocarditis. Analysis of factors affecting outcome of therapy. Journal of Thoracic & Cardiovascular Surgery 92: 776-83	Case series	N=116 USA	Inclusion: diagnosis of PVE based on a strict case definition, mean age 59.6±10.7, median 60.5yrs (range (21 to 79yrs), [12]			Study period 1st January 1975 to 31st December 1982 Mean follow-up 20.2mths (range 0.5 to 79mths)	Factors associated with complicated PVE, medical-surgical therapy, mortality	Not stated
Effect size: **Factors associated with complicated PVE** N=74/116 (64%) had complicated PVE Logistic regression models of complicated PVE in a single vale recipient showed aortic valve infection, early onset of IE to be factor associated with complicated								

[12] Complicated PVE was defined as infection associated with any of the following; a new or increasing murmur of prosthetic valve dysfunction; new or worsening CHF related to dysfunction of the prosthesis; fever doe 10days or more days during appropriate antibiotic therapy; new or progressive abnormalities of cardiac condition
Relapse – if infection occurred in the 12mths after hospital discharge and either was caused by the same organism or else no pathogen was identified

infection

Factors associated with medical-surgical therapy for PVE[13]
N=45/115 (39%) received medical-surgical therapy
Logistic regression identified three factors as associated with a decision foe medical-surgical therapy; complicated PVE, infection with coagulase negative staphylococci, infection of a single prosthesis (may reflect bias against operating on those with multiple prosthesis

Factors associated with mortality of PVE
N=27/116 (23%) died during initial hospitalisation for the treatment of PVE
Logistic regression showed complicated PVE to be the best predictor of mortality
The mortality rate was significantly lower in those with coagulase-negative staohylococci (OR<1)
None of the other variables exerted an independent effect on mortality from PVE

Follow-up
N=89 survived hospitalisation, on discharge N=71 had no or mild CHF, N=13 moderate and N=5 severe
The presence of moderate to severe CHF on discharge affected survival after therapy compared to no or mild CHF (p=0.03)
NS effect on mortality after discharge; position of the infected valve, porcine vs. mechanical prosthesis, patient sex, medical vs. medical-surgical therapy

N=11/89 (12%) relapsed; NS difference in medical vs. medical-surgical treatment
Valve site originally infected or infecting organism did not affect relapse rate

N=14/56 (25%) who had had medical therapy vs. N=2/33 (6%), p=0.04, who had had medical-surgical therapy required an operation for late sequelae of infection (other than relapse)

Including death, relapse of PVE and subsequent cardiac operation for late sequelae of infection as bad outcomes of initial therapy; the medical group showed significantly worse outcome than those who had medical-surgical therapy (p=0.02)
NS influence were patient sex, position of infected valve, porcine vs. mechanical prosthesis, infecting organism and early vs. late onset

Analysis of outcome of complicated PVE
Survival of patient with complicated PVE without the need for additional therapy was more frequently found with initial medical-surgical vs. medical therapy (p=0.008)

[13] Medical-surgical therapy was considered to be where patient underwent repair or replacement of the infected prosthesis during the initial hospitalisation for treatment of PVE

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Cecchi E, Forno D, Imazio M, Migliardi A, Gnavi R, Dal C, I *et al*. New trends in the epidemiological and clinical features of infective endocarditis: results of a multicenter prospective study. *Italian Heart Journal: Official Journal of the Italian Federation of Cardiology* 2004;**5**:249-56	Prospective multicentre survey	N=147 cases Italy	Patients with a definite diagnosis of IE in a region of Italy, diagnosis was based on Duke University criteria and 3-mth follow-up data These cases constituted the samples population for the purposes of this study			January 2000 to December 2001	Predisposing heart disease	Not stated

Effect size:

Predisposing heart disease
N=104/147 considered to be related to predisposing heart disease

Prosthetic valves	**37(25%)**	Aortic insufficiency	6
Native valves	**67(45%)**	Mitral insufficiency	3
Mitral valve prolapse	25	Mitral & aortic insufficiency	5
Aortic stenosis	5	Bicuspid aortic valve	8
Aortic stenosis & insufficiency	6	Interventricular septal defect	1

Mitral stenosis	2	Previous mitral valvuloplasty	2
Mitral stenosis & insufficiency	3	Aortic valve sclerosis	2

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Choudhury R, Grover A, Varma J, Khattri HN, Anand IS, Bidwai PS *et al*. Active infective endocarditis observed in an Indian hospital 1981-1991. *AM J CARDIOL* 1992;**70**:1453-8	Retrospective review	N=186 patients (N=190 episodes of IE) India	Data from patient records at a hospital in Northern India, diagnostic criteria: vegetation on echocardiography; ≥2 positive blood cultures growing the same organism with ≥2 specified clinical features N=133 males, N=53 females, mean age 25±12yrs SD (range 2-75yrs)			January 1981 to July 1991	Underlying heart disease, outcomes	Not stated

Effect size:

Underlying heart disease

N=190 episodes (N=186 patients) of IE, underlying heart disease (rheumatic heart disease N=79(42%), normal N=17(9%))

Congenital heart disease - total	**62(33%)**	**Uncertain aetiology**	**24(13%)**
Bicuspid aortic valve	25	Aortic regurgitation	15
VSD	15	Mitral regurgitation	9

Patent ductus arteriosus	7		
Tetralogy of Fallot	3	**Prosthetic valves**	**2(1%)**
Ruptured sinus of Valsalva	3	**Mitral valve prolapse**	**2(1%)**
Double-outlet right ventricle	2		
Aortic stenosis	2		
Pulmonary stenosis	2		
Atrial septal defect	2		
Coronary AV fistula	1		

Outcome
For those with congenital heart disease N=11(23%) died and N=53(38%) recovered
For those with mitral valve prolapse N=2 recovered

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Chu J, Wilkins G, Williams M, Chu J, Wilkins G, Williams M. Review of 65 cases of infective endocarditis in Dunedin Public Hospital. *New Zealand Medical Journal* 2004;**117**:U1021	Case review	N=62 patients N=65 episodes	IE diagnosed using the Duke criteria, N=42 male, N=20 female; mean age 65.0±18.1yrs (range 7-89yrs)			5years November 1997 to October 2002	Underlying heart disease, outcome	Not stated
Effect size:								

Underlying heart disease
N=65 episodes (N=62 patients) of IE, predisposing heart conditions (normal valves N=25; 40.3%)

Congenital heart disease – total	**8**	**Acquired heart disease – total**	**29**
Bicuspid aortic valve	5(8.1%)	RHD with mitral stenosis	1(1.6%)
Tetralogy of Fallot *	1(1.6%)	Aortic stenosis	8(12.9%)
Transposition of Great Arteries *	1(1.6%)	Mitral valve prolapse	4(6.5%)
Abnormal pulmonary valve	1(1.6%)	Prosthetic valves	15(24.2%)
		Automated implantable cardioverter defibrillator	1(1.6%)

*post repair

Outcome
Mortality for those with NVE was N=11/20(55.0%), N=33/42 (78.5%) recovered
Mortality for those with PVE was N=6/20 (30.0%), N=6/42 (14.3%) recovered

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Clemens JD, Horwitz RI, Jaffe CC, Feinstein AR, Stanton BF, Clemens JD *et al*. A controlled evaluation of the risk of	Case-control	N=204	Inclusion: hospital inpatients who had undergone echocardiography and who lacked any known cardiovascular risk factors for endocarditis apart from mitral valve prolapse and isolated mitral-regurgitant murmurs; age ≥15yrs at the time of hospital admission[14] Inclusion: cases: data extracted from medical records, who fulfilled the diagnostic and/or pathological criteria for	N=51 cases	N=153 control group Similar for age, sex and prevalence of white patients	4yrs of cases Between 1st Nov 1976 to 1st Nov 1980	Mitral valve prolapse	Not stated

[14] The one exception was the inclusion of those with antecedent findings of isolated mitral regurgitation, since mitral valve prolapse is commonly accompanied by auscultatory findings of mitral regurgitation
[15] The eligibility of patients was determined by a 'blinded' researcher, without knowledge of the echocardiograph findings

bacterial endocarditis in persons with mitral-valve prolapse. *N ENGL J MED* 1982;**307**:776-81. Ref ID: 1272			bacterial endocarditis Exclusion: cases: antecedent heart disease acting as a risk factor for endocarditis; discharge diagnosis referable only to episodes occurring in previous admissions; inadequate diagnostic evidence of BE; no echocardiogrem Inclusion: controls: selected from those who had undergone echocardiography during the period covered by the study; matched with age, sex and nearest date of echocardiography (excluded those with antecedent heart disease) Exclusion: controls: antecedent heart disease acting as a risk factor for endocarditis; medical records not located MVP was defined by either auscultatory or echocardiographic data The 2 groups were similar in age and sex, the cases groups had higher proportions of those with a history of parenteral drug use, recommendations for prophylaxis before instrumentation and high-risk cardiovascular lesions that were unsuspected before echocardiogaraphy, adjustment was made for these inequalities 15					

Effect size:

Mitral valve prolapse
N=13 (25%) of the cases and N=10 (7%) of the controls had mitral valve prolapse
In 16 matched sets, the cases and controls were discordant for the presence or absence of mitral-valve prolapse; the matched OR for the association was 8.2 (2.4 to 28.4, CI 95%), p<0.001

Analysis was completed using only the echocardiographic criteria for MVP (the association was unaffected) and also to adjust for risk factors for endocarditis that were unequally distributed between the cases and the controls (the association remained substantial for both addicts and non addicts).

(the authors consider that these results demonstrate a substantial association between MVP and BE)

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Danchin N, Voiriot P, Briancon S, Bairati I, Mathieu P, Deschamps JP *et al*. Mitral valve prolapse as a risk factor for infective endocarditis. [see comment]. *Lancet* 1989;**1**:743-	Case-control	N=144 France	Inclusion: cases; records of all those with bacterial endocarditis admitted to cardiology and cardiovascular surgery Bacterial endocarditis considered present in those with pathological evidence of endocarditis at operation or necropsy; or if the patients had fever and 2 major diagnostic criteria; or fever with 1 major and 3 minor diagnostic criteria. All had ≥1 echocardiography, only those with echocardiographic evidence of mitral valve endocarditis were entered into the study Exclusion: cases; endocarditis of the	N=48 cases	N=96 controls, matched for age and sex[16]	Between 1st Jan 1981 to 31st March 1986	Mitral valve prolapse, risk of BE	Not stated

[16] Mitral valve prolapse diagnosed by echocardiography

5. Ref ID: 7167			aortic valve or of one of the right sided valves without mitral valve endocarditis or endocarditis on a mitral valve prosthesis Controls; 2 groups; a random sample of N=71 under 60yrs, who were examined echocardiographically during routine family screening who attended between 5th to 16th January 1987; and N=25, over 60yrs, randomly selected from patients admitted for surgery of the limbs					

Effect size:

Frequency of mitral valve prolapse[17]
Cases; N=9 (19%) of the N=48 with mitral valve endocarditis had mitral valve prolapse
(the characteristics of the patients with or without mitral valve prolapse identified that these groups did not differ significantly in the infective organism)
Controls; N=6 (6%) of the N=96 controls had echocardiographic evidence of mitral valve prolapse
Mitral valve prolapse identified in x3 in those with IE (19%) than those without (6%), this increased to x14 for those with mitral valve prolapse and a previously recognised systolic murmur

Risk of bacterial endocarditis
Whole group:
All MVP; cases N=9, controls N=6, OR 3.5 (1.1 to 10.5, 95%CI)
MVP with systolic murmur; cases N=7, controls N=1, OR 14.5 (1.7 to 125, 95%CI)
MVP without systolic murmur; cases N=2, controls N=5, OR 1.0 (0.2 to 5.5, 95%CI)

Excluding those with rheumatic heart disease:
All MVP; cases N=9/48, controls N=6/96, OR 5.7 (1.8 to 18.4, 95%CI)
MVP with systolic murmur; cases N=7/41, controls N=1/91, OR 27.4 (3.1 to 239, 95%CI)
MVP without systolic murmur; cases N=2/41, controls N=5/95, OR 1.6 (0.3 to 8.7, 95%CI)

(author conclusion: only those with mitral valve prolapse and systolic murmurs are at increased risk of IE and may need antibiotic prophylaxis)

Reference	Study type/	Number of	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of

[17] The authors note that the frequency of mitral valve prolapse in the general population varies according to the diagnostic criteria used

	Evidence level	patients						funding
Diz DP, Tomas C, I, Limeres PJ, Medina HJ, Fernandez FJ, Alvarez FM. Comparative efficacies of amoxicillin, clindamycin, and moxifloxacin in prevention of bacteremia following dental extractions. *Antimicrobial Agents & Chemotherapy* 2006;**50**:2996-3002.	RCT [18]	N=221 Spain	Inclusion: patients who for behavioural reasons underwent dental extractions under GA, 57% male, 43% female, mean age 24.9±5.7yrs (range 18 to 57yrs) Exclusion: under 18yrs, antibiotics in the previous 3mths, routine use of oral antiseptics, history of allergy or intolerance to amoxicillin, clindamycin or moxifloxacin, any type of congenital or acquired immunodeficiency, any known risk factor for BE There was NS difference in age, sex, oral health grade and number of dental extractions between the four groups	N=56 2g amoxicillin N=54 600mg clindamycin N=58 400mg moxifloxacin	N=53 control Blood samples: baseline, 30secs, 15min and 1hr after dental extraction	January 2003 to December 2004	Bacteraemia Resistance 829 pairs of blood cultures were processed in a BACTEC 9240 instrument, a gram stain was performed on each positive blood culture, the positive blood cultures in the aerobic media were subcultured on blood agar and chocolate agar and on MacConkey agar, in the anaerobic media subcultured on Schaedler agar	Xunta de Galicia of Spain

[18] randomisation not specified; power calculated

Effect size:

Oral health scale grades 0 and 1 (N=46, 21%), grade 2 (N=84, 38%), grade 3 (N=91, 41%)
Median number of teeth extracted per patient N=4

Bacteraemia
At baseline; control group (9.4%), amoxicillin (5%), clindamycin (12.5%), moxifloxacin (7.5%)

At 30sec; control group (96.2%) vs. amoxicillin (46.4%), p<0.001, vs. moxifloxacin (56.9%), p<0.001, vs. clindamycin (85.1%), NS. Amoxicillin vs. clindamycin (p<0.001) moxifloxacin vs. clindamycin (p≤0.001)

At 15min; control group (64.2%) vs. amoxicillin (10.7%), p<0.001, vs. moxifloxacin (24.1%), p<0.001, vs. clindamycin (70.4%), NS. Amoxicillin vs. clindamycin (p<0.001) moxifloxacin vs. clindamycin (p<0.001)

At 1hr; control group (20%) vs. amoxicillin (3.7%), p≤0.01, vs. moxifloxacin (7.1%), p<0.05, vs. clindamycin (22.2%), NS. Amoxicillin vs. clindamycin (p<0.01) moxifloxacin vs. clindamycin (p<0.05)

Overall there were significant differences in the percentages of positive blood cultures between the control group (47.8%) vs. amoxicillin (17.5%) and vs. moxifloxacin (25.5%), p<0.001, but not vs. clindamycin (50%)

There was a significant difference in the proportion of polymicrobial blood cultures in the control group (29%) vs. amoxicillin (0%) p<0.001, vs. moxifloxacin (14.8%) p<0.05, NS vs. clindamycin (31.7%)

Most frequent in the positive blood cultures was Streptococcus (63.1%), followed by Staphylococcus (11.3%) and Neisseria (7.5%)

Of the Streptococcus spp 1.5% were highly resistant to penicillin, 0.8% to ampicillin, 0.8% to amoxicillin, 45.9% to erythromycin, 22.6% to clindamycin

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding

Duval X, Alla F, Hoen B, Danielou S, Larrieu F, Delahaye F *et al*. Estimated risk of endocarditis in adults with predisposing cardiac conditions undergoing dental procedures with or without antibiotic prophylaxis. *Clinical Infectious Diseases.* 2006;**42**:e102-e107. Ref ID: 10629	Epidemiological study France	N=2805 interviewed adults, N=104 native valve PCC N=24 prosthetic valve PCC	Included: 25-84yrs from the French population	To assess the risk of developing IE after an at-risk dental procedure using estimations of: the estimated annual number of IE cases that occur after at-risk dental procedures in adults with known predisposing cardiac conditions (PCC)[19] (numerator)[20] and the annual number of at-risk dental procedures performed in adults with known PCCs (denominator)[21]		1-year study 1999	An estimate of the number of IE cases that would have been prevented during 1-yr if antibiotic prophylaxis had been administered in 100% of cases of at-risk dental procedures	Programme hospitalier de recherché clinique, the federation francaise de cardiologie, Aventis and SmithKilne Beecham Labs

[19] PCC were defined according to the French recommendations for IE prophylaxis
[20] Data used was taken from a 1-yr French epidemiological study on IE in 1999
[21] Sample drawn from 2 studies ongoing in 1998, a structured and previously validated questionnaire was administered by phone interview to classify subjects as having a PCC or not

Effect size:

Prevalence of PCC and number of at-risk dental procedures
N=104 native valve PCC, N=15 of which had undergone an at-risk dental procedure, unprotected in N=12
N=24 prosthetic valve PCC, N=4 of which had undergone an at-risk dental procedure, unprotected in N=2
Applying these to the adult French population, in 1999, resulted in the following estimates: N=1,287,296 (CI; 999,196 to 1,575,396) had a known PCC, corresponding to 3.3% (CI; 2.6 to 4%) of the 39 million adults

In 1999, a total of 2,746,384 at-risk dental procedures (CI; 2,304,094 to 3,188,384) were performed in these adults, a rate of 2.1 procedures per subject per year
N=1,704,195 (62%) of these procedures were performed without antibiotic prophylaxis

Annual number of IE cases after at-risk dental procedures in adults with known PCC
N=12/182 cases of IE that occurred in adults with PCC in the 1999 survey occurred after an at-risk dental procedure and were due to an oral micro-organism (N=10 unprotected)
With the estimated 1370 cases of IE, 714 would have occurred in adults with PCC, 44 attributable to dental procedures (37 without and 7 with antibiotic prophylaxis)

Risk of IE after at-risk dental procedures in adults with known PCC
The estimated risk of IE was:
1 case per 46,000 (CI; 36,236 to 63,103) unprotected at-risk dental procedures
1 case per 54,300 (CI; 41,717 to 77,725) unprotected at-risk dental procedures in adults with native valve PCC
1 case per 10,700 (CI; 6,000 to 25,149) unprotected at-risk dental procedures in adults with prosthetic valve PCC
1 case per 149,000 (88,988 to 347,509) protected dental procedures, a 70% reduction in the risk compared with unprotected procedures

Assessment of IE prophylaxis strategies intact
Using the annual number of procedures and the risk estimates if antibiotics have been administrated in 100% of at-risk dental procedures[22], N=41 cases (CI; 29 to 53) of IE would have been prevented in those with native valve PCC and 39 cases (CI; 11 to 72) in those with prosthetic valve PCC in France in 1999

Estimated incidence of IE
Annual incidence 35 cases per million (CI; 32 to 39) in the entire 25-84yr French population
555 cases per million (CI; 520 to 588) in those with known PCC
980 cases per million (CI; 875 to 1090) in those with known prosthetic valve PCC
460 cases per million (CI; 415 to 500) in those with known native valve PCC
18 cases per million (CI; 16 to 21) in those without known PCC

[22] 2.7 administered antibiotic courses, corresponding to 2,228,545 for those with native valve PCC and 512,829 for those with prosthetic valve PCC

(Author's conclusion: antibiotic prophylaxis reduces the risk of IE after a dental procedure. However, because of the very limited risk of "spontaneous" IE after unprotected dental procedures in adults with known PCCs, a huge number of doses of prophylaxis must be prescribed to prevent a very low number of IE cases)

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Dyson C, Barnes RA, Harrison GA, Dyson C, Barnes RA, Harrison GA. Infective endocarditis: an epidemiological review of 128 episodes.[see comment]. *Journal of Infection* 1999;**38**:87-93	Epidemiological review	N=125 patients N=128 episodes Wales	those within a hospital in Wales, including those transferred from other units for specialised medical/surgical treatment, episodes included where clinical and investigational criteria were met; mean age 53.1yrs, N=87(69.6%) male and N=38(30.4%) female			9years March 1987 to March 1996	Cardiac risk factors, outcome	Not stated

Effect size:

Frequencies of predisposing cardiac risk factors NVE episodes

N=128 episodes (N=125 patients) of IE, predisposing cardiac risk factors for NVE episodes (no identifiable risk factor N=29(37.7%)

Congenital heart lesion	**21(26.9%)**	Mitral valve prolapse	9(11.5%)
Biscuspid aortic valve	13(16.7%)	Rheumatic heart disease	8(11.1%)
Ventricular septal defect	3(3.8%)	Marfan syndrome	2(2.6%)
Congenital aortic stenosis	2(2.6%)		

Complex structural malformation	2(2.6%)		
Hypertrophic obstructive cardiomyopathy	1(1.3%)		

Outcome
Mortality rate 17.2% (N=21)
Mortality rate for PVE, 24.5 % (N=12) and for NVE, 12.3% (N=9)
For early PVE the mortality rate was 30.8%, for late PVE the mortality rate was 22.2%

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
El Baba M, Tolia V, Lin CH, Dajani A. Absence of bacteremia after gastrointestinal procedures in children. *Gastrointestinal Endoscopy* 1996;**44**:378-81. Ref ID: 627	Case series	N=95 (N=108 procedures) Children's Hospital of Michigan, Detroit	Inclusion: requiring gastrointestinal endoscopy, N=43 females, N=52 males Exclusion: receiving or had received antibiotics in the preceding week, none of the patients had fever, chills or clinical evidence of any intercurrent illness prior to endoscopic procedure Those with a specific need for prophylactic antibiotics prior to the procedures were excluded	N=68 oesoagogastro duodenoscopies N=29 colonscopies N=11 flexible sigmoidoscopies	Blood samples: just before endoscopy and within 5mins of withdrawal of the endoscope[23]	October 1992 to October 1993	Blood cultures Microbiology: 2ml per sample, injected into a sterile Dupont isolator 1.5 microbial tube, specimens were processed within 1hr. 0.3ml was inoculated on chocolate agar (4dyas in 5 to 10% Co2 at 37˚C) and 0.3ml on Columbian anaerobic blood agar (6days at	Not stated

[23] An additional blood sample was obtained 5mins after ET intubation but before endoscopy in those who had a GA to assess if the endotracheal intubation may have resulted in bacteraemia

							37˚C). All isolated were identified using standard microbiologic techniques	

Effect size:

Blood cultures
Of the N=236 samples obtained, N=10 from N=9 patients were positive (N=4 pre-endoscopy, N=2 post ET intubation which were negative after endoscopy)
A total of N=4 post endoscopy blood cultures were positive, the organisms isolated were Micrococcus, S.epidermidis, Bacillus sp., diptheroids; all organisms were normal skin flora or environmental contaminants, none were indigenous oropharyngeal or GI flora (Micrococcus and Bacillus species were considered to be contaminants

All those with positive cultures remained afebrile and without any evidence of sepsis during the 72hrs following procedure

The risk of bacteraemia was not affected by the procedure, underlying GI pathology, method of bowel prep, duration of procedure, performance of endoscopic biopsies or ET intubation

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding

Gentry LO, Khoshdel A (1989) New approaches to the diagnosis and treatment of infective endocarditis. Review of 100 consecutive cases 1813. Texas Heart Institute Journal 16: 250-7	Retrospective review, case series	Between 1983 to 1989 N=94 confirmed cases of IE	Medical records of the 100 most recent patients whose discharge diagnosis included IE. Diagnosis of endocarditis was made on the basis of positive blood cultures or other convincing evidence of systemic infection, as well as the lack of an obvious focus for the infection and the presence of significant underlying risk factors for endocarditis.				Special attention was paid to predisposing underlying conditions	Not stated
Effect size: **Valves** N=54 (57%) had NVE, N=40 (43%) had PVE, as the percentage of the population with prosthetic heart valves is much smaller than 43%, prosthetic valves appear to increase the risk of endocarditis								

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Gersony WM, Hayes CJ, Driscoll	Cohort	N=2401 entered into	Those with aortic stenosis (AS), pulomonary stenosis (PS) or ventricular septum defect (VSD), most patients with	N=462 aortic stenosis	N=1,347 VSD with or without aortic	NHS-2 from 1983-1989	Prevalence and incidence,	Not stated

DJ, Keane JF, Kidd L, O'Fallon W *et al*. Bacterial endocarditis in patients with aortic stenosis, pulmonary stenosis, or ventricular septal defect. *Circulation* 1993;**87**:I-121-I-126. Ref ID: 539		NHS-1[24],this study reports on the extended follow-up, NHS-2[25]	severe defects were managed surgically and most with mild defects were managed medically NHS-1 the prevalence of a history of BE was determined, new occurrences were noted and confirmed. NHS-2 all participants were asked about occurrences of BE, all questionnaire items were reviewed by the examining physician and medical and surgical records were reviewed (full details O'Fallon et al, 1993)	N=592 pulmonary stenosis	regurgitation	Overall; 40,855 person-years (average 17.4±8.3 person-years of follow-up per patient) Aortic stenosis; 8,115 person-years (17.9±8.0 person-years) Pulmonary stenosis; 10,688 person-years (18.1±7.8 person-years) VSD; 22,077 person-years (16.4±8.6 person-years)	outcome	
Effect size: (all CI 95%)								

[24] The First Natural History Study of Congenital Heart Defects between 1958-1965
[25] The Second Natural History Study between 1983-1989

Prevalence – on admission to NHS-1
Overall; N=25/2401 had or either had or had experienced BE, prevalence of a history of BE was 104 per 10,000 patients (CI; 67.4 to 153.6)
AS; N=1/462 had or either had or had experienced BE, prevalence of a history of BE was 21.6 per 10,000 patients (CI; 0.5 to 120.6)
PS; N=1/592 had or either had or had experienced BE, prevalence of a history of BE was 16.9 per 10,000 patients (CI; 0.4 to 94.1)
VSD[26]; N=23/1347 had or either had or had experienced BE, prevalence of a history of BE was 170.6 per 10,000 patients (CI; 108.2 to 256.0)

Incidence
Follow-up; N=55 had BE, incidence rate of 13.5 per 10,000 person-years (CI; 10.1 to 17.5)

Aortic stenosis:
N=22 had a diagnosis of BE, incidence rate of 27.1 per 10,000 person-years (CI; 17.0 to 41.0)
Medical management N=7 had BE for an incidence rate of 15.7 per 10,000 person-years (CI; 6.3 to 32.4)
Surgical management N=15 had BE for an incidence rate of 40.9 per 10,000 person-years (CI; 22.9 to 67.4)
Ratio (post-op to nonoperated) is 2.6 (CI; 1.1 to 6.6), this is significantly >1 (p=0.0150), BE is more than twice as likely to be experienced post-op than when medically managed for those with aortic stenosis

The ratio of severity of AS (≥50mmHg vs. <50mmHg, peak systolic gradient) is 12.0 (CI; 4.0 to 43.8), p<0.0001, those with more severe AS are more likely to experience an episode of BE

N=8 cases of BE occurred before a diagnosis of aortic regurgitation and N=14 after; a non-aortic regurgitation rate of 19.8 per 10,000 person-years and a post-aortic regurgitation of 34.3, the difference in these rates was NS

Pulmonary stenosis:
N=1 experienced BE, an incidence rate of 0.9 per 10,000 (CI; 0.02 to 5.2), further analysis not possible due to low incidence.

Ventricular septum defect:
N=32 experienced BE, for an overall incidence rate of 14.5 per 10,000 person-years of follow-up (CI; 9.9 to 20.5)
N=564/1347 had surgical attempts to close the VSD, N=6 developed BE (7.3 per 10,000 person-years CI; 2.7 to 15.9)
N=26 of BE in the nonoperated patients (18.7 per 10,000 person-years CI; 12.2 to 27.5)
The ratio (nonoperated to post-op) is 2.6 (CI; 1.1to 6.7), significantly >1 (p=0.0122), BE is more than twice as likely to occur before attempts to surgically close the VSD

Using 5 categories of severity rates of VSD the development of BE were NS different

[26] VSD and VSD plus aortic regurgitation

N=25 cases of BE with non-aortic regurgitation, incidence 12.5 per 10,000 person-years, N=7 in post-aortic regurgitation, incidence 34.8, the difference in rates was significant (p=0.0002), suggesting that after AR, VSD patients are more likely to experience BE than before AR

Outcomes
AS complications N=7 aortic regurgitation ruptured aorta sinus; N=5 emboli; N=1 shock, VF; N=10 none
PS complications N=1 none
VSD complications N=7 aortic regurgitation ruptured aorta sinus; N=6 emboli; N=1 meningitis; N=1 shock, VF; N=15 none
N=10 deaths, not analysed by underlying complication

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Griffin MR, Wilson WR, Edwards WD, Ofallon WM, Kurland LT. Infective endocarditis - olmsted county, minnesota, 1950 through 1981. *Jama Journal of the American Medical Association* 1985;**254**:1199-202. Ref ID: 10723	Population based study	N=78 patients N=78 episodes USA	Records of all County residents with a diagnostic code of endocarditis, cases defined using Von Reyn criteria; mean age 58yrs (range <1yr to 90yrs), there was no change in the age distribution over the 32yrs of the study, N=45 male, N=33 female			32years 1950 to 1981	Incidence, underlying cardiac disease	National Institutes of Health
Effect size: **Incidence rate**								

Mean annual incidence rate 3.8 per 100,000 person-years (3.2 per 100,000person-years for definite and probable cases only)
Mean annual incidence rate 2.8 (women) and 5.2 (men) per 100,000 person-years

Underlying cardiac disease
N=78 residents with IE identified

Rheumatic heart disease	20(26%)
Mitral valve prolapse	13(17%)
Congenital heart disease	11(14%)
Degenerative heart disease*	7(9%)
Aortic arch prosthesis	1(1%)
Prior systolic murmur	15(19%)

*calcific aortic stenosis, calcified mitral valve, papillary muscle dysfunction

Outcome
N=13(17%) were diagnosed at autopsy, of the remaining N=65(29%) died within 2mths of diagnosis

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Habib G, Tribouilloy C, Thuny F et al. (2005) Prosthetic valve endocarditis: Who needs surgery? A multicentre study of 104 cases. Heart 91: 954-9	Multicentre study	N=104 France	Inclusion: consecutive from two centres who fulfilled the Duke criteria for PVE, N=71 male, mean age 60 (SD 16), all patients underwent blood culture and systematic transthoracic and transoesophageal studies	All patients were scheduled for a 4 to 6week antibiotic regimen		Study from January 1991 to March 2003	Outcomes, mortality, influence of surgery	Not stated

Effect size:

Outcomes
Embolic events N=35 (33%) patients, rates similar between early and late PVE[27]
Early surgery was more often needed in the early group than in the late group (80% vs. 41%)

N=22/104 (21%) died in hospital (causes of death; N=10 multiorgan failure; N=3 uncontrolled infection; N=6 congestive heart failure or cardiogenic shock, N=3 cerebral haemorrhage
N=5 recurrent PVE

N=82 in-hospital survivors, N=21 (26%) died during a mean 32mths follow-up

Cumulative mortality was higher in early than in late PVE (65% vs. 36%, p=0.01)

After a mean 32mths follow-up, only N=61 (58%) patients were still alive

Factors affecting in-hospital and long term mortality
Univariate analysis identified factors associated with in-hospital mortality were severe co-morbidity (p=0.05), renal failure (p=0.05), moderate-to-severe regurgitation (p=0.006), staphylococcal infection (p=0.001), severe heart failure (p=0.001), and occurrence of any complication (p=0.05)

Multivariate analysis identified severe heart failure (OR 5.5, 1.9 to 16.1, 95% CI) and S aureus infection (OR 6.1, 1.9 to 19.2, 95% CI) were the only predictors of in-hospital death

Influence of surgery
N=51 (49%) underwent surgery during the active phase of endocarditis
In-hospital mortality was NS different between surgical and non-surgical patients
In those with staphylococcal PVE in-hospital mortality was lower in those treated surgically than non-surgically (27% vs. 73%, p=0.03)
Long-term mortality was lower in staphylococcal PVE treated surgically than in the medical group (p=0.03)

Among N=69 with complicated PVE, in-hospital mortality was lower in N=44 (N=8 deaths, 18%) surgical patients compared with N=25 (N=12 deaths, 48%) non-surgical, p=0.05
In-hospital mortality was low in the remaining N=35 with non-complicated PVE for both surgical and non-surgical patients

[27] Early PVE; PVE occurring during the first 12mths after surgery

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Hall G, Hedstrom SA, Heimdahl A, Nord CE. Prophylactic administration of penicillins for endocarditis does not reduce the incidence of postextraction bacteremia.[see comment]. *Clinical Infectious Diseases* 1993;**17**:188-94	RCT [28]	N=60 Sweden	Inclusion: healthy patients referred to the department of oral surgery for dental extraction, N=42 male, mean age 47yrs (range 23 to 74yrs) Exclusion: allergy to penicillins, cardiovascular, renal, hepatic or GI diseases None of the patients were receiving any medication except analgesics	N=20 penicillin V (2g) N=20 amoxicillin (3g) Orally 1hr before dental extraction Blood samples: before, during and 10mins after dental extraction	N=20 matched placebo		Bacteraemia Lysis filtration under anaerobic conditions	Not stated

Late PVE; PVE occurring after 12mths
[28] Randomisation not specified

Effect size:

Bacteraemia
No microorganisms were observed in any pre-treatment blood samples

During dental extraction; placebo (90%), penicillin V (90%), amoxicillin (85%)
10mins after surgery; placebo (80%), penicillin V (70%), amoxicillin (60%)

NS difference in the incidence or magnitude of bacteraemia, of bacteraemia due to viridans streptococci, or of bacteraemia due to anaerobic bacteria among the three patient groups at any of the sampling times

10mins after dental extraction, the number of microorganisms had decreased in similar ways in all three patient groups from that found during extraction ($p<0.01$)

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Hall G, Heimdahl A, Nord CE. Effects of prophylactic administration of cefaclor on transient bacteremia after dental extraction. *European journal of clinical microbiology*	RCT [29] Double-blind	N=39 Sweden	Inclusion: those undergoing dental extraction	N=19 1g cefaclor, 1hr prior to dental extraction Blood samples before, during and 10min after dental extraction	N=20 placebo, 1hr prior to dental extraction Blood samples before, during and 10min after dental extraction		Processed by lysis filtration under anaerobic conditions, aerobic and anaerobic microorganisms were identified using standard methods	Swedish Medical Research Council

[29] Randomisation not specified

& infectious diseases : official publication of the European Society of Clinical Microbiology 1996;**15**:646-9								

Effect size:

Bacteraemia
None of the patients were bacteraemic prior to dental extraction

Post-extraction bacteraemia had a dominance of gram-positive strains (>90%) in both groups

During dental extraction positive blood cultures; 79% cefaclor group; 85% placebo group
Viridans streptococci during extraction; 79% cefaclor; 50% placebo group

10mins after extraction positive blood cultures; 53% cefaclor group; 47% placebo group
Viridans streptococci 10mins after extraction; 26% cefaclor; 30% placebo group
Strains of streptococcus intermedius most frequently, followed by streptococcus sanguis and streptococcus mitis in both patient groups

Anaerobic bacteraemia during extraction; 74% cefaclor; 47% placebo group
Anaerobic bacteraemia during extraction; 75% cefaclor; 35% placebo group
Actinomyces spp. Most commonly identified (Veilloneela and Prevotella isolated from single patients)

Susceptibility
More than 99% of the viridans streptococci were classified as susceptible to cefaclor (≤8mg/l), penicillin V (≤0.125mg/l), clindamycin (≤0.5mg/l) and erythromycin (≤0.5mg/l); ampicillin (0.125mg/l) inhibited 90% of the viridans strains

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Hall G, Nord CE, Heimdahl A. Elimination of bacteraemia after dental extraction: comparison of erythromycin and clindamycin for prophylaxis of infective endocarditis. *Journal of Antimicrobial Chemotherapy* 1996;**37**:783-95	RCT Double-blind	N=38 Sweden	Inclusion: referred to the department of oral surgery for dental extraction because of dental caries or chronic periradicular ostetis, N=24 males, mean age 48.5yrs (range 25 to 74yrs), except for analgesics and oral contraceptives, none of the patients was on any medication Exclusion: those with a history of allergic reaction or systemic symptoms following clindamycin or erythromycin therapy, those with cardiovascular, renal, hepatic or GI diseases	N=19 x2 0.5g erythromycin stearate tablets 1.5hr before dental extraction Blood samples: before, during and 10min after dental extraction	N=19 x2 0.3g clindamycin capsules 1.5hr before dental extraction		Bacteraemia Vacuum filtration and the filters placed on brain heart infusion agar plates for anaerobic incubation at 37C for 10days. Aerobic and anaerobic microorganisms were identified using methods described by Lennette et al (1985)	Swedish Medical Research Council and the Swedish National Association against heart and Chest Diseases
Effect size: **Bacteraemia** All pre-extraction blood samples showed no growth Post-extraction bacteraemia; erythromycin (79%), clindamycin (84%) 10mins post-extraction bacteraemia; erythromycin (58%), clindamycin (53%) Anaerobic bacteria dominated the findings of post-extraction bacteraemia, aerobic bacteria (other than viridans streptococci) were recovered infrequently								

Overall incidence of viridans streptococcal bacteraemia; 79% erythromycin, 74% clindamycin
Anaerobic bacteraemia (Actinomyces, Eubacterium, Lactobacillus most commonly) during extraction was; 58% erythromycin, 74% clindamycin

N=38, all samples obtained before dental extraction showed no growth (despite evidence of chronic dentoalveolar pathology in most cases)
Anaerobic bacteria dominated postextraction bacteraemia, gram-positive strains outnumbered gram-negative, aerobic bacteria other than viridans streptococci were infrequent

Incidence of bacteraemia during dental extraction was 79% in the erythromycin group and 84% in the clindamycin group
At 10mins; 58% erythromycin and 53% clindamycin

There was NS difference in the incidence or magnitude of total bacteraemia, bacteraemia with viridans streptococci or bacteraemia with anaerobic bacteria between the two groups at any sampling time

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Harris A, Chan AC, Torres-Viera C et al. (1999) Meta-analysis of antibiotic prophylaxis in endoscopic retrograde cholangiopancreatograp	Meta-analysis	N=7 RCT, placebo controlled trials (2 double blinded)	Clinical trials were identified Medline using “ERCP”, “antibiotic”, “antibiotic prophylaxis” as subject words and text words; bibliography reviews of relevant articles, and contacts with experts in the fields of gastroenterology and infectious disease, the search was not limited to the English language. A similar search was completed in Pubmed[30] Inclusion: RCTs, placebo controlled studies of the efficacy of antibiotic prophylaxis in ERCP using oral or	Antibiotic prophylaxis for ERCP			Required end points included bacteraemia, sepsis or cholangitis	

[30] Titles or abstracts identified by the search were reviewed independently by two investigators regarding suitability for inclusion in the meta-analysis, if there was disagreement an assessment was made by a third investigator

hy (ERCP). Endoscopy 31: 718-24			intravenous antibiotics Exclusion: had received other antibiotics in addition to prophylaxis, were diagnosed with sepsis or cholangitis prior to ERCP					
Effect size: **Bacteraemia** 4 studies reported bacteraemia, the RR in those receiving antibiotics compared with those receiving the placebo was NS [31] **Sepsis/cholangitis** The RR for sepsis/cholangitis for prophylaxis compared with no prophylaxis was NS								

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Hickey AJ, MacMahon SW, Wilcken DE, Hickey AJ, MacMahon SW, Wilcken DE. Mitral valve prolapse and bacterial endocarditis: when is antibiotic	Case-control	N=224 Australia	Inclusion: cases ≥15yrs admitted to hospital, all who had echocardiography, met the criteria set for diagnosis for endocarditis Inclusion: controls inpatients who did not have bacterial endocarditis and underwent echocardiography during the period of the study, 3 controls were chosen for each case Exclusion: for both cases and controls, known to have had antecedent cardiovascular lesions warranting	N=56 cases[32] (N=66 met the criteria, N=10 excluded due to antecedent lesions)	N=168 controls (N=4620 met the criteria) matched for age, sex and date of echocardiography	Between Jan 1976 to Jan 1984	Prevalence of mitral valve prolapse, systolic murmur, probability of developing endocarditis	Not stated

[31] There was little heterogeneity between the results
[32] 7 of the cases were on chronic haemodialysis and 6 were parenteral drug users

prophylaxis necessary? *American Heart Journal* 1985;**109**:431-5. Ref ID: 1242			antibiotic prophylaxis					

Effect size:

Prevalence of mitral valve prolapse
MVP was identified in N=11/56(20%) of cases and in N=7/168 (4%) of controls
11 sets had BE and MVP were present, in one of these MVP was also present in a control
39 sets had BE without MVP, in 6 of these MVP was present in a control[33]
OR for the association of MVP and BE was 5.3 (2.0 to 14.4, 95% CI)

Systolic murmur
In N=9/11 of those with MVP and BE, there were pre-existing systolic murmurs
OR for the association between BE and MVP with pre-existing systolic murmurs was 6.8 (2.1 to 22.0, 95%CI)

Probability of developing endocarditis
(the incidence of BE in the adult population of New South Wales in 1980 was 145 out of 3,852,638[34], also assuming that 15% of patients with BE had known high-risk lesions other than MVP and mitral regurgitation, as was the case in this study)
The probability of BE occurring in a person with MVP in a 1-year period is 0.00014, this is x4.7 greater than in the general population
Results suggest that 14 out of every 100,000 adult patients with MVP will develop BE over a 1-year period, compared with 3 people in every 100,000 in the general population

(authors conclude that antibiotic prophylaxis is not warranted fro all patients with MVP, the risk of developing BE is slight; findings suggest that antibiotics prophylaxis is required for those patients with MVP who have systolic murmur)

Reference	Study	Number	Patient characteristics	Intervention	Comparison	Length of	Outcome	Source

[33] In no set was MVP present in more than one of the 3 controls
[34] Taken from the New South Wales State hospital morbidity and mortality statistics for 1980

	type/ Evidence level	of patients				follow-up	measures	of funding
Ho H, Zuckerman MJ, Wassem C. A prospective controlled study of the risk of bacteremia in emergency sclerotherapy of esophageal varices. [Review] [44 refs]. *Gastroenterology* 1991;**101**:1642-8. Ref ID: 829	Case series	N=72 (N=126 endoscopies)	Inclusion: patients admitted for upper GI bleeding or elective oesophageal variceal sclerotherapy (EVS) Exclusion: had received any antibiotics in the last 2 weeks before admission The emergency endoscopy and sclerotherapy groups were comparable in age and sex distribution	N=36 (N=37 sessions) emergency endoscopy group	N=36 sclerotherapy groups (N=14 the emergency EVS group, N=33 sessions) (N=36 the elective EVS group, N=56 sessions) Blood samples: Before endoscopy, at 5min and 30min after the procedure	July 1985 to April 1987	Significant bacteraemia group[35] Nonsignificant bacteraemia group[36] Microbiology: 5ml per sample inoculated into each Trypiticase Soy Broth for both aerobic and anaerobic, bacterial growth was monitored for 7days with Bactec 360 Microscan system	Not stated

[35] Any positive blood culture in which the isolated microorganism is one of the following: coliform bacteria (including Escherichi coli and Proteus) Bacteroides, Hemophilus, group A Streptococcus, and Streptococcus pneumoniae, or more than one blood culture, drawn at different times, positive for the same organism. Patients were not necessarily symptomatic

[36] A single positive blood culture in which the isolated microorganism is one of the following: Staphylococcus coag negative (including S. epidermidis anf S. warneri), Corynebacterium, Propionibacterium and Bacillus species, unless a patient has a prosthetic valve, graft or shunt, or a single blood culture for Clostridia (including C. perfringens and C. sordelli) without clinical correlation of active infection

Effect size:

Blood cultures
Positive blood cultures were found in N=30/378 cultures (7.9%), of these N=11 were considered to be potentially significant

Emergency endoscopy group blood cultures
N=5 positive[37], the incidence of endoscopy-related bacteraemia was considered to be 11% (N=4) with a predominance of skin flora

Sclerotherapy groups
Elective EVS sclerotherapy;
N=8 positive blood cultures (N=3 drawn before endoscopy), no significant bacteraemia was noted and no patients had signs or symptoms of infection
Emergency EVS sclerotherapy;
N=17 positive blood cultures (N=7 drawn before endoscopy), N=4 (7.1%) sessions had significant pre-endoscopic blood cultures and N=5 (8.9%) sessions had six significant post-endoscopic blood cultures
N=8/17 (47%) testing positive for E coli, Campylobacter coli, Pseudomonas fluorescens, Bacteroides fragilis, or they were polymicrobial with Clostridium. The other N=9/17 (53%) positive blood culture results were with oral and skin flora
In this group there were positive blood cultures in N=8/56 (14%) of sessions, excluding those with the same organisms identified pre and post procedure, bacteraemia was N=6/56 (11%), this was significant bacteraemia in N=3/56 (5.4%)

Differences in bacteraemia between groups
There were NS differences in the positive blood culture results in:
- the post endoscopy groups between: emergency EVS vs. emergency endoscopy; emergency EVS vs. elective EVS; elective EVS vs. emergency endoscopy
- within groups (post endoscopic vs preendoscopic); elective EVS; emergency EVS
The difference within groups (post endoscopic vs preendoscopic) in the emergency group was significant p=0.03

There was no difference in postendoscopic bacteraemia compared with preendoscopic bacteraemia in emergency alone, or for elective ECS or emergency EVS

Analysis of significant bacteraemia
There was NS differences in the significant bacteraemia in the postendoscopy groups; emergency EVS vs. emergency endoscopy; emergency EVS vs. elective EVS; elective EVS vs. emergency endoscopy

Reference	Study type/	Number of	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of

[37] none of the blood culture results drawn before endoscopy were positive

	Evidence level	patients						funding
Horstkotte D, Rosin H, Friedrichs W, Loogen F. Contribution for choosing the optimal prophylaxis of bacterial endocarditis. *Eur Heart J.* 1987;**8**:379-81.	Comparison of 2 patient groups	N=533 Germany	Both patient groups showed a nearly similar distribution in the site of implantation and the type of prosthesis including a similar relationship between mechanical (84%) and biological (16%) valves Exclusion: other procedures that could have caused bacteraemia of febrile conditions during a 6mth period prior to the procedure in question and before the onset of symptoms of endocarditis	Group A N=229 in whom N=287 diagnostic and therapeutic procedures were performed using a prophylactic antibiotic regime considered correctly administered[38]	Group B N=304 (out of N=1898 patients questioned) in whom N=390 procedures were performed who gave reliable information that they had undergone one of the procedures regarded as requiring endocarditis prophylaxis without having received any antibiotic regime		Cases of PVE	Not stated

[38] The prevention used was similar to that recommended earlier by the AHA

Effect size:

Prosthetic valve endocarditis[39]
In group A no PVE was observed, in group B N=6 cases of PVE which corresponds to an incidence of 1.5 cases per 100 procedures. The highest incidence (N=2/39 procedures, 5.1%) after urological procedures, followed by oropharyngeal surgery (2.6%) and gynaecological (2.2%). Streptococci and enterococci were identified as causative organisms for PVE after oral, urological or gynaecological procedures

N=2 cases of PVE in N=117 dental procedures, both of which occurred after tooth extraction, a case of enterococcal PVE after spontaneous passage of a renal calculus without having undergone any invasive intervention

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding

[39] PVE was considered related to the diagnostic or therapeutic procedure only if symptoms of endocarditis occurred within 2weeks

Hricak V, Kovacik J, Marx P et al. (1998) Etiology and risk factors of 180 cases of native Valve Endocarditis : Report from a 5-year national prospective survey in Slovak Republic 3598. Diagnostic Microbiology & Infectious Disease 31: 431-5	National survey	N=180 Slovakia	Inclusion: cases from 12 clinics/departments, Duke Endocarditis Service Criteria were used as inclusion criteria and to define the probability			Study from 1st January 1992 to 31st December 1996	Positive cultures, infected valves Blood culturing performed in all centres with a BACTEC blood culturing system	Not stated
Effect size: N=169 definitive and N=11 probable/possible cases of IE N=48 (26.7%) were culture negative **Positive cultures**; Staphylococci (N=60, 33.3%), viridans Streptococci (N=22, 12.2%), Enterococcus faecalis (N=21, 11.7%), Haemophilus spp. (N=11, 6.1%) **Infected valves**; aortic valve (46.7%), mitral valve (47.2%) Univariate analysis of the differences between deaths and surviving patients showed NS difference between the two groups; only age >60yrs (40% vs. 21.4%), p<0.05; staphylococcal aetiology (56% vs. 27.1%), p<0.04; antibiotic therapy <21days without surgery (65% vs. 3.6%), p<0.001 were significantly more often								

associated with deaths Therapy with antibiotics only (without surgery) was observed more in those who died than those who survived (92.5% vs. 59.3%), p<0.05

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Ishiwada N, Niwa K, Tateno S et al. (2005) Causative organism influences clinical profile and outcome of infective endocarditis in pediatric patients and adults with congenital heart disease. Circulation Journal 69: 1266-70	Case series	N=188 (N=113 paediatric, N=75 adult) Japan	Inclusion: members of the Japanese Society of Paediatrics Cardiology and Cardiac Surgery in 66 institutions registered paediatric and adult patients with CHD and IE; N=107 male, mean age 15.1±14.3yrs (range 14days to 63yrs),			Study over a 5yr period 1997 to 2001	Causative organism Source of infection Complications	Japanese Society of Pediatric Cardiology and Cardiac Surgery Joint Working Groups for Guidelines for Prophylaxis, Diagnosis and Management of Infective Endocarditis in Patients with Congenit

								al Heart Disease

Effect size:

Streptococcus (N=94, 50%) and Staphylococcus species (N=68, 36.2%) were the commonest pathogens
N=58/94 streptococcus mitis; N=57/68 staphylococcus aureus

The likely source of infection was identified in N=59 (31.4%);
- Streptococcal IE; dental procedure (N=17/28, 60.7%), pneumonia (N=4/28, 14.3%)
- Staphylococcal IE; cardiac surgery (N=7/21, 33.3%), dental procedure (N=3/21, 14.3%), atopic dermatitis (N=2/21, 9.5%)

Complications

Total complications N=126/188, 67.0%, NS difference in the incidence of complications among the different causative species;
- vegetation N=109, 58.0%
- valvular regurgitation N=58, 30.9%
- cardiac failure N=38, 20.2%
- arrythmias N=10, 5.3%
- CNS embolism N=13, 6.9%
- Other embolism N=17, 9.0%
- Abscess N=9, 4.8%
- Aneurysm N=3, 1.6%

Mortality

N=20 (10.6%) died of IE, mean age of 10.5yrs (2mths to 25yrs), mortality was highest in those <1yr (N=5/16, 31.3%)
N=14/20 (70%) had undergone cardiac surgery, N=11 of whom had had prophylactic antibiotics before the onset of IE
S. aureus was isolated from N=11/20, N=7 with MRSA
Overall mortality was higher for S. aureus (N=11.57, 19.3%) than for Streptococcus species (N=5/94, 5.3%), $p<0.05$
Candida mortality (N=2/5, 40.0%), Pseudomonas mortality (N=2/4, 50.0%)

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding

Jokinen MA. Prevention of postextraction bacteremia by local prophylaxis. *International Journal of Oral Surgery* 1978;**7**:450-2.	Controlled study [40]	N=152 Finland	Inclusion: patients from various departments of the hospital for a cleaning of the mouth or because of acute symptoms in the teeth or periodontal tissues indicating dental extraction There were NS differences among the four groups in regard to sex or age	N=38 mouth rinsing with 1% iodine solution N=38 operative field isolation with cotton rolls and saliva ejector N=38 operative field isolation and disinfection with 10% iodine solution	N=38 operative field isolation and disinfection with 0.5% chlorhexidine			Not stated
Effect size: **Bacteraemia** Positive cultures; iodine mouth rinses N=21/38, 55%; operative field in isolation N=13/38, 34%; operative field isolation and disinfection with iodine N=12/28, 32%; operative field isolation and disinfection with chlorhexidine N=5/38, 13%, p=0.05 78% of the bacterial strains isolated from the positive cultures in the prophylactic groups were streptococci of the viridans type The strains isolated were most sensitive to chloramphenicol, ampicillin, erythromycin and penicillin								

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding

[40] The bacteriologic determinations were made in the laboratory without the investigator having any knowledge of the nature of the individual samples

Kullman E, Borch K, Lindstrom E, Ansehn S, Ihse I, Anderberg B. Bacteremia following diagnostic and therapeutic ercp. *Gastrointestinal Endoscopy* 1992;**38**:444-9. Ref ID: 10028	Consecutive case series	N=180 (N=194 examinations) University Hospital, Sweden	Inclusion: median age 66yrs (range 26 to 92yrs), N=104 female, N=76 male Exclusion: those with signs of localised or general infection, antibiotic treatment with the preceding 7 days, treatment with corticosteroids or other immunosuppressive drugs, history or signs of endocarditis or valvular heart disease	Diagnostic ERCP N=115 participants (N=126 procedures) Therapeutic ERCP N=65 participants (N=68 procedures)	Blood samples: taken at 5min after cannulation and at 5 and 15min after the end of examination	November 1988 to December 1990	Bacteraemia Microbiology: A 2-phase blood culture system, one aerobic and one anaerobic flask was inoculated with 4ml of blood and each incubated at 37˚C, the flasks were inspected for bacterial growth twice daily for 2days and then once daily for an additional 8days. When growth was observed or suspected a gram stain was done. Subcultures were performed on blood-agar, hematin-agar and anaerobic blood-agar plates, which were incubated at 37˚C in air, carbon dioxide and in an anaerobic box	Not stated

Effect size:

Bacteraemia
N=19/126 (15%) of diagnostic procedures and N=18/68 (27%) of therapeutic procedures were associated with bacteraemia during and/or within 15min after the endoscopy, NS between the groups

There was NS difference in the frequency of bacteraemia between diagnostic ERCP and biliary manometry or between endoscopic sphincterotomy and endoprosthesis

Of the N=37 bacteraemic patients, N=9 had polymicrobial bacteraemia with 16 detected groups of microorganisms. Different Streptococci, mainly α-haemolytic, were the most common, they were identified in N=14(38%) of the bacteraemic patients either alone or with other species

There was no correlation between the occurrence of bacteraemia and the age of participants or the duration of the endoscopic procedure

During follow-up for 4 to 26mths of bacteraemic patients none developed clinically overt endocarditis

There was no correlation of bacteraemia with subsequent fever, pancreatitis, or sepsis in patients with partial or complete obstruction of the pancreaticobiliary system due to stones, strictures or cancer

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Kullman E, Jonsson KA, Lindstrom E, Dahlin LG, Ansehn S, Borch K. Bacteremia associated with extracorporeal	Consecutive case series	N=76 (N=107 treatments) University hospital, Sweden	Inclusion: all patients undergoing extra corporeal shock wave lithotripsy (ESWL), median age 52yrs (range 21 to 87yrs), N=55 female, N=21 male, mean BMI 25.9±0.4kg/m2 Exclusion: those with signs of localised or general infection, antibiotic treatment within the preceding 7 days, history or signs of endocarditis or valvular heart disease, treatment with corticosteroids or		Blood samples: prior to ESWL, immediately after stone fragmentation during treatment, at 5mins, 20mins and 18hrs after the end of treatment	Mean follow-up time was 29±1 (range 6 to 48mths)	Blood cultures Microbiology: A 2-phase blood culture system, one aerobic and one anaerobic flask was inoculated with 4ml of blood and each incubated at	Not stated

shockwave lithotripsy of gallbladder stones. *Hepato-Gastroenterology* 1995;**42**:816-20. Ref ID: 669			other immunosuppressive drugs				37˚C, the flasks were inspected for bacterial growth twice daily for 2days and then once daily for an additional 8days. When growth was observed or suspected a gram stain was done. Subcultures were performed on blood-agar, hematin-agar and anaerobic blood-agar plates, which were incubated at 37˚C in air, carbon dioxide and in an anaerobic box	

Effect size:

Blood cultures
No patient had positive blood cultures at more than one treatment (repeat treatment was performed within 10days in N=10 patients)

Positive blood cultures:
- during ESWL N=16 (N=15 S epidermidis; N=1 S aureus)
- after 5min N=12 (N=11 S epidermis; N=1 Propionibacterium acnes)
- after 20min N=6 (N=11 S epidermis; N=1 Propionibacterium acnes; N=1 Enterococcus)
- after 18hrs N=3 (all S epidermis)

N=24/107 (22%) of the EWSL sessions were associated with bacteraemia during and/or with 18hrs of the procedure, N=3 of the 24 had polymicrobial bacteraemia

with 4 detected groups of organisms. Staphylococcus epidermidis was the most common and was identified in N=23 (96%) of the treatments associated with bacteraemia There was no difference between the patients with and without bacteraemia regarding age and sex distribution, or BMI, or regarding the duration of treatment, the number of shock waves, the energy index, the mean stone volume, or the occurrence of calcified gallstones During follow-up no patient developed sepsis or clinically overt endocarditis

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Lacassin F, Hoen B, Leport C, Selton-Suty C, Delahaye F, Goulet V *et al*. Procedures associated with infective endocarditis in adults. A case control study.[see comment] 1013. *European heart journal* 1995;**16**:1968-74.	Prospective epidemiological study Case-control	N=171 pairs Public and private medical facilities in 3 regions in France	Inclusion: cases: definite and probable IE defined according to revised Von Reyn's criteria with modifications; possible IE defined according to non revised Von Reyn's criteria Exclusion: cases: patients younger than 15yrs, valve replacement within the previous year, prematurely dead, intravenous drug users, those with *Coxiella burnetti* IE (unlikely to be related to any procedure) Cases: those without IE who satisfied the same exclusion criteria as the cases. Cases were recruited randomly from cardiology or medicinal wards either during a consultation for echocardiography or during hospitalisation in the same period of	N=171 cases were interviewed as soon as possible after the diagnosis of IE Following a pre-established list, they were requested to indicate all the procedures involving cutaneous and	N=171 controls were interviewed under the same conditions as cases using the same questionnaire form Following a pre-established list, they were requested to indicate all the procedures involving cutaneous and	1st November 1990 to 31st October 1991	The relative risk of IE for each procedure, causative organisms, antibiotic prophylaxis	Several grants from medical societies in France and from the following companies: Baxter, Dideco-Shiley, Eli-Lily, Medtronic, St Jude Medical Compani

[41] To adjust for factors which could potentially influence the risk of IE associated with procedures, the questionnaire requested items concerning general co-morbid conditions such as alcohol and tobacco consumption, and diabetes mellitus

Ref ID: 1013			observations as cases. Cases and controls were distributed into 3 groups of underlying cardiac conditions: native valve disease, prosthetic valve or no known cardiac disease Each case was matched to one control as regards sex, age (±5yrs) and group of underlying cardiac conditions. The proportion of those with diabetes mellitus, or who consumed alcohol and tobacco did not differ between the 2 groups. Cases had significantly more often an infectious episode or a skin wound than controls (39% and 19% vs. 15% and 5% respectively)	mucosal surfaces they had undergone within the 3mths prior to diagnosis In case of medical consultation or procedure, the information was checked by the cited practitioner [41]	mucosal surfaces they had undergone within the 3mths prior to diagnosis In case of medical consultation or procedure, the information was checked by the cited practitioner			es
Effect size: **Procedures** N=88 (51.5%) of cases and N=70 (41%) of controls had undergone at least one procedure, the adjusted OR for the risk of IE related to a procedure 1.6 (1.01 to 2.53, 95%CI), p<0.05 Taking the frequency of the procedures in the control group (40%) as an estimation of the frequency in the general population, the risk of IE attributable ≥1 procedure (attributable risk) was 20% Any dental procedure – no increased risk (cases N=37 (22%), controls N=33 (19%)); Dental extraction no higher risk of IE; scaling and root canal work showed a trend towards a higher risk (NS) Any urological procedure – no increased risk (cases N=6 (3.5%), controls N=2 (1%)) Any GI procedure – no increased risk (cases N=14(8.2%), controls N=8 (4.7%)) Any surgical procedure – cases N=11[42](6%), controls N=2 (1%); adjusted OR for the risk of IE 4.7 (1.02 to 2.53, 95%CI)								

[42] Abdominal surgery N=3, soft tissue surgery N=6, gynaecological surgery N=2. Two of the 7 clean surgical procedures were done with antibiotic prophylaxis and five without antibiotic prophylaxis

All procedures, the mean number of procedures was significantly higher in cases than in controls (2.0 vs. 4.5, p<0.05)
The risk of IE increased with the number of procedures per case, RR for one procedure 1.2; 1.7 for two procedures; 3.6 for three or more procedures (p=0.005)
No control had had >1 dental procedure in the previous 3mths, N=3 cases had undergone 2 procedures

Multivariate analysis:
Variables included; extraction, scaling, root canal treatment, urological, GI and surgical procedures, skin wound, infectious episode. Only infectious episodes (OR 3.9; 2.1 to 7.3, p<0.05, 95%CI) and skin wounds (OR 3.9; 1.6 to 9.6, p<0.05, 95%CI) significantly and independently contributed to the explanation of the risk of IE. The procedures were NS

Causative organism
The only procedure associated with a risk for IE due to viridans streptococci was scaling (N=9/50 in the cases; N=2/50 in the controls, OR=5.25, p=0.025)
The only procedure associated with the subsequent occurrence of IE was surgery for staphylococcal IE (N=4/27 in the cases; N=0/27 in the controls, p=0.03)
In multivariate analysis, scaling was associated with a significant risk for IE due to viridans streptococci, independently of an infectious episode. Conversely, only infectious episodes contributed to the risk of staphylococcal infective endocarditis, the risk after skin wound and surgery being non-significant in this analysis

Antibiotic prophylaxis
N=8 cases of IE occurred in those who had received an appropriate antibiotic prophylaxis, (N=4 PVE, N=4 NVE). Procedures included multiple extractions within a single session (N=3), scaling (N=3), ENT procedure (N=1) and urethrocystoscopy (N=1)

N=6 controls had received appropriate antibiotic prophylaxis (N=2 PV disease, N=4 NV disease)

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding

Li W,.Somerville J. Infective endocarditis in the grown-up congenital heart (GUCH) population. *European Heart Journal* 1998;**19**:166-73. Ref ID: 3609	Retrospective and prospective cohort	N=185 (N=214 episodes of IE) London	Up to 1993 data were collected retrospectively from patient notes, from 1993 to 1996 data were collected prospectively from patients. Diagnosis by Duke criteria N=111/185 male, N=7 previous IE at age 6-11yrs Divided into 2 groups according to whether or not the definitive repair surgery had been performed on the main lesion The number of males was more than females in Group II compared to Group I ($p<0.05$)	Group I N=128 (N=155 episodes) unoperated or palliated (N=25 palliative procedures, including systemic to pulmonary shunts or pulmonary artery banding)	Group II N=57 (N=59 episodes) after definitive and/or valve repair/replacement (including aortic, pulmonary, mitral and/or tricuspid valvotomy, repair or valve repair)	The grown-up congenital disease database (GUCH), 13yrs of data Between 1983 to 1996	Cardiac lesions, predisposing events, organisms, echocardiography/site of infection, delay in diagnosis, recurrence, specific problems, surgery during infective endocarditis, outcome	Not stated

Effect size:

Cardiac lesions

Left ventricular outflow tract lesions were the most frequent lesions, N=42 patients (N=45episodes), this significant incidence showed a similar incidence was found in those with and without previous surgery

The differences in the rates of IE for those with a ventricular septal defect are noted to raise the question about whether closing a small ventricular septal defect would improve prognosis

Lesions	**Group I (episodes)**	**Group II (episodes)**
Left ventricular outflow tract	22 (24)	20 (21)*
VSD	31 (37)	6 (6)*
Fallot (shunt 6, valvotomy 1)	12 (13)	11 (11)
Corrected transposition	11 (18)	2 (2)

Mitral valve prolapse	17 (18)	(1)
Pulmonary atresia (shunt 7)	10 (13)	2 (2)
One ventricle (shunt 7, PA banding 1)	12 (15)	-
Classic transposition (shunt 2)	5 (9)	3 (3)
Atrioventricular defect	2 (2)	8 (8)
Coarctation	1 (1)	3 (3)
Common trunk	2 (2)	1 (1)
Infundibular pulmonary stenosis	2 (2)	-
Duct	1 (1)	-
Ebstein	-	1 (1)

* p<0.05

Recurrence
Recurrence occurred in N=21(11%) of patients, N=19 of whom were in Group I

Outcome

	Group |	Group II
Cured	106 (83%)	50 (88%)
Recurrent	19 (15%)	2 (3%)*
Death	3 (2%)	5 (9%)*

*p<0.05

The cardiac lesions of the N=8 patients who died during endocarditis were: VSD; aortic stenosis/aortic regurgitation; pulmonary atresia/VSD (N=2); aortic stenosis/aortic regurgitation/mitral regurgitation (N=2); aortic stenosis/Coarctation; transposition of the great arteries/VSD/pulmonary stenosis

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Lindert KA, Kabalin JN, Terris MK. Bacteremia	RCT	N=50 USA	Inclusion: men scheduled for prostate ultrasound and ultrasound guided biopsy to rule out prostate cancer	N=25 preoperative enema[43]	N=25 no preoperative enema		Blood cultures Microbiology: 10ml samples,	Not stated

[43] usual procedure is to administer an enema with antibiotics before the procedure and a repeat dose of antibiotics 12hrs after the procedure

and bacteriuria after transrectal ultrasound guided prostate biopsy. *Journal of Urology* 2000;**164**:76-80. Ref ID: 447			Exclusion: patients with a history of prosthetic devices and/or valvular heart disease that mandated prophylactic antibiotics before biopsy	Blood culture was taken 15mins after biopsies No antibiotics were given before the procedure, immediately after all cultures were obtained patients were given oral antibiotics, including 500mg ciprofloxacin and 500mg metronidazole			inoculated into aerobic and anaerobic bottles, blood cultures were assayed colorimetrically every 15mins for 5days, when any bacterial growth was detected, colonies were harvested to identify further the organisms involved	
Effect size: **Blood cultures** N=8 (16%) of blood cultures taken after biopsy had bacterial growth[44] (including enteric flora in N=5 (62.5%) N=4 patients had pre-biopsy bacteriuria and post-biopsy bacteraemia, however the same organism was present in pre-biopsy urine culture and post-biopsy blood culture in only N=1 man, and none had the same organism in post-biopsy urine and blood cultures There was no correlation of bacterial growth in blood cultures with patient age, history of dysuria and/or UTI, PSA, number of biopsies, obstructive voiding symptoms, prostate volume, cancer, or post-biopsy haematuria or voiding symptoms								

[44] organisms identified; Staphylococcus, Streptococcus, Diptheroids, Bacteeroides fraglis, E coli, Proprionibacterium, Gemella morbillum (all N=1 patient), Enterobacter, Gram-pos rods (all N=2 patients)

N=7 (28%) who did not receive an enema before biopsy had positive blood cultures, N=1 (4%) of those given an enema had a positive blood culture, p=0.0003 for the difference

N=1 patient with a fever of >37.5C after the procedure, the remaining men were asymptomatic

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Lo GH, Lai KH, Shen MT, Chang CF. A comparison of the incidence of transient bacteremia and infectious sequelae after sclerotherapy and rubber band ligation of bleeding esophageal-varices. *Gastrointestinal Endoscopy* 1994;**40**:-679.	Case series	N=105 Veterans General Hospital, Kaohsiung, China	Inclusion: patients admitted with acute variceal bleeding, all underwent EIS or EVL not more than 24hrs after onset of bleeding Exclusion: signs of infection before treatment, blood or body fluid culture before endoscopy showed bacterial growth, antibiotics within 2 wks before admission, required balloon tamponade or placement of a central venous catheter or Foley catheter which can cause bacteraemia Both groups were comparable with regard to age, sex, underlying cause of liver disease, incidence of hepatocellular carcinoma, episodes of active bleeding and Pugh's grade	N=50 (N=58 admissions) endoscopic injection sclerotherapy (EIS)	N=55 (N=60 admissions) endoscopic variceal ligation (EVL) Blood samples: before the procedure, 5mins, 30mins and 24hrs after completion of the procedure	July 1990 to June 1991	Blood cultures Microbiology: 10ml samples, 5ml inoculated into a trypic soy broth (Bactec 6B, aerobic) and pre-reduced tryptic soy broth (Bactec 7C, anaerobic), they were incubated at 37˚C for 7days and monitored using Bactec 460	Not stated

Ref ID: 4770								
Effect size: **Blood cultures** N=10/58 (17.2%) EIS had positive blood cultures; N=2/60 (3.3%) EVL had positive blood cultures, p<0.03 Organisms grown; Staph aureus (N=3), Staph epidermidis (N=1), Strep pneumoniae (N=1), E coli (N=3), Klebsiella pneumoniae (N=2), Proteus vulgaris (N-=1), Clostridum fallax (N=1) In the EIS group N=5/10 episodes of bacteraemia were associated with fever and leukocytosis, with positive blood cultures in all at 24hrs In the EVL group N=1/2 episodes of bacteraemia were associated with fever and leukocytosis, blood culture positive at 24hrs Infectious complications Spontaneous bacterial peritonitis (N=4), empyema (N=2), pneumonia (N=1) The frequency of infectious complications (included sustained bacteraemia) after EIS (18%) was significantly higher than that after EVL (1.8%), p<0.01								

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Lockhart PB. An analysis of bacteremias during dental extractions. A double-blind,	RCT, double blind [45]	N=70 USA	Inclusion: >18yrs, no valvular heart disease, no infectious disease, no poorly controlled systemic disease, facial cellulitis, N=37 male, mean age 37yrs (range 21 to 72yrs) Exclusion: use of steroids or chlorhexidine during the previous 2mths, use of antibiotics during the previous 2wks, any	N=35 10ml 0.2% chlorhexidine hydrochloride (peridex) rinse for 30sec, rinsing was repeated 1min later	N=35 10ml placebo rinse for 30sec, rinsing was repeated 1min later		Bacteraemia Blood bottles processed and tested on a blood culture system (BACTEC 660) for 5days or until yields were	Not stated

[45] study patients were selected consecutively from a large pool of outpatients who underwent dental extractions; randomised by a random number generator in the hospital pharmacy, unmarked identical bottles; power analysis

placebo-controlled study of chlorhexidine. [Review] [67 refs]. *Archives of Internal Medicine* 1996;**156**:513-20			manipulation of the gingival within 1hr of the extraction There was an equal distribution between maxillary and mandibular teeth	Blood samples: 1min following initiation of surgery, 3min mark			positive	
Effect size: 70% were multirooted, the majority were molars (87%) N=57 (81%) of these teeth had peridontitis with a mean alveolar bone loss of 33% N=16 (22%) had tooth mobilities of 2 or 3 due to peridontitis and alvelolar bone loss The mean greatest pocket depth was 6.4mm and the mean total pocket depth was 29mm **Bacteraemia** N=62 (89%) had positive blood cultures at either the 1 or 3min point; at 1min N=43 (61%); at 3min N=56 (80%) The majority of organisms at the 1 and 3min samples were gram-positive cocci, with a predominance of Streptococci viridans and α-haemolytic pyogenic streptococci There was NS difference between the 1 and 3min samples in either the incidence of blood cultures or between the chlorhexidine and the placebo groups; placebo group positive cultures in N=31 (94%); chlorhexidine group N=31 (84%) Chlorhexidine had NS difference on either the incidence of polymicrobial cultures or the incidence of blood cultures and the three surgeons in the incidence of positive blood cultures The mean time for surgery was 4.7mins (range 1 to 48mins). Patients who had surgery times of less than 3mins showed significantly increased number of positive blood cultures vs. those with surgery >3mins (p=0.04); those with times >6mins had significantly increased positive blood cultures vs. those with surgery times of <6mins (p=0.04)								

The degree or severity of odontogenic disease did not correlate with the results of the blood cultures

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Lockhart PB, Brennan MT, Kent ML, Norton HJ, Weinrib DA. Impact of amoxicillin prophylaxis on the incidence, nature, and duration of bacteraemia in children after intubation and dental procedures. *Circulation* 2004;**109**:2878-84.	RCT [46]	N=100	Inclusion: children who required dental treatment in the operating room setting because of behaviour, young age and/or the scope of treatment needs Exclusion: poorly controlled systemic illness, medical conditions requiring antibiotic prophylaxis, allergy to penicillin-type drugs, weight <12kg, exposure to systemic antibiotics within the past 2wks There was NS difference in the baseline characteristics for all subjects, stratified by treatment group	N=49 amoxicillin Blood samples: 2mins after the initiation of intubation; dental restorations, pulp therapy and cleaning were then completed and a second sample drawn; 10mins later a third sample for a baseline culture before dental extraction, 90secs after the initiation of	N=51 placebo Blood samples: 2mins after the initiation of intubation; dental restorations, pulp therapy and cleaning were then completed and a second sample drawn; 10mins later a third sample for a baseline culture before dental extraction, 90secs after the initiation of		Incidence, nature and duration of bacteraemia Aerobic and anaerobic were processed according to standard methods, cultures with bacterial growth were gram stained and subcultured onto appropriate media; blood cultures were continued monitored for growth with the use of an automated Microscan	Health Services Foundation Inc, Carolinas HealthCare System, Charlotte, NC

[46] A computer-generated random number system was used by our pharmacy to assign identically appearing syringes containing placebo or study drug. All investigators were blinded as to the assigned treatment

				the first extraction a fourth draw was taken, the remaining teeth were extracted and a fifth blood draw 90secs after the final extraction. Further draws at 15, 30 and 45mins after the end of extraction	the first extraction a fourth draw was taken, the remaining teeth were extracted and a fifth blood draw 90secs after the final extraction. Further draws at 15, 30 and 45mins after the end of extraction		(Baxter) system and standard biochemical tests were done manually to complete the identity; blood cultures were incubated for up to 14days before considered no growth to avoid missing more slow-growing oral pathogens	

Effect size:

Bacteraemia was defined as the occurrence of a positive culture at any of the 8 blood draws, only bacteria considered as likely or possibly from the oral cavity were included in the analysis of draws 2 to 8[47].

Incidence bacteraemia
The overall incidence from all 8 draws was greater in the placebo group than the amoxicillin group (N=43, 84% vs. N=16, 33%), p<0.0001
Highest incidence at a single time point occurred at 1.5mins (fifth draw) after extraction, placebo vs. amoxicillin (N=34, 76% vs. N=6, 15%), p<0.0001
Incidence after intubation (D1) 18% placebo vs. 4% amoxicillin , p=0.05
Incidence restorative and cleaning procedures (D2) 20% placebo vs. 6% amoxicillin, NS
Bacteraemia incidence in the placebo group; 15mins (N=7, 18%); 30mins (N=6, 16%); 45mins (N=5, 14%)
Bacteraemia incidence in the amoxicillin group; N=1 at 15mins

Statistically significant decrease in the incidence of bacteraemia from amoxicillin at all but one draw (D2); D1 (p=0.05), D3 (p=0.03), D4 (p=0.0001), D5 (p=0.0001), D6 (p=0.04), D7 (p=0.01), D8 (p=0.03)

[47] All bacteria were considered in the analysis of the intubation blood draw, number 1, because the skin and nasopharynx are more likely to harbour other bacteria

Logistic regression analysis suggests that the incidence of bacteraemia associated with extraction draws increase with the age of the subject (p=0.025) and number of teeth extracted (p=0.002) and that the use of amoxicillin significantly reduced the incidence of bacteraemia (p<0.0001)

No subject had a positive culture at D6,7 or 8 who did not have a positive extraction blood draw

Logistic regression analysis demonstrated that amoxicillin significantly reduced the incidence of bacteraemia (p=0.03)

Nature
There was a >5-fold difference in the number of positive blood cultures with placebo vs. amoxicillin, N=128 vs. N=24. Streptococci made up 45% (N=57) of the total bacteria in the placebo group vs. 33% (N=8) of the amoxicillin group

Duration
Positive draw 4/5 N=38 placebo, N=11 amoxicillin; D6 15mins N=12 placebo, N=1 amoxicillin; D7 30mins N=9 placebo, N=0 amoxicillin; D8 45mins N=5 placebo, N=0 amoxicillin

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
London MT, Chapman BA, Faoagali JL, Cook HB. Colonoscopy and bacteraemia: an experience in 50 patients. *New Zealand Medical Journal*	Case series	N=50 New Zealand	Inclusion: patients undergoing colonoscopy, N=24 males, N=26 females, mean age 58.8yrs (range 22 to 80yrs) Exclusion: patients with evidence of infection or who had taken antibiotics in the previous 2 weeks Biopsies, often multiple were taken from N=26 patients, N=19 had neither a biopsy or a polypectomy N=45 were prepared for colonoscopy by a whole gut lavage usually 8 litres of an isotonic solution, N=5 were prepared with soap and water enemas		Blood samples: before colonoscopic insertion, 5mins after insertion,		Blood cultures Microbiology: 7-10ml was inoculated into 40ml BBL(vacutainer) supplemented broth, cultures were incubated at 30˚C for 3wks and examined daily, aerobic and anaerobic subcultures were made at 24hrs,	Not stated

1986;**99**:269-71. Ref ID: 952							6days, 14days and 21days and the cultures identified	
Effect size: **Blood cultures** N=204 blood cultures from N=5 patients, N=6 positive blood cultures from N=5 patients (N=2 patients had samples positive prior to colonoscopy not from later samples) In N=2 patients the positive culture was considered to be directly related to the colonoscopy, the blood samples were collected at the limit of insertion of the colonoscope and were for Bacteroides fragilis and Bacillus sp. (these N=2 patients were from the N=7 group with carcinoma of the colon) Positive blood cultures were in N=4/45 patients who had whole gut lavage and in N=1/5 who had an enema								

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Low DE, Shoenut JP, Kennedy JK, Sharma GP, Harding GK, Den Boer B *et al*. Prospective assessment of risk of bacteraemia with colonoscopy and	Prospective case series	N=270 (N=280 procedures) St. Boniface General hospital, Winnipeg Canada	Inclusion: patients undergoing colonoscopy with or without polypectomy, a high saline enema was given prior to the colonoscopy Exclusion: none of the patients had received antimicrobial agents during the 2 weeks prior to the procedure	N=165 colonoscopy-only (N=169 procedures) N=105 colonoscopy with polypectomy (N=111 procedures)	Blood samples: colonoscopy-only group, postinsertion blood cultures at 10min in N=86 procedures and at 15min in N=83 procedures; Polypectomy group post-polypectomy	August 1983 to March 1985	Blood cultures, patients were observed for 24hrs after the procedure for evidence of sepsis Microbiology: 5ml samples, innocaulated into 45ml of supplemented peptone broth	Not stated

polypectomy . *Digestive Diseases & Sciences* 1987;**32**:1239-43. Ref ID: 930					blood cultures at 5min in N=42 procedures, at 5 and 10min in N=26 procedures and at 30sec, 5 and 10min in N=43 procedures		(Becton-Dickinson) and inculbated at 37˚C for 7days, subcultures were made onto sheep blood agar at 24hr and 7days	

Effect size:

Blood cultures
N=7 (2.5% preprocedural blood cultures were positive but were negative post-colonoscopy or post-polypectomy
In the colonoscopy-only group N=7/169 (4.1%) blood cultures were positive at either 10 or 15min (microorganisms isolated: Corynebacterium spp., Escherichia coli, Bacteroides spp., Bacillus spp., S. epidermidis, Clostridium spp.)
In the polypectomy group N=8/223 (3.6%) blood cultures were positive at either 30sec, 5 or 10min (microrganisms isolated: Veionella spp., Pseudomonas spp., Bacillus spp., Peptostreptococcus spp., Escherichia coli, Bacillus spp., S. epidermidis, Streptomyces spp.)
There was NS difference between pre and postprocedural positive blood culture rates in the 2 groups

No patient developed clinical evidence of sepsis during the 24hr following the procedure

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding

Lucas VS, Omar J, Vieira A, Roberts GJ. The relationship between odontogenic bacteraemia and orthodontic treatment procedures 9668. *European Journal of Orthodontics* 2002;**24**:-301. Ref ID: 9668	RCT	N=142 (N=81 undergoing GA, N=61 receiving treatment in the O/P department London	Inclusion: mean age 13.5yrs (range 9.2 to 17.9), N=64 males, N=78 females Indices were recorded for bacterial dental plaque and gingival inflammation. A separate score was recorded for the teeth involved in the orthodontic procedure	N=39 upper alginate impression N=42 separator N=25 fit/placement of band N=36 archwire adjustment	Blood samples: baseline sample and 30 second sample taken after the orthodontic procedure		Prevalence and intensity of bacteraemia following 4 orthodontic procedures Microbiology: 6ml per sample, inoculated into sodium polyanethol sulphonate and added to the lysing solution and 3ml of a proprietary streptokinase-streptodornase compound and incubated at 37˚C for 10mins. One plate was incubated aerobically and the other anaerobically for 10days, from day3 they were checked daily for bacterial growth	Not stated

Effect size:

Prevalence of bacteraemia
There was NS difference in the number of positive blood cultures between baseline and the dentogingival manipulations
There was NS association between the mean plaque and gingivitis scores and the number of positive blood cultures for any of the procedures

Intensity of bacteraemia
The mean total number of aerobic and anaerobic bacteria isolated from the blood samples (cfu of bacteria per ml of blood) was significantly greater following the placement of a separator ($p<0.02$)
There was NS difference in the mean number of aerobic or anaerobic, or the combined total bacteria isolated from the blood samples between baseline and an upper alginate impression or placement of a band or archwire adjustment

Identity of bacteria
The identity of bacteria isolated from blood cultures were similar to those following dental operative procedures, these included S. gordonii, S. sanguis, S. salivarius, S. vestibularis and coagulase negative staphylococci

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Lucas V, Roberts GJ, Lucas V, Roberts GJ. Odontogenic bacteremia following tooth cleaning procedures in children 891. *Pediatric dentistry*	RCT Not blinded	N=155 cleaning procedures Guy's Dental Hospital or Great Ormond Street Hospital	Inclusion: children referred for dental treatment under general anaesthetic (GA), N=79 male, N=76 female, aged 21mths to 16yrs 11mths Exclusion: antibiotics within the previous month, haemorrhagic disorders, known viral carriage Bacterial dental plaque and gingivitis were assessed	N=52 toothbrushing group N=53 professional cleaning group N=50 scaling group Blood samples: baseline	N=50 control group (data taken from a previous study)	1991 to 1994	Blood cultures, intensity of bacteraemia, bacteria isolated Microbiology: 3ml volume of blood was inoculated into each of the aerobic and anaerobic bottles, two commercial broth culture	Not stated

2000;**22**:96-100. Ref ID: 891		London		sample and 30 seconds after the procedure			systems were used: the Bactec 460 radiometric system and the Bactec 760, bacteria were identified using standard laboratory methods and the oral streptococci were further identified using API Strep20. A further 1.5ml was inoculated into the Isolator system vial which estimates the intensity of bacteraemia by lysis centrifugation and gives cfu/ml of blood	
Effect size: **Positive blood cultures** There was NS difference in the number of positive blood samples in the groups studies There was NS difference in the intensity of bacteraemia (colony forming units per millilitre of blood) in any of the 3 cleaning groups **Intensity of bacteraemia** There was NS difference in the intensity of bacteraemia (cfu/ml blood) in any of the three cleaning groups **Bacteria isolated** There were similar to bacteria isolated from blood cultures following dental operative procedures, these included S. mitis, S. sanguis and coagulase negative								

staphylococci (the bacteria isolated from the baseline group included S. sanguis, coagulase negative staphylococci and Oerskovia species)

(authors conclude that even the professional cleaning procedures with a rubber cap and scaling should be carried out with benefit of pre-procedure antibiotic prophylaxis)

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
MacFarlane TW, Ferguson MM, Mulgrew CJ. Post-extraction bacteremia : role of antiseptics and antibiotics. *Br Dent J* 1984;**156**:179-81.	Case control	N=60 Glasgow	Inclusion: patients attending the department of oral surgery for tooth extraction, had normal medical history and required an uncomplicated extraction of a single premolar or first or second molar tooth under local anaesthetic, extractions were confined to lower teeth in order to reduce variability Exclusion: cases of gross decay, advanced periodontal disease, or dental abscess with facial swelling, a history of antibiotic therapy during the previous 3mths The groups were matched for age and sex, and the ratios of premolar to molar teeth in each group were similar	N=20, 10mls 1% chlorhexidine N=20, 10mls 1% povidine-iodine Solutions irrigated the gingival crevice through a blunted needle, the patient was asked to retain the solution in the mouth for 2mins before rinsing out	N=20, 10mls normal saline Blood samples: before and 30sec after tooth extraction		Bacteraemia, antibiotic sensitivity The blood cultures were incubated at 37C and subcultured on 1,4 and 8days after initial collection	Not stated
Effect size: **Bacteraemia** Pre-extraction all cultures were negative Post-extraction; saline (N=4) vs. chlorhexidine (N=15) p<0.001, povidone-iodine (N=12) p<0.01								

NS difference between chlorhexidine vs. povidone-iodine

46 isolates; anaerobic streptococci (N=11), Streptococcus sanguis (N=8), Streptococcus mitior (N=5), Streptococcus mutans (N=6), Diptheroids (N=3), other N=2 or less

Antibiotic sensitivity
Sensitive; penicillin (N=43/46), ampicillin (N=46/46), cephaloridine (N=46/46), erythromycin (N=45/46), spiromycin (N=46/46), clindamycin (N=45/46), vancomycin (N=46/46), streptomycin (N=27/46)

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Mansur AJ, Dal Bo CM, Fukushima JT, Issa VS, Grinberg M, Pomerantzeff PM. Relapses, recurrences, valve replacements, and mortality during the long-term follow-up after infective endocarditis. *American Heart*	Cohort study	N=420 Brazil	Included: adult and paediatric patients discharged after first treatment of endocarditis from a tertiary care hospital; aged 34.2±17.2 (mean ±SD), 2mths to 83yrs; N=270 (64.3%) men, N=150 (35.7%) women Infecting micro-organism Streptococci N=237 56.4% Staphylococcus aureus N=70 16.7% Coag negative staphylococci N=21 5% Gram-negative bacteria N=20 4.58% Other gram-positive bacteria N=9 2.2% fungi N=5 1.2% Negative blood cultures N=58 13.8% Underlying cardiac conditions			Mean follow-up 6.1±4.3yrs for survivors, 3.7±3.7yrs for those who died during follow-up N=28 (6.7%) were lost to follow-up	Relapses[48] Recurrence[49] Valve replacements, death	Not stated

Journal 2001;**141** :78-86. Ref ID: 551			Valvular heart disease: N=177, 42.1% Congenital heart disease: N=49, 11.7% Hypertrophic cardiomyopathy: N=3, 0.7% Chagas cardiomyopathy: N=1, 0.2% Endocardial fibroelastosis: N=1, 0.2% Prosthetic heart valve: N=91, 21.7% - bioprostheses: N=82 Endocarditis timeframe First 2 mths post-op: N=9, 9.9% 2mths – 1yr after valve replacement: N=18, 19.8% >1yr after valve replacement: N=64, 70.3%					

Effect size:

Relapses
First episode of endocarditis N=14 (3.3%); second N=1 (0.2%)

Cardiac defect:
Prosthetic valve N=7 (50% of relapses)
Valvular heart disease N=2
Congenital heart disease N=1
Cardiac pacemaker N=1
No known heart disease N=3

[48] Resumption of clinical picture of endocarditis in the first 6mths after treatment, an infecting micro-organism of the same genus and species, no change in underlying cardiac condition

[49] Clinical picture and isolation of a micro-organism different from previous episode of endocarditis, change in underling cardiac condition, clinical picture and micro-organism consistent with previous episode of endocarditis greater than 6mths since the previous episode

Outcomes:
Surgical treatment N=5, 35.7% (N=3 native value endocarditis, N=2 prosthetic valve infection)
Death N=5 (N=4 due to endocarditis)

Recurrence
One episode (N=48, 11.4%); two (N=2, 0.5%); three (N=1, 0.2%); five (N=1, 0.2%)

One recurrence was observed from 1-15mths (4.5±3.9yrs)
There was a significant male predominance in those who had 2 episodes of recurrence compared with those who had one (N=39, 81.2% vs. N=228, 62.0%), p=0.009.

Cardiac defect:
Unchanged underlying condition N=24 (50%)
First on a native valve, second on a prosthetic valve N=18 (37.5%)
Second on a native valve regurgitant resulting from damage by previous endocarditis N=6 (12.5%)

Outcomes:
Mortality was also higher for those with 2 episodes (N=26, 54.2% vs. N=71, 20.8%), p=0.001.
Complications were significantly more frequent in those with 1 compared to 2 recurrences (N=267, 72.6% vs. n=24, 50.0%), p=0.001

Survival free recurrence
The probability of survival free recurrence decreased progressively, there was a significant difference for curves of increasing ages (in classes), p=0.0026.
The probability of survival free recurrence was NS for the duration of the symptoms of endocarditis; antimicrobial administration before hospital admission; the observation of vegetation on echo; infecting micro-organism; native value compared with prosthetic valve endocarditis; medical or surgical treatment; cardiac, neurological or septic complications; valve replacement

For those with prosthetic valve endocarditis, endocarditis in the first post-op year was a risk factor for recurrent endocarditis (p=0.0264, risk ratio 2.05)

Valve replacements
The probability of survival free valve replacement decreased progressively and was lower for those with recurrent endocarditis (p=0.0157), with prosthetic valve endocarditis (p=0.0091) and with prosthetic valve endocarditis in the first post-op year (p=0.0234).
The probability of survival free valve replacement was NS affected by increasing age; sex; duration of endocarditis symptoms; antimicrobial administration before hospital admission; detection of vegetation on echo; infecting micro-oraganism; comparison of aortic to mitral valve replacement; frequency of surgical treatment of the endocarditis; frequency of cardiac, neurologic or septic complications; finding of annular abscess at operation

Risk factors for valve replacement were recurrent endocarditis (p=0.0169, risk ratio 1.62) and prosthetic valve endocarditis (p=0.0099, risk ration 1.61)

Deaths
N=20 died as a result of a new episode of endocarditis

The probability of survival decreased over time, curves showed significant decreases in the age strata (p=0.003).
There was a lower probability of survival in those with recurrent endocarditis (p=0.0007).
The probability of long-term survival was not influenced by sex; duration of symptoms; antimicrobial administration before hospital admission; micro-oraganism; native or prosthetic valve endocarditis; prosthetic valve endocarditis in the first opst-op year; the detection of vegetations on echo; occurrence of cardiac or septic complications; frequency of surgical treatment of the endocarditis; annular abscess at operation; valve replacement during follow-up.

Risk factors for death were increasing age (p=0.001, risk ratio 1.03) and recurrent endocarditis (p=0.0015, risk ratio 2.06)

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Martin JM, Neches WH, Wald ER (1997) Infective endocarditis: 35 years of experience at a children's hospital. Clin Infect Dis. 24: 669-75	Case series, retrospective analysis	N=73 (N=76 cases of endocarditis) New Zealand	Inclusion: medical records from a children's hospital, database created by the department of cardiology and the records of the department of pathology; criteria cited by Saiman et al were modified to be more specific and used to substantiate the diagnosis of endocarditis; median age 9yrs (1mth to 18yrs) Exclusion: >18yrs, endocarditis did not fulfil the criteria			January 1958 to December 1992	Risk factors, antibiotic use, outcome	Not stated
Effect size: N=62 had congenital heart disease, N=8 more-complex congenital heart disease								

Risk factors
N=8 had a dental procedure or cleaning in the mouth; dental work was the only risk factor for bacteraemia in N=6 of these cases
N=11 had multiple caries at the time of their admission
N=7 underwent cardiac catheterisation in the 2mths before endocarditis was diagnosed
N=3 had a central venous catheter in place before endocarditis developed
N=7 who had a structurally normal heart developed endocarditis

Antibiotic use
N=44/76 (58%) episodes the patient had received an antibiotic in the week before the diagnosis of IE was made, the most frequently used were penicillins
There was NS difference in positive cultures between those who had had antibiotics N=40/44 (91%) and those who had not N=30/31 (97%)

Outcome
N=30/73 (41%) recovered without any complications; N=30/73 (41%) had complicated endocarditis and did not die; N=13/73 (18%) died
Children with blood cultures positive for S. aureus were more likely to have complications than were those whose cultures were positive for viridans streptococci (p=0.001)
N=15/73 required surgery during initial hospitalisation for endocarditis for complications of their infection; valve replacement (N=7), vegetation removal (N=3), drainage of a brain abscess (N=3), removal of an infected ventricular patch (N=1), pacemaker insertion (N=1)
N=13/73 (18%) died of immediate complications; N=7 were early (<4days after admission), N=6 were due to late complications (>21dyas after hospital admission)
46% of those who died had blood cultures that were positive for S. aureus compared with 28% of those who did not die

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding

Melendez LJ, Chan KL, Cheung PK, Sochowski RA, Wong S, Austin TW. Incidence of bacteremia in transesophageal echocardiography - a prospective-study of 140 consecutive patients. *J AM COLL CARDIOL* 1991;**18**:1650-4. Ref ID: 9109	Consecutive case series	N=140 2 tertiary hospitals, Canada	Inclusion: consecutive ambulatory patients scheduled for transoesophgeal echocardiography (TOE) at 2 tertiary hospitals Age 53±15yrs (range 19 to 84yrs), N=69 male, N=71 female, N=34 patients with a valve prosthesis Exclusion: those with a potential source of bacteraemia (known or suspected bacterial infection, indwelling urinary catheter, multiple venipuncture sites, recent surgery or trauma) None of the patients received prophylactic antibiotic agents before or after transoesophageal echocardiography	Blood samples: immediately before the procedure, within 5mins after termination of the procedure, 1hr after the procedure		12 weeks	Blood cultures Microbiology: 10ml per sample, 5ml were inoculated into aerobic and anaerobic culture, cultures were assessed for bacterial growth with use of a semiautomated instrument (Bactec 460) that detects carbon dioxide generated by bacterial metabolism, cultures were considered negative if no bacterial growth was observed after 7days	Not stated

Effect size:

Positive blood cultures
Blood cultures were positive in N=4 patients before TOE, in N=2 in immediately after (bacteria species, coagulase negative staphylococci) and in N=2 late samples (bacteria species, coagulase negative staphylococci, Propionibacterium), both these organisms were considered to be likely contaminants

There was no correlation between difficulty in intubation and a positive blood culture, or between a positive culture and the presence of an indwelling intravenous line

The relative risks of bacteraemia immediately after and 1hr after TOE were NS different from baseline

All patients were contacted 12 weeks after transoesophageal echocardiography, none had developed bacterial endocarditis or other infections requiring the administration of antimicrobial therapy

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Mellow MH,.Lewis RJ. Endoscopy - related bacteremia. Incidence of positive blood cultures after endoscopy of upper gastrointestinal tract. *Archives of Internal Medicine* 1976;**136**:667-9. Ref ID: 1065	Consecutive case series	N=100 Harlem Hospital Center, New York	Inclusion: patients undergoing endoscopy of the upper GI tract Exclusion: patients who had received antibiotics within 96hrs prior to the time of endoscopy	Additional manipulations performed during endoscopy included biopsy in N=58 patients and exfoliative cytology in N=55	Blood samples: blood cultures were taken prior to endoscopy and 10mins after endoscopy in all patients, for the final N=28 blood cultures were also taken 5mins after endoscopy		Blood cultures, no organisms were excluded as being possible contaminants Microbiology: Thiogylcollate and trypticase soy were the bllod culture media used, bottles were incubated for 7days at 37C and checked visually for growth each day, if there was any sign of growth the broth was subcultured to blood agar, MacConkey agar and chocolate agar plates	Not stated

Effect size:

Blood cultures
N=3/100 patients had positive blood cultures after endoscopy (type of bacteria; Enterococcus, Diphtheroids, Staphylococcus epidermidis)
There was no correlation between associated medical conditions, GI lesions, or endoscopic manipulation and the occurrence of postendoscopy bacteraemia

None of the patients with bacteraemia had any detectable clinical sign or symptom of bacteraemia or subsequent sepsis

(Cultures of samples from equipment and environment identified in the bacteriologic surveys for items in the room and the equipment were considered unacceptable in an operating room environment, the endoscopy room being essentially a dirty area)

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Mollison LC, Desmond P, V, Stockman KA, Andrew JH, Watson K, Shaw G *et al*. A prospective-study of septic complications of endoscopic retrograde cholangiopancreatography. *Journal of*	Consecutive case series	N=150 (N=179 procedures)	Inclusion: ERCP, mean age 58yrs (range 18 to 96yrs), 61% were female Therapeutic procedures were performed in 54%(N=96), comprising stenting in 21%(N=37), stone removal in 16%(N=28) and sphincterotomy alone 17%(N=31) Exclusion: patients undergoing combined ERCP and concomitant percutaneous transhepatic cholangiography	ERCP[50]	Blood samples: pre-ERCP and within 10mins of the completion of the procedure Bacteraemia was deemed to be significant if the organisms isolated were consistent with a biliary origin or if anaerobes were found	June to November 1991	Blood cultures Microbiology: 10ml samples, 5ml was inoculated into anaerobic (NR-7A) and 5ml into aerobic (NR-6A) Bactec NR-660 system blood culture bottles and then routinely processed in the microbiology laboratory	Not stated

[50] If prophylactic antibiotics were deemed necessary they were not administered until after the collection of the second set of cultures

Gastroenterology and Hepatology 1994;**9**:55-9. Ref ID: 8945								

Effect size:

Blood cultures
Positive blood cultures were detected in association with N=20 (11%) of procedures
N=9 (5,2%) of cases were considered to be significant, that the organisms were likely to have come from the biliary tree
N=7 were after the procedure, N=1 was prior to the procedure and in N=1 pre- and post-procedure were positive (post procedure organisms were; Enterobacter aerogens, Enterobacter cloacae, Escgerichia coli, Bacteriodes fragillis, Klebsiella oxytoca, Enterobacter faecalis)

During follow-up clinical septic events occurred in N=22 (12.6%) of cases

N=5 of the patients with positive cultures at the time of ERCP subsequently developed clinical sepsis (N=4 of these had been given prophylactic antibiotics appropriate for the organism)

There was an association between therapeutic procedures and sepsis (p=0.0001) and therapeutic procedures and bacteraemia (p=0.015)

(N=110 (61%) of ERCP patients ahd antibiotics peri-ERCP, most commonly gentamicin and ampicillin
N=70 others received antuibiotics at the time of the procedure N=51 gentamicin alone, N=29 gentamicina dn ampicillin, N=11 gentamicin plus ampicillin and metronidazole and N=19 other complications
Antibiotic complications occurred in N=7/109 (6.4%), N=4 developed rashes and N=2 had GI disturbance

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Morris CD, Reller MD, Menashe	Cohort	From 1958 to present (from	Inclusion: Oregan residents who had surgical repair of major congenital heart defects at less than 19yrs of age	Follow-up status of all individuals in		Data from the follow-up cycle	Risk of endocarditis, after surgery,	National Institutes of Health

<table>
<tr>
<td>VD, Morris CD, Reller MD, Menashe VD. Thirty-year incidence of infective endocarditis after surgery for congenital heart defect. JAMA 1998;279:599-603.
Ref ID: 6086</td>
<td></td>
<td>population based register started in 1982)[51] [52]

N=3860, follow-up data available for 88%

USA</td>
<td>Expanded to include 12 major heart defects:

<table>
<tr><th>Defect</th><th>Sample size</th><th>Total pt-yrs follow-up</th></tr>
<tr><td>Tetralogy of Fallot</td><td>497</td><td>7025</td></tr>
<tr><td>VSD</td><td>557</td><td>6310</td></tr>
<tr><td>ASD secundum</td><td>624</td><td>7890</td></tr>
<tr><td>ASD primum</td><td>114</td><td>1117</td></tr>
<tr><td>Coarctation of the aorta</td><td>563</td><td>6675</td></tr>
<tr><td>Aortic valve stenosis</td><td>178</td><td>1814</td></tr>
<tr><td>Pulmonary valve stenosis</td><td>252</td><td>3567</td></tr>
<tr><td>Dexotransposition of the great arteries</td><td>208</td><td>1390</td></tr>
<tr><td>Patent ductus arteriosis</td><td>620</td><td>8751</td></tr>
<tr><td>Complete atrioventricular SD</td><td>165</td><td>996</td></tr>
<tr><td>Pulmonary atresia</td><td>32</td><td>157</td></tr>
<tr><td>Pulmonary atresia with VSD</td><td>50</td><td>262</td></tr>
</table>

Endocarditis was determined using 3 criteria applied to medical records
The median age at operation ranged from 0.005yr (2days) for pulmonary atresia to 7.0yrs for aortic valve stenosis, the age of surgery has decreased over time

Exclusion: children who had palliative surgery only</td>
<td>the registry was obtained by a medical questionnaire every 2yrs</td>
<td></td>
<td>that began in late 1993 are included in this analysis</td>
<td>overall</td>
<td></td>
</tr>
</table>

[51] To inform the registry, medical records departments in all Oregon hospitals that performed cardiac or thoracic surgery were asked to identify cases
[52] To obtain long term follow-up information, subjects were traced through next of kin, physicians, employment records, motor vehicle registrations, city and telephone directories, and the National Death Index

Effect size:

Secundum ASD was the most common defect, pulmonary atresia the least common.

Risk of endocarditis

Risk for endocarditis		No. of cases per pt-yrs
High	Pulmonary atresia with VSD	11.5
	Tetralogy of Fallot with palliative systemic-to-pulmonary shunt	8.2
	Aortic valve stenosis*	7.2
	Pulmonary atresia *	6.4
	Unoperated VSD	3.8
Moderate to low	Primum ASD with cleft mitral valve*	1.8
	Coarctation of the aorta*	1.2
	Complete atrioventricular septal defect*	1.0
	Tetralogy of Fallot*	0.7
	Dextrotransposition of the great arteries*	0.7
	VSD* (no cases occurred with closed VSD in the absence of other abnormalities)	0.6
No documented risk	ASD*	0
	Patent ductus arteriosus*	0
	Pulmonic stenosis*	0

* after definitive surgical repair

After surgery:
Aortic valve stenosis
The highest incidence following surgery was in the cohort with aortic valve stenosis (this includes those with isolated supraventricular or subvalvular aortic stenosis, in whom there were no cases of IE before or after surgery)
Incidence of IE appears to increase more rapidly after 5yrs and by 25yrs the cumulative incidence was 13.3% (3.8%), (SE)

Valve replacement
For those with aortic stenosis the risk for those with valve replacement was compared with those with native valves, 16% (N=28) had aortic valve replacement
For prosthetic valve N=3 cases of endocarditis, 10-year incidence of 26% (13%)
For native valve N=10 cases of endocarditis, 10-year incidence of 5% (2%), 20-year 11% (4%), 25-year 15% (6%)

Coarctation of the aorta
N=8 cases after surgery, the risk appears to increase with age or time after surgery, at 30yrs cumulative incidence was 3.5% (1.6%)

Tetralogy of Fallot
N=5 cases after surgery, all occurred within the 10yrs after surgery, cumulative incidence 1.3%(0.6%), this remains constant to 30yrs
N=3/5 had a residual VSD

Pulmonary atresia with VSD
N=3 episodes of IE after reparative surgery, (N=2/3 had a pulmonary homograft)
At 10yrs the cumulative incidence was 6.4% (4.4%)

VSD
Following surgery, N=4 cases of IE, cumulative incidence at 30yrs, 4.1% (2.1%)
The risk appears to increase 20yrs after surgery, cumulative incidence at 20yrs 0.5%, 25yrs 2.7%

Primum ASD
N=2 cases of IE, cumulative incidence from 10yrs on 2.8% (2.0%)

Overall
N=38 cases after surgical repair, N=7 (18%) deaths distributed among different heart defects
At 25years after surgery the cumulative incidence of IE was 1.3% for tetralogy of Fallot, 2.7% for isolated VSD, 3.5% for coarctation of the aorta, 13.3% for valvular aortic stenosis and 2.8% for primum ASD
Endocarditis occurred in the immediate post-op period in 22% of the cases occurring in children with tetralogy of Fallot, primum ASD, coarctation, pulmonary atresia, and pulmonary atresia with intact septum

(The infection was presumed by the treating physician to be of dental origin in 14%, based on recent dental procedure or poor oral hygiene)

(the authors consider the important outcome of this study to be the recognition of the high risk of endocarditis with aortic stenosis)

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Niederau C, Pohlmann U, Lubke H et al. (1994)	RCT	N=100	Inclusion: consecutive patients likely to undergo a therapeutic or complicated diagnostic ERCP	N=50 Group I 2g cefotaxime IV 15mins before	N=50 Group II control group	Patients were followed up 3days after	Bacteraemia Rectal temperature	Not stated

Prophylactic antibiotic treatment in therapeutic or complicated diagnostic ERCP: results of a randomized controlled clinical study.[see comment]. Gastrointestinal Endoscopy 40: 533-7			Exclusion: history of endocarditis or valvular heart disease, history of allergy to antibiotics, antibiotic therapy less than 48hrs before ERCP	endoscopy Blood samples: before endoscopy, 5, 15, 30 and 120mins after beginning the procedure		ERCP	Culture vials were incubated for 7days	
Effect size: **Bacteraemia** Bacteraemia detected (15 and 30mins) N=4 of the control group, N=0 cefotaxime group (E.coli, Peptostreptococcus, S. aureus) None of the episodes of bacteraemia was followed by clinically evident cholangitis or sepsis N=4 of the control group developed cholangitis or sepsis during the 3day follow-up, all had a temperature of 38.5C or more Bacteraemia or clinical sepsis developed in N=8/50 control group vs. N=0 cefotaxime, p<0.01								

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding

Peterson LJ,.Peacock R. The incidence of bacteremia in pediatric patients following tooth extraction. *Circulation* 1976;**53**:676-9. Ref ID: 1066	Controlled trial	N=107 children	Inclusion: healthy paediatric patients, between the ages of 5 and 13yrs, all teeth were removed using local anaesthesia and forceps extraction technique, the ages of the patients show little variation among the 4 groups	Group I N=28 required extraction of healthy primary teeth for space management and interceptive orthodontic purposes; removed for reasons other disease Group II N=34 required removal of primary or permanent teeth which had diseased or necrotic pulps and associated abscesses Group III N=18 removal of permanent teeth for orthodontic reasons Group IV N=27 restorative dental treatment, this	Blood samples: Groups I, II and III had blood drawn within 2mins following the removal of the tooth, while Group IV had blood for cultures taken prior to their dental treatment		Extractions, blood cultures Microbiology: 2ml samples were drawn into Becton-Dickinson Vactainer, the first tube was grown aerobically, the second anaerobically, the culture medium was a peptone broth supplemented with yeast extract, vitamins, and amino acids to increase microorganism growth, cultures were incubated at 35˚C, tubes with growth were subcultures at 24 and 48hrs, the original culture tubes were incubated and observed for 16days before being reported as negative	Not stated

				group served as a negative control				

Effect size:

Extractions
Average number of teeth extracted: Group I (1.4); Group II (1.2); Group III (3.4); Group IV (0)

Blood cultures
Group I, nondiseased primary teeth, positive cultures N=10/28 (35.7%)
Group II, nondiseased primary teeth, positive cultures N=18/34 (52.9%)
Group III, diseased teeth, positive cultures N=11/18 (61.1%)
Group IV, negative controls, no positive cultures

NS correlation between number of teeth extracted and resultant condition of the culture

Of the N=39 positive cultures, N=23 grew two or more organisms

Organisms found; Streptococcus (N=20, 29%), Peptostreptococcus (N=7, 10%), Diptheroids (N=16, 23%), Staphylococcus (coagulase negative, N=8, 12%), Bacteroids (N=8, 12%), Veillonella (N=3, 4%), Neisseria (N=6, 9%), Vibrio (N=1, 1%)

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Qiang W, Jianchen W, MacDonald R et al. (2005) Antibiotic prophylaxis for	Systematic review	N=4694 N=28 trials (N=10 placebo controlled, N=18						Not stated

transurethral prostatic resection in men with preoperative urine containing less than 100,000 bacteria per ml: a systematic review. [Review] [40 refs]. Journal of Urology 173: 1175-81		no treatment control)						

Effect size:

Criteria
Inclusion: electronic databases searched; MEDLINE 1966 to 2003, EMBASE from 1980 to 2002, Cochrane Library for RCTs and quasi-RCTs comparing antibiotic prophylaxis and placebo/or controls in men undergoing TURP. Search strategy made with MeSH headings including prostatectomy, prostatic hyperplasia, transurethral resection of the prostate, antibiotic prophylaxis, antibiotics and postoperative complications. Bibliographies of included studies were hand searched. The Journal of Urology and European Urology 1998 to 2004 for study abstracts.

RCTs or quasi-RCT were included if they met the criteria of comparing antibiotic prophylaxis with placebo or no treatment control patients undergoing TURP, no local or systemic signs of urinary infection, sterile preoperative urine specimen, reports of at least 1 of postoperative bacteriuria, fever, bacteraemia, septicaemia, additional antibiotic treatment, urethral stricture, catheteisation or hospitalisation duration, and were published in English

Exclusion: studies were excluded from analysis if patients had a preoperative temperature greater than 38C, a preoperative indwelling catheter, kidney dysfunction, bladder tumour, hypersensitivity to antibiotics, preoperative UTI and antibiotic treatment within a week before TURP

Missing or additional information was sought from authors and sponsors

Studies
N=28 trials, N=4694 patients, mean age 69yrs, N=10 trials placebo controlled N=18 no treatment control
N=23 compared a single type of antibiotic with placebo or no treatment, N=5 compared 2 different antibiotic groups with placebo or no treatment

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Rahn R, Schneider S, Diehl O, Schafer V, Shah PM. Preventing post-treatment bacteremia: comparing topical povidone-iodine and chlorhexidine.[see comment]. *Journal of the American Dental Association* 1995;**126**:1145-9	RCT Single-blind	N=120	Inclusion: those who were scheduled for dental treatment involving either intraligamental injection (N=60), or elective extraction of a molar (N=60); N=28 female, mean age 33.6yrs (range 22 to 77yrs) Exclusion: those receiving antibiotics or immunosuppressive therapy or who had a history of bacterial endocarditis, rheumatic fever or congenital heart disease The mean oral hygiene scores and periodontal scores (plaque index, gingival index, sulcus bleeding index, clinical pocket depth) were similar among the patients of all three groups	N=40 0.2%chlorhexidine N=40 10% povidone-iodine Into the sulcus of the affected tooth with an endodontic syringe	N=40 control sterile water Blood samples: before antiseptic, 2, 4, and 6mins after the dental procedure was finished		Bacteraemia Blood samples processed as recommended by the American Society for Microbiology, all micro-organisms were identified by standard identification procedures	Mundipharma/Limburg

Effect size:

Bacteraemia
The blood samples obtained before the dental procedure were completely negative for bacteraemia

Post-procedure bacteraemia; control (N=21, 52.5%), povidone-iodine (N=11, 27.5%), chlorhexidine (N=18, 45.0%)
Bacteraemia povidone-iodine vs. control, $p<0.05$
Viridans streptococci povidone-iodine and chlorhexidine vs. control, $p<0.01$; NS chlorhexidine vs. control

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Roberts GJ, Radford P, Holt R. Prophylaxis of dental bacteraemia with oral amoxycillin in children. *British Dental Journal* 1987;**162**:179-82.	Controlled study	N=108 [53] UK	Inclusion: under 16yrs and required admission for extensive conservative dental work as well as the extraction of at least one tooth Exclusion: allergy to one of the penicillin group or a significant medical disorder The randomised groups were comparable in age and sex	N=47 oral amoxicillin 50mgs/kg 2hrs before the scheduled time for surgery (mean dose 50.4mg/kg) Blood samples: prior to nasotracheal intubation, 2mins after nasotracheal intubation, extensive	N=8 with cardiac abnormalities given oral amoxicillin[54] N=6 refusers		Bacteraemia, sampling time 4x1ml blood samples processed using differing broths, plates were incubated and positive results recorded as cfu, bacteria grown were identified by a described procedure (a broad spectrum penicillinase was	Not stated

[53] allocation decided at random
[54] N=2 vomited the oral amoxicillin and were given IV 250mg upon attainment of anaesthesia

				conservative dental work was carried out before extraction; 2mins after extraction of the first tooth samples were taken. (supplementary studies; one had additional samples taken at 45secs post extraction, another 5mins post extraction).			added to all samples from those who had received amoxicillin, a pilot study confirmed that the addition did not alter culture results)	

Effect size:

Bacteraemia
All samples taken at the pre-intubation sampling time were negative
2mins after intubation N=3/47 in the control group and N=2/6 in the refusers had positive blood cultures (these were typical of those commonly colonising the upper respiratory tract
The post extraction samples; N=18/47 positive in the control group, N=1/47 in the amoxicillin group and N=2/6 in the refusers group, control vs. amoxicillin, $p<0.001$ (the organisms isolated were typical of those normally found in bacterial dental plaque)

Sampling time
Samples taken 45secs after extraction showed N=1/9 positive, none of the corresponding samples taken at 5mins was positive. At 5mins N=5/20 were positive, for the corresponding samples at 2mins N=10/20 were positive *(the authors note that these results suggest that the optimal sampling time is 2mins or less)*

Reference	Study type/	Number of	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of

	Evidence level	patients						funding
Roberts G,.Holzel H. Intravenous antibiotic regimens and prophylaxis of odontogenic bacteraemia. *British Dental Journal* 2002;**193**:525-7.	Retrospective study	N=92	Inclusion: children and adolescents with severe congenital heart disease, mean age 8yrs2mths (range1yr5mths to 19yrs8mths) undergoing dental treatment under GA; dental treatment consisted of a mixture of dental extractions and restorations Exclusion: anticoagulant treatment, antibiotic therapy within the last month and known viral carriage	All children received intravenous antibiotic drugs immediately upon attainment of anaesthesia but before the start of dental treatment, the antibiotics used were those advised by the child's cardiac physician [55] Where appropriate the dose was adjusted to match the weight of the child			Bacteraemia Bacteria was speciated using standard microbiological methods with oral streptococci speciated using the API Strep 20 system The extent of dental disease was graded using simplified indices for dental plaque, gingivitis and spontaneous gingival bleeding	Not stated

[55] ampicillin was used as first choice, the use of teicoplanain and amikacin combined was required as part of the hospital infection control policy where there were concerns about antibiotic resistant Staphylococcus aureus

Effect size:

The two major antibiotic groups used were ampicillin (N=42) and teicoplanin & amikacin (N=35)(clindamycin N=6, teicoplanin N=2, amikacin N=1 vancomycin N=2, ampicillin & clindamycin N=1, ampicillin & vancomycin N=1, ampicillin & amikacin N=4)
There was no identifiable pattern of antibiotic usage in relation to underlying cardiac condition

Bacteraemia
There was NS difference in the positive blood cultures with ampicillin (16.7%) and teicoplanin & amikacin (22.2%)
Data were compared with a contemporaneous examining the percentage positive cultures following multiple extractions
The ampicillin group was significantly less than the multiple extractions, 16.7% vs. 54.2%, p=0.0001. this was also seen with the teicoplanin & amikacin group vs. multiple extractions, 22.2% vs. 54.2%, p<0.003
There was NS relationship between the presence or absence of bacterial dental plaque and/or gingivitis

All isolated organisms exhibited full antibiotic sensitivity during routine testing

Follow-up
All patients had an uneventful recovery without any signs and symptoms of endocarditis

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Roberts GJ, Holzel HS, Sury MR, Simmons NA, Gardner P, Longhurst P. Dental bacteremia	RCT [56]	N=735	Inclusion: children referred to Guy's Dental Hospital or GOSH for dental treatment under general anaesthetic, N=383 male, N=352 female, mean age 9yrs 3mths	Group A – nonmanipulation group; baseline and dental examination Group B – cleaning	Blood samples: one sample taken 30sec after each procedure	1991 to 1993	Blood cultures Microbiology: Two commercial blood culture systems were used; the Bactec radiometric	Not stated

[56] randomisation was using random number tables, there were three exceptions, extractions which could only be performed if clinically needed, mucoperiosteal flap because of its relative infrequency was studied each time it was needed for treatment of the patient, the third was the cardiac group all of whom had antibiotic prophylaxis and therefore formed a separate group of patients

in children. *SO: Pediatric cardiology* 1997;**18**:24-7. Ref ID: 4116				procedures; toothbrushing, polishing and scaling Group C – minimal manipulation group; intraligamental injection and nasotracheal tube Group D – conservative dentistry procedures; rubber dam placement, slow drill, fast drill, and matrix band placement Group E – oral surgery group; single extractions, multiple extractions, and mucoperisoteal flaps Group F – groups having antibiotic prophylaxis; cardiac patients			system and the Bactec 760, a 3ml volume of blood was inoculated into each of the aerobic and anaerobic bottles. Bacteria were speciated using standard methods, streptococci were speciated using API Strep 20	

Effect size:

Blood cultures
All procedures were associated with a bacteraemia, highest association intraligamental injection, lowest fast drill

Positive blood cultures;
- baseline N=5/53 (9.4%)
- dental examination N=9/53 (17.0%)
- toothbrushing N=20/52 (38.5%)
- polishing teeth N=13/53 (24.5%)
- scaling teeth N=20/50 (40.0%)
- intraligamental injection N=28/29 (96.6%)
- nasotracheal tube N=3/31 (9.7%)
- rubber dam placement N=15/51 (29.4%)
- slow drill N=6/47 (12.8%)
- fast drill N=2/47 (4.3%)
- matrix band placement N=18/56 (32.1%)
- single extraction N=17/44 (38.7%)
- multiple extractions N=30/59 (50.9%)
- mucoperiosteal flap N=20/51 (39.2%)
- cardiac patients N=6/59 (10.2%)

Comparison of proportions compared to baseline (95% CI):
- toothbrushing 12.8 to 45.4%
- polishing teeth 0.7 to 29.4%
- scaling teeth 14.0 to 47.2%
- intraligamental injection 76.9 to 97.3%
- rubber dam placement 4.8 to 35.1%
- matrix band placement 7.4 to 38.0%
- single extraction 12.5 to 45.9%
- multiple extractions 24.2 to 58.6%
- mucoperiosteal flap 13.4 to 46.2%

NS; dental examination, nasotracheal tube, rubber dam placement, slow drill, fast drill,

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Roberts GJ, Simmons NB,	RCT	N=143 children	Inclusion: healthy children attending for dental extractions under general anaesthetic, average age 8yrs 7mths	N=50 baseline, blood taken before any	Blood samples: taken 30sec after injection[58]		Blood cultures Microbiology:	Not stated

[57] for the study groups, one of the three injection techniques was selected using random number tables

Longhurst P, Hewitt PB. Bacteraemia following local anaesthetic injections in children. *British Dental Journal* 1998;**185**:295-8. Ref ID: 2440		Guy's Dental Hospital, London	(differences between the baseline and test groups was NS) Exclusion: children who had had antibiotics within the previous month, those with a history of Hepatitis B or HIV	dento-gingival manipulation N=32 buccal infiltration N=32 modified intraligamental N=29 conventional intraligamental [57]			Two commercial blood culture systems were used; the Bactec radiometric system and the Bactec 760, a 3ml volume of blood was inoculated into each of the aerobic and anaerobic bottles. Bacteria were speciated using standard methods, streptococci were speciated using API Strep 20. A further 1.5ml was inoculated into the Isolator system vial	
Effect size: **Blood cultures** Positive blood cultures: - baseline N=4/50 (8.0%; 0.5 to 15.5% 95% CI) - buccal infiltration N=5/32 (15.6%; 2.8 to 28.5%, 95% CI) - modified intraligamental N=16/32 (50.0%; 29.2 to 64.5% 95% CI) - conventional intraligamental N=28/29 (96.6%; 75.2 to 99.2%, 95% CI)								

[58] only one sample of blood was taken from each child

Significant differences:
- baseline vs. modified intraligamental (p<0.0001
- baseline vs. conventional intraligamental (p<0.0001)
- buccal infiltration vs. modified intraligamental (p<0.003)
- buccal infiltration vs. conventional intraligamental (p<0.0001)
- modified intraligamental vs. conventional intraligamental (p<0.0001)

NS differences:
- baseline vs. buccal infiltration

Colony forming units (cfu):
The results for infiltration, modified intraligamental and the baseline were always zero. Positive cultures were only obtained in those who had had a conventional intraligamental injection, mean value 252cfu/ml, with a range of 0 to 3018cfu/ml

Micro-organisms isolated
The organisms isolated are typical of those associated with bacteraemia of dental or oral origin

Peridontal indices and bacteraemia
There was no positive association between the presence of plaque on the tooth surface adjacent to the conventional intraligamental injection, similarly there was no association with gingivitis

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Roberts GJ, Gardner P, Longhurst P, Black AE, Lucas VS. Intensity of	RCT[59]	N=257 children GOSH and Guy's	Inclusion: healthy children receiving dental treatment under general anaesthetic, N=141 male, N=116 female, mean age 9yrs 1mth (range 2yrs to 19yrs 6mths)	N=54 baseline (no procedure) N=51 rubber bam placement	Blood samples: baseline before any dento-gingival manipulation was carried out		Blood cultures Microbiology: Two commercial blood culture systems were	Not stated

[59] randomisation by random number table

bacteraemia associated with conservative dental procedures in children.[see comment]. *British Dental Journal* 2000;**188**:95-8. Ref ID: 460		and St Thomas' Hospital Trust, London	Exclusion: those who had taken antibiotics within the previous month, known viral carriage and haemorrhagic disorders	N=49 slow drill (60seconds) N=47 fast drill (60seconds) N=56 matrix band and wedge	and 30sec after each of the procedures		used; the Bactec radiometric system and the Bactec 760, a 3ml volume of blood was inoculated into each of the aerobic and anaerobic bottles. Bacteria were speciated using standard methods, streptococci were speciated using API Strep 20. A further 1.5ml was inoculated into the Isolator system vial	

Effect size:

Blood cultures
Positive blood cultures: baseline N=5/54 (9.3%); rubber dam placement N=16/51 (31.4%); slow drill n=6/49 (12.2%); fast drill N=2/47 (4.3%; matrix band and wedge N=18/56 (32.1%)
Significant differences in the number of positive cultures for:
- baseline vs. rubber dam placement ($p<0.005$)
- baseline vs. matrix band ($p<0.003$)
- rubber dam placement vs. slow drill ($p<0.02$)
- rubber dam placement vs. fast drill ($p<0.001$)
- slow drill vs. matrix band ($p<0.02$)
- fast drill vs. matrix band ($p<0.0001$)

NS difference:

- baseline vs. slow drill; baseline vs. fast drill; rubber dam placement vs. matrix band; slow drill vs. fast drill

Intensity of bacteraemia
There was NS differences between any of the groups in the cfu (colony forming units per/ml of blood)

Micro-organisms
The organisms isolated are typical of those associated with bacteraemia of dental origin

Exploration by each group of samples did not reveal showed NS relation between plaque accumulation, gingival inflammation, gingival bleeding and the presence or absence of bacteraemia

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Roberts GJ, Jaffray EC, Spratt DA, Petrie A, Greville C, Wilson M *et al*. Duration, prevalence and intensity of bacteraemia after dental extractions in children. *Heart (British Cardiac Society)* 2006;**92**:1274-7.	RCT Not blinded	N=500	Inclusion: children attending Eastman Dental Hospital for treatment under general anaesthetic, the mean age of the children was 7.6yrs (range 3.4 to 18.9) Exclusion: antibiotic usage within the previous month, viral carriage, haemorrhagic disorders and body weight less than 17.5kg An orodontic examination was carried out according to the WHO criteria for dental caries, plaque and gingivitis were assessed Age, plaque index, gingivitis index, number of teeth present at the start of the operation and number of teeth extracted were all similar between the various groups	Children were allocated to one of the time groups in random permuted blocks; 10sec, 30sec, 1min, 2min, 4min, 7.5min, 15min, 30min, 45min, 1hr	Other comparison time groups		Percentage prevalence of positive cultures, intensity of bacteraemia, speciation of the organism isolated Microbiology: The samples were processed automatically in the Bactec 9480, for the lysis filtration samples the blood was processed by a well-established method, positive cultures from	British heart foundation grant

Ref ID: 2375							both broth culture and lysis filtration were isolated and identified. Negative controls were processed with every 10th run of broth culture and each run of lysis filtration and identify contamination	

Effect size:

Intensity of bacteraemia (cfu/6ml sample)
10sec; before extraction median 2.9 (range 0 to 46); after extraction median 9.8 (range 0 to 149), p=0.001
30sec; before extraction median 0.5 (range 0 to 4); after extraction median 2.6 (range 0 to 17), p=0.001
1min; before extraction median 0.4 (range 0 to 4); after extraction median 16.4 (range 0 to 247), p=0.003
2min; before extraction median 1.2 (range 0 to 23); after extraction median 8.1 (range 0 to 162), p=0.009
4min; before extraction median 0.4 (range 0 to 4); after extraction median 1.7 (range 0 to 15), p=0.002
7.5min; before extraction median 0.4 (range 0 to 4); after extraction median 1.2 (range 0 to 14), p=0.002
15min; before extraction median 1.7 (range 0 to 53); after extraction median 1.9 (range 0 to 33), NS
30min; before extraction median 0.3 (range 0 to 6); after extraction median 0.6 (range 0 to 8), not determined
45min; before extraction median 0.7 (range 0 to 3); after extraction median 2.4 (range 0 to 46), NS
1hr; before extraction median 1.0 (range 0 to 28); after extraction median 2.1 (range 0 to 49), NS

The intensity was significantly greater at the post-extraction time than at the pre-extraction time up to and including 7.5min; however by 15min and beyond, the difference was NS

The odds of having a positive culture were significantly greater in the post-extraction time than in the pre-extraction time (OR>1) at each time point up to an including a post-procedure time of 7.5min but not beyond this time

The genera most often detected were Streptococcus, Actinomyces and Staphylococcus[60]

(it is appropriate to estimate that dental bacteraemia is quenched within about 12min of completing dental extractions)

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Rolando N, Gimson A, Philpott-Howard J et al. (1993) Infectious sequelae after endoscopic sclerotherapy of oesophageal varices: role of antibiotic prophylaxis. Journal of Hepatology 18: 290-4	RCT [61]	N=97 (N=115 procedures) London	Inclusion: patients admitted for sclerotherapy for bleeding oesophageal varicies Exclusion: <18yrs, antimicrobials within the preceding 72hrs, history of allergy to imipenem/cilastatin Groups were comparable for age, sex, encephalopathy grade, ascites and biochemical parameters	N=47 IV imipenem/cilastatin over 20min Blood samples: before and immediately after each endoscopic procedure	N=50 control IV dextrose-saline		Bacteraemia Blood culture bottles examined twice a day for the first 2days and daily for a further 5days	Merck, Sharpe & Dohme Ltd

[60] some of the staphylococci may be contaminants, it is not possible to identify the skin as a source of contamination without carrying out DNA typing of the isolates and matching them to skin swabs taken at the time of the blood sample

[61] Patients were sequentially assigned using computer-generated randomisation tables

Effect size:

Bacteraemia
N=2/97 bacteraemia in the pre-endoscopy samples (excluded in the analysis for efficacy of prophylaxis)

Early bacteraemia (isolation of any pathogen from cultures taken 30-min post-sclerotherapy without clinical signs of infection and with a negative blood culture taken before sclerotherapy); N=1/57 (1.8%) sessions imipenem/cilastatin group; N=5/58 (8.6%) sessions control group, NS difference (organisms; Staphylococcus aureus, Eschericha coli, Enterobacter cloacae, Xanthomonas maltophilia)

Clinical bacteraemia (isolation of any pathogen from blood cultures with clinical signs of infection) was detected in N=8 patients in the first 4days after sclerotherapy and occurred in equal numbers in both groups (organisms; Staphylococcus aureus, Staphylococcus epidermis, Escherichia coli, Kledsiella pneumoniae)

There were NS differences in outcome between the two groups

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Roudaut R, Lartigue CM, Texier-Maugein J, Dallocchio M. Incidence of bacteraemia or fever during transoesophageal echocardiog	Consecutive case series	N=82 France	Inclusion: patients referred fro transoesophageal echocardiography Exclusion: had received antibiotics before the procedure, was febrile, had any suspicion of infective endocarditis The mean procedure duration was 19min and no complications occurred There was NS differences in the clinical characteristics of the two groups, N=8 patients had prosthetic heart valves	N=44 (group I) N=38 (group II)	Blood samples: - group I blood cultures taken before procedure, immediately after the procedure, 15min after procedure - group II blood cultures taken before	Rectal temperature of the N=62 hospitalised patients was measured twice a day for a mean of 6 days after the procedure.	Bacteraemia, fever, follow-up Microbiology: Aerobic and anaerobic blood culture bottles (BCB system roche) were inoculated and incubated for 10days at 37˚C	Not stated

[62] in addition in group II cotton swabs were used to take smear samples from the surface of the endoscope after the procedure

raphy: A prospective study of 82 patients. *European Heart Journal* 1993;**14**:936-40. Ref ID: 3797					procedure, during procedure (10min after the first attempt to introduce the endoscope), immediately after procedure[62]	A third (34%) were examined a few months later to evaluate any occurrence of endocarditis		
Effect size: **Incidence of bacteraemia** N=2/82 (2.4%) patients had a single positive blood culture (Corynebacteria from a group I patient at the end of the procedure, Staphylococcus epidermis from a group II patient during the procedure from the second patient)[63] **Incidence of fever** The rectal temperate rose above 37.5Cin N=9 patients within the first 24hr after examination but returned to normal within the subsequent 24hr (maximum temperature observed was 38.4C) **Follow-up** A third (34%) of the patients were seen within the first months after the procedure, average follow-up 4mths No sign of endocarditis was detected in these patients[64]								

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding

[63] the smear samples from the surface of the endoscope after the procedure were positive in N=29/38 (79%), the organisms were essentially haemolytic Streptococcus or Neisseria

[64] for those who were lost to follow-up the authors assumed that patients would have been referred back to them in the event of an episode of endocarditis

Salman L, Prince AS, Gersony W. Pediatric infective endocarditis in the modern era. *The Journal of Pediatrics* 1993;**122**:847-52. Ref ID: 11630	Case review	N=62 cases of paediatric IE USA	Children treated at a hospital in Columbia, to be included patients had to meet blood culture and/or clinical criteria; N=39(63%) male, ages ranged from 1mth to 19yrs (median age 8.2yrs)			15years January 1977 to February 1992		Not stated

Effect size:

Prior medical conditions

N=62 cases of paediatric IE, 70% had structural heart disease

Complex cyanotic heart disease	22
VSD	9
Other acyanotic lesions	5
Mitral valve prolapse	4
Rheumatic heart disease	3

Outcome

Mortality rate N=13 (21%)

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding

Sauter G, Grabein B, Huber G et al. (1990) Antibiotic prophylaxis of infectious complications with endoscopic retrograde cholangiopancreatography. A randomized controlled study. Endoscopy 22: 164-7	RCT [65]	N=96 (N=100 procedures)	Inclusion: ERCP Exclusion: history or signs of endocarditis or valvular heart disease, history of allergy to antibiotics, antibiotic therapy less than one week prior to ERCP Two groups were matched for age, underlying disease of the pancreaticobiliary tract, duration of ERCP, interventions during ERCP (such as sphincterotomy or stone extraction)	N=50 cefotaxime 2g IV 15min before starting ERCP Blood samples; during and 5mins after ERCP	N=50 control group, no antibiotic therapy		Bacteraemia Two pairs of bottles of enriched trypticase soy broth for aerobic and anaerobic culture, one of the pairs containing a resin for the absorption of antibiotics (Bactec NR6A, NR7A, NR16A, NR17A), culture vials were incubated for 7days	Not stated
Effect size: **Bacteraemia** No blood cultures were positive prior to ERCP Significant difference between cefotaxime (N=1/50, 2%) vs. control group (N=8/50, 16%), p<0.02 Duration of the procedure NS difference between those who had a bacteraemia and those who did not Manipulations such as papilotomy, stone extraction, or balloon dilatation of the bile duct NS difference the frequency of bacteraemia when compared with simple diagnostic ERCP N=2 patients with a bacteraemia developed fever >38C (not accompanied by leukocytosis or sings of cholangitis) Most of the micro-organisms found in the blood cultures were bacteria of the normal oropharyngeal flora (streptococcus milleri, streptococcus salivarius,								

[65] Randomised using a closed envelope method

streptococcus mitis, streptococcus pneumoniae, enterococus faecalis, enterococcus faecium, aerococcus viridans, corynebacterium pseudotuberculosis, klebsiella pneumoniae)

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Selby WS, Norton ID, Pokorny CS et al. (1994) Bacteremia and bacterascites after endoscopic sclerotherapy for bleeding esophageal varices and prevention by intravenous cefotaxime: a randomized trial. Gastrointestinal Endoscopy 40: 680-4	RCT [66]	N=31 (N=39 episodes of bleeding) Australia	Inclusion: those undergoing emergency endoscopic sclerotherapy, defined as performed within 48hrs of bleeding Exclusion: antibiotics within 72hrs, antibiotics required for other indications, patients who met the criteria for spontaneous bacterial peritonitis, allergy to penicillin or cephalosporins Patients could enrol in the study on more than one occasion Post allocation patients were stratified into those with and those without ascites There was no difference between the groups in cause of liver disease, use of ET tubes, need for vasopressin or balloon tamponade	N=19 1g cefotaxime IV immediately before procedure Blood samples: before endoscopy, 5mins, 4hrs and 24hrs after sclerotherapy	N=20 No antibiotic	Study between August 1989 to December 1991	Bacteraemia Cultures were performed using standard aerobic and anerobic techniques at 37C, organisms were identified using conventional means	Not stated

[66] Allocation by selection of a sealed envelope containing a random number

Effect size:

Blood cultures
N=1/19 positive at 5mins with cefotaxime (alpha-haemolytic streptococcus)
N= 6/19[67] control groups positive cultures (p=0.04 vs. cefotaxime); N=5 positive at 5mins, N=2 positive at 4hrs (alpha-haemolytic streptococci, veillonella sp, streptococcus milleri, streptococcus salivarius, neisseria sp – were identified)
At 24hrs no positive cultures with either group

Oral flora including alpha-haemolytic streptocci were found on the endoscope

Follow-up
The presence of bacteraemia was not correlated with fever after sclerotherapy
Clinical sepsis did not develop in any of the patients during the 24hrs after sclerotherapy
N=7 (18%) died during hospital admission, this was NS difference between those who received antibiotics and the control group

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Sett SS, Hudon MP, Jamieson WR et al. (1993) Prosthetic valve endocarditis. Experience with porcine bioprostheses 6739. Journal of Thoracic & Cardiovascu	Retrospective review	N=56 Canada	Inclusion: patients who had endocarditis related to a porcine bioprosthesis between 1975 and 1988, those who had undergone concomitant procedures, such as coronary artery bypass, were included; diagnosis was based on two positive blood cultures and histopathologic evidence; mean age at initial surgical intervention 57yrs (range 27 to 81yrs)				Outcomes, death, survival	Not stated

[67] N=1 with staphylococcus epidermis not considered in further analysis

lar Surgery 105: 428-34								

Effect size:

PVE diagnosed in N=56/3200

Outcomes
Overall mortality N=18/56, 32%; mortality rate N=6/8, 75% with early PVE and N=12/48, 25% with late PVE [68]

The most common organism was Staphylococcus epidermis (N=12, N=4 died), Streptococcus viridans (N=8, N=2 died), Staphylococcus aureus (N=7, N=3 died), Candida albicans (N=4, N=2 died)

Causes of death with early PVE were septicaemia, congestive heart failure, thrombotic occlusion of a mitral prosthesis
Causes of death with late PVE were congestive heart failure, hepatic and renal failure, septicaemia, ruptured mycotic aneurysm, adult respiratory distress syndrome

N=6 had previous NVE, in only N=1 was the organism the same as with the original NVE, Streptococcus viridans

91% of those with late PVE survived after combined medical and surgical treatment vs. 62% with medical therapy alone, $p<0.01$

N=26 reoperated cases, findings showed perforation (N=8, 31%), vegetations (N=9, 35%), dehiscence (N=11, 42%), annular abscess (N=7, 27%)

Both early and late groups, univariate analysis showed renal status, presence of ongoing sepsis, mode of treatment, presence of fever, previous dental procedure, lack of dental prophylaxis, time to diagnosis, and age >65yrs, were predictors of death ($p<0.05$)
Multivariate analysis, renal status ($p<0.05$), mode of treatment ($p<0.05$), time to diagnosis ($p<0.04$) and age ($p<0.05$) were predictors of early death

Follow-up; N=1 subsequent death related to recurrent PVE

[68] Endocarditis diagnosed within 60days of operation was classed as early endocarditis, cases that occurred after 60days were classed as late endocarditis

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Shanson DC, Akash S, Harris M, Tadayon M. Erythromycin stearate, 1.5 g, for the oral prophylaxis of streptococcal bacteraemia in patients undergoing dental extraction: efficacy and tolerance. *Journal of Antimicrobial Chemotherapy* 1985;**15**:83-90	RCT [69] Double-blind	N=109 side effects study N=82 dental bacteraemia study London	Inclusion: adult patients undergoing dental extractions in the out-patient department, age range 18 to 78yrs, male:female ratio 3:1, Inclusion: healthy adults aged between 18 and 71yrs attending the out-patient department were also studied	N=56 1.5g erythromycin stearate orally 1hr before dental extraction N=40 erythromycin	N=53 matched placebo N=42 placebo	7days	Bacteraemia, side-effects	Abbott Laboratories

[69] Random code and coded envelopes containing either erythromycin or placebo of identical appearance, the number of the envelope issues to each patient was recorded and numbers decoded only after the trial on side-effects was completed

Effect size:

Streptococcal bacteraemia
Streptococci were isolated from the nutrient broth cultures in N=18/42 (43%) in the control group compared with N=6/40 (15%) erythromycin group, p=0.01
The total numbers of 1litre blood culture bottles yielding growth of viridans streptococci were N=20/240 (8%) inoculated with blood from those receiving erythromycin and N=87/252 (35%) inoculated from the placebo group

Side-effects
N=29/56 (52%) receiving erythromycin reported GI side-effects compared with N=10/53 placebo group

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Shull HJ, Jr., Greene BM, Allen SD, Dunn GD, Schenker S. Bacteremia with upper gastrointestinal endoscopy. *Annals of Internal Medicine* 1975;**83**:212-4. Ref ID: 1069	Case series	N=50 USA	Inclusion: male patients referred for upper GI endoscopy Exclusion: intravenous or urinary catherter or other obvious mechanical breaches of the skin, febrile, leukocytosis (total leukocyte count greater than 10000/mm3), had received antibiotics for 2wks before the procedure, other evidence of infection from clinical records		Blood samples: before, during, at 5min after and 30min after the procedure		Bacteraemia Microbiology: Cultures were incubated at 37˚C, bottles were examined visually for growth after 18hrs incubation and daily or every other day thereafter, each bottle was subcultured at 48hrs and after 10days	Veterans Administration, National Institute of Mental Health

Effect size:

Bacteraemia [70]
Bacteraemia was detected in N=4/50 (8%) of the participants, none of the blood specimens taken during endoscopy were positive, bacteraemia was detected at 5min or 30min or both (organisms identified; Neisseria perflava, Streptococcus salivarius, Propionobacterium acnes, S. mitis, Acinetobacter calcoaceticus, Staphylococcus epidermidis)
N=11 participants had biopsies taken, none had any positive blood cultures

Follow-up of those with positive cultures showed no clinical manifestations of bacteraemia

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Shyu K-G, Hwang J-J, Lin S-C, Tzou S-S, Cheng J-J, Kuan P *et al*. Prospective study of blood culture during transesophageal echocardiography. *American Heart Journal*	Case series	N=132 (N=135 procedures) National Taiwan University Hospital Taiwan	Inclusion: patients undergoing transoesophageal echocardiography, N=66 male, N=66 women, ranging in age from 17 to 73yrs (mean age 44.6yrs) Exclusion: absence of fever (<37.5C) within 3days of the procedure, no leukocytosis (total white cell count <10000/mm3), no use of antibiotics for 3days before the procedure, other evidence of infection from clinical record review No procedure related complications were noted in any of the N=132 patients		Blood samples: 30 to 60mins before the procedure, immediately after, 180 to 240mins after the procedure[71]	October 1990 to August 1991	Blood cultures, throat swaba Microbiology: blood cultures were incubated at 35˚C for 7days, aerobic culture vials were tested twice on days 1 and 2 and once on days 3 through 7, anaerobic culture vials were tested once on days 1 through 7.	Not stated

[70] the following organisms were excluded as contaminants unless they were found in both flasks, or in one flask and in significant numbers on the corresponding pour plate; Staphylococcus epidermis, Bacillus species and aerobic diptheroids
[71] A cotton swab took smear samples from the throat 30 to 60mins before the procedure

1992;**124**:1541-4. Ref ID: 3820							Positive vials were subcultured on appropriate media and gram staining was performed	

Effect size:

The mean time (±SD) of introducing the endoscope into the oesophagus was 50.1(±64.8)secs, the insertion time was less than 30sec in N=61 procedures, 30 to 60sec in N=52 procedures, and >60sec in N=22 procedures
The mean procedure time was 10.2(±4.3)mins

Blood cultures [72]
N=3/270 pre-echocardiographic cultures were positive, the N=3 patients were asymptomatic and subsequent cultures were negative

None of the blood samples obtained immediately after the procedure was positive

N=2/270 cultures from N=1 patient 4hrs after the procedure were positive

No evidence of endocarditis was subsequently found in these patients and the positive cultures were considered to be transient bacteraemia, no positive blood samples were obtained in N=21 patients with prosthetic valves

Throat swabs
N=135 throat swabs, the majority of isolated microorganisms were Neisseria species and Streptococcus viridans, these are normal flora of the oral cavity. The microorganisms isolated from blood cultures were different to those isolated from the throat swab (post procedure, Staphylococcus epidermidis)

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Silk KL, Ali	Case	N=50	Inclusion: patients having nasal		Blood samples:		Blood cultures,	Not

[72] The threshold of the growth value indicating a positive result was set at 25 to 30, a change in growth value of >10 to 15 between two consecutive readings was also indicative of a positive result

MB, Cohen BJ, Summersgill JT, Raff MJ. Absence of bacteremia during nasal septoplasty. *Archives of Otolaryngology Head Neck Surgery* 1991;**117**:-55. Ref ID: 4847	series	USA	septoplasty, age range 15 to 87yrs (mean age 33.3yrs), N=21 female, N=29 male, all patients had septal deviation		immediately prior to surgical incision, 5 and 15min following the onset of surgery		nasal swabs Microbiology: 10ml sample, 5ml were injected into each of two blood culture bottles containing trypticase soy broth incubated at 37˚C, subcultured onto blood and mannitol salt agar plates at 24hrs and examined for turbidity daily for 2wks	stated
Effect size: **Blood cultures** None of the blood cultures taken from the N=50 patients either prior to surgery or during the procedure showed bacterial growth **Nasal swabs** N=23/50 (46%) of patients showed S aureus in nasal swabs (N=19 (82.6%) of these yielded S aureus in all four cultures), N=6/50 yielded coagulase negative staphylococci and N=1/50 Pseudomonas aeruginosa								

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding

Sontheimer J, Salm R, Friedrich G, Vonwahlert J, Pelz K. Bacteremia following operative endoscopy of the upper gastrointestinal-tract. *Endoscopy* 1991;**23**:-72. Ref ID: 4843	Controlled study	N=160	Inclusion: patients undergoing interventional endoscopy, patients were included irrespective of age, sex, general condition or endoscopic measures taken Exclusion: antibiotic treatment within the previous 48hrs, indwelling venous or arterial catheters, signs of localised or general infection or sepsis	N=120 endoscopic operative measures Blood samples: prior to the examination, 3 to 5min after the potentially dispersing event, 30min after the end of the examination	N=40 control group (N=15 diagnostic endoscopies without therapeutic measures; N=25 who in addition had sample biopsies taken)		Bacteraemia (certain, questionable, contamination) Microbiology: Aerobes were cultivated by incubation for 4 to 6days at 36˚C under 5 to 10% CO2, the colonies were then inoculated to CO agar in order to obtain pure cultures. Anaerobes were streaked on HCB agar and cultivated in an anerobian receptacle for a minimum of 6days at 36˚C.	Not stated
Effect size: **Endoscopic measures** N=15 diagnostic control group N=25 gastroscopy with biopsy excision N=25 dilative oesophageal interventions N=25 sclerotherapy N=25 ERCP and interventional measures N=25 endoscopic percutaneous N=20 laser treatment of tumours								

Bacteraemia
Certain bacteraemia[73] was identified in N=18/160 (11.25%), the germ spectrum comprised aerobic and anaerobic, which were found as flora of the upper GI tract, mixed cultures of two different germs were found in N=7/18

Positive culture findings were classified as questionable bacteraemia[74] in N=29 (18.12%), in the other N=10 (6.25%) the culture findings were identified as contamination, in N=3 cases the entire culture medium batch had been contaminated

Bacteraemia appears to occur significantly more frequently ($p<0.05$) following operative endoscopies (gastroscopy including sample excision N=5 positive bacteraemia, 12.5%) than after diagnostic endoscopies (surgical endoscopy N=42 positive bacteraemia, 35.0%)

Within the group of patients in whom bacteraemia was not identified, N=113, leukocytes (5700 to 6700) and rectal temperature (37.3 to 37.4) showed slight increases, whereas there was a greater increase in those where bacteraemia was identified, N=47, leukocytes (4700 to 9700) and in rectal temperature (37.2 to 38.8)

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Strom BL, Abrutyn E, Berlin JA, Kinman JL, Feldman RS, Stolley PD *et al*. Risk factors for infective endocarditis: oral hygiene	Case-control	N=416 enrolled potential case-patients N=287 community acquired IE not	Information was abstracted from medical records and obtained from structural telephone interviews with controls and endocarditis cases (medical records were requested to validate individual diagnosis and procedures, agreement between interviews and medical records exceeded 90% Cases were more likely than controls to suffer from self-reported severe kidney		Controls and case-patients were matched for age, sex, race, education, occupation and dental insurance Cases were		Prior infection, medical procedures and therapies, oral hygiene	NIH grant

[73] minimum of 3 colonies of the same germ species in ≥2/6 media, provided the germ is known to be local flora at the site of intervention; strictly anaerobic germs were isolated, irrespective of the number of their colonies on the media
[74] germ count below 3/10ml of blood, germs were not identified in the patient's secretion and not known to be at the site of intervention, 3 or more colonies of the same germ species grew on one culture medium only, one and the same germ species was found at time 0, 3to5, and 15min

and nondental exposures. *Circulation* 2000;**102**:2842-8. Ref ID: 31		associated with IV drug use N=273 interviewed case-patients From August 1988 – November 1990 surveillance for IE in 54 hospitals Philadelphia	disease, they were also more likely to report physician diagnosed diabetes. Cases did not differ from controls in history of living with pets, animal bites, smoking, menopausal status, history of rheumatoid arthritis, other autoimmune disease, thyroid disease, alcoholism, cancer, stroke, ischaemic heart disease, cardiomyopathy, arrhythmia, heart operation other than valve replacement, cardiac disease other than prior history of endocarditis, valvular heart disease, congenital heart disease, rheumatic fever, heart murmur Cases and controls were similar with respect to age and sex, race, education, occupation, and dental insurance		more likely to have self-reported prior kidney disease, to report physician diagnosed diabetes			

Effect size:

Prior infection as a risk factor
An association between endocarditis and skin infection was NS with multivariate analysis[75]
The elevated OR for skin infection disappeared after the analysis was restricted to subjects with cardiac valvular abnormalities
When restricted to cases who were infected with skin flora and their matched controls the OR for skin infections increased markedly to 6.0 (CI; 1.3 to 27), p=0.019.

UTIs were not associated with IE
Initially pneumonia showed an increase among cases, but this occurred in the month before study dates and may be an early manifestation of endocarditis

Medical procedures and therapies
Only barium enema remained significant after multivariate adjustment OR 11.9 (CI; 1.34 to 106), p=0.026 (review indicated that in some cases the procedure was performed as part of the workup for the illness finally diagnosed as IE, or for a comorbidity, accordingly this cannot be interpreted as indicating a causal relationship

[75] The elevated OR for skin infection disappeared after the analysis was restricted to subjects with cardiac valvular abnormalities

between the procedure and IE)(NS were pulmonary procedures, lower GI endoscopy, upper GI endoscopy, gynaecological surgery, urinary catheterisation, other genitourinary, cardiac procedure, other surgery, intravenous therapy, nasal-oxygen therapy)

Overall IV fluid administration was not associated with IE, when analysis was restricted to those with infected skin flora and their controls the unadjusted OR increased from 1.8 to 5.0(CI: 1.1 to 23), p=0.04. Adjusted[76] OR was 6.7 (CI; 1.1 to 41), p=0.04

Tests of interaction between procedures and antibiotic use provided no evidence that anti biotic use modified the risk associated with those procedures

Oral hygiene
No association was found between IE and the frequency of routine dental care within the previous year, tooth brushing, or use of a toothpick, Water Pik or gum stimulator, there was no association between IE and complete denture prosthesis for edentulous mouths

There was no evidence that of a risk in having teeth vs. being edentulous, when this was repeated considering only cases affected with dental flora (N=106 and matched controls) there was an increased risk associated with having teeth, adjusted OR 7.02 (CI; 1.25 to 2.14), p=0.03.
Edentulousness was associated with decreased risk compare woth having teeth and not flossing, OR 0.11 (CI; 0.02 to 0.71), p=0.02

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Strom BL AEBJeal. Dental and cardiac risk factors for infective endocarditis: a population-based case-	Case-control	N=416 enrolled potential case-patients N=287 community acquired	Surveillance completed for IE in 54 hospitals Philadelphia Case-patients and controls were similar for age (range 18-98yrs, mean 59.1±17.1 and 59.1±17.0, respectively), sex, ethnicity, education, occupation, and dental insurance status. Excluded: <18yrs, IV drug users, those	Cases; information was obtained from case-patients by a structured telephone interview, medical and dental records were	One control from the community selected for each case-patient (using a modification of the Waksberg random-digit dialing method)	From August 1988 – November 1990	Primary risk factor variables were host characteristics[78], (reflecting the information that would be available to a practitioner about to	National Heart, Lung and Blood Institute

[76] Adjusted for cardiac valvular abnormality and diabetes
[77] Interviewers and medical records abstractors were not blinded but were extensively trained in good interviewing and abstracting techniques
[78] Due to the study focusing on indications for an antibiotic prophylaxis

control study. *Ann Int Med* 1998;**129**:761-9. Ref ID: 492		IE not associated with IV drug use N=273 interviewed case-patients	who developed endocarditis in the hospital Case records were examined and classified by experts in IE, agreement in 2 out of 3 was required to determine a case or not a case [77]	subsequently requested	Controls and case-patients were matched for age, sex and neighbourhood of residence		perform a procedure for which prophylaxis might be indicated) (Any valvular heart abnormality - defined from self-reporting structured telephone interviews, dental visit information was obtained from dental records)	

Effect size: (all CI 95%)

Infecting organisms
N=272/287 had multiple positive blood cultures[79]

Cardiac risk factors
Patient-reported history of any cardiac valvular abnormality was highly associated with IE (adjusted[80] odds ratio 16.7, CI 7.4 to 37.4)

Risk factor	**Cases (N=273)**	**Controls (N=273)**	**Adjusted OR[81] (CI 95%)**
Mitral valve prolapse	52(19.0%)	6(2.2%)	19.4 (6.4 to 58.4)
Congenital heart disease	26(9.5%)	7(2.6%)	6.7 (2.3 to 19.4)
Rheumatic fever	32(11.7%)	10(3.7%)	13.4 (4.5 to 39.5)
Cardiac valvular surgery	37(13.6%)	2(0.7%)	74.6 (12.5 to 447)
Other valvular heart disease	12(4.4%)	1(0.4%)	131 (6.9 to 2489)
Heart murmur	37(13.6%)	14(5.1%)	4.2 (2.0 to 8.9)
Any cardiac valvular abnormality *	104 (38.1%)	17(6.2%)	16.7 (7.4 to 37.4)

(previous episode of endocarditis)	17(6.2%)	1(0.4%)	37.2 (4.4 to 317)

*includes any of; mitral valve prolapse, congenital heart disease, rheumatic fever with heart involvement, cardiac valvular surgery, previous episode of endocarditis and other valvular heart disease, those reporting >1 of these factors were only reported once

Case patients were substantially more likely than controls to report previous known mitral valve prolapse; history of CHD; rheumatic fever; cardiac valvular surgery; previous endocarditis; other valvular heart disease; heart murmur without other known cardiac abnormalities

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding

Takeda S, Nakanishi T, Nakazawa M, Takeda S, Nakanishi T, Nakazawa M. A 28-year trend of infective endocarditis associated with congenital heart diseases: a single institute experience 4882. *Pediatrics International* 2005;**47**:392-6. Ref ID: 4882	Case series	N=183	Inclusion: patients with congenital heart diseases, patients who were diagnosed as definite endocarditis according to Duke criteria Exclusion: any patients with IE who were within 1yr post cardiac surgery			1971 to 1998	Preceding events, microorganisms	Not stated
Effect size: **Preceding events** Preceding events were documented in N=61/183 patients with N=122 (69%) where preceding events were unclear N=38 (21%) included dental treatment[82], of these N=15 (9%) were prevention, N=3 (2%) periapical infection and N=7 (4%) dental caries N=3 (2%) had atopic dermatitis as a preceding events and N=10 (5%) were others **Microorganisms** The most frequently isolated organism was Streptococcus sp. N=106/185 (57%), with Staphylococcus sp. N=26 (14%), Enterococcus sp. N=4 (2%), negative blood								

culture N=29 (16%)
The microbiological profile did not change during the 28yrs of the study

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Tleyjeh IM, Steckelberg JM, Murad HS, Anavekar NS, Ghomrawi HM, Mirzoyev Z *et al*. Temporal trends in infective endocarditis: a population-based study in Olmsted County, Minnesota. *JAMA* 2005;**293**:3022-8. Ref ID: 534	Population based survey	N=102 patients N=107 episodes USA	Data from a centralised system which links diagnostic and procedure information from virtually all sources of healthcare in the county; adults ≥18yrs; cases defined by Beth Israel and Duke criteria; mean age 54.1yrs in 1980-84 to 67.4yrs in 1995-2000; male predominance which was consistent (67 to 83%)			30years 1970 to 2000	Incidence, underlying heart disease	Public Health Service National Institutes of Health

Effect size:

Incidence
The overall adjusted incidence of IE ranged from 5.0 to 7.0 cases per 100,000 person-years, NS change during the study period

Underlying heart disease

N=107 episodes of IE, underlying cardiac disease

Prosthetic valve	23(21%)
Rheumatic heart disease	14(13%)
Mitral valve prolapse	18(17%)
Congenital heart disease	8(7%)
Bicuspid aortic valve	7(7%)
Acquired valvular disease	12(11%)
(Previous IE)	8(7%)

The proportions of cases with MVP and congenital heart disease NS changed over time

In the subgroup of IE cases with identified underlying heart disease there was a significant increasing trend in MVP over time (p=0.04), and a decreasing trend in rheumatic heart disease NS, however numbers were small

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Tomas I, Alvarez M, Limeres J, Tomas M, Medina J, Otero JL *et al*. Effect of a chlorhexidine mouthwash on the risk of postextraction bacteremia. *Infection*	RCT [83]	N=106 Spain	Inclusion: patients with mental and behavioural disabilities who underwent dental extractions under GA, N=52 male, mean age 25.8±11.4yrs (range 8 to 57yrs) Exclusion: use of antibiotics in the previous 3mths, use of oral antiseptics, any type of congenital or acquired immunodeficiency , disease that predisposes the patient to infections or bleeding There were NS differences between the groups with regard to age, sex, oral health status, or number of teeth extracted	N=53 underwent endotracheal intubation and oesophageal packing and then had their mouths filled with 0.2% chlorhexidine digluconate solution for 30sec	N=53 control group Blood samples: baseline, 30sec after final dental extraction , 15mins and 1hr[84] after finishing surgical procedure		Bacteraemia Blood cultures were processed in the bactec 9240, gram staining was performed	Xunta de Galicia, Spain

Control & Hospital Epidemiology 2007;**28**:577-82								
Effect size: **Bacteraemia** Positive blood cultures at baseline; 9% chlorhexidine, 8% control Bacteraemia 30sec; chlorhexidine 79% vs. control 96%, p=0.008 Bacteraemia 15min; chlorhexidine 30% vs. control 64%, p<0.001 Bacteraemia 1hr; chlorhexidine 2% vs. control 20%, p=0.005 The risk of bacteraemia after dental extraction at 30sec was x1.21 (1.04 to 1.40, 95%CI) higher in the control group; x2.12 (1.34 to 3.35, 95%CI) higher at 15mins; x10 (1.32 to 75.22, 95%CI) higher at 1hr Percentage blood cultures with positive results 48% chlorhexidine vs. 30% control, p<0.001 Polymicrobial culture results 29% vs. 11%, p=0.005 The most frequently identified were Streptococcus species (64% control, 68% chlorhexidine), then Staphylcoccus species (11% control, 8% chlorhexidine), Neisseria species (8% control, 5% chlorhexidine)								

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Tomas I, Alvarez M, Limeres J, Potel C, Medina J, Diz P. Prevalence,	Case series	N=53 Santiago de Compostela Universit	Inclusion: patients, who for behavioural reasons, underwent dental extractions under general anaesthesia; N=29(55%) male and N=24(45%) female, mean age 26.1±12.3yrs (range 8 to 52yrs) Exclusion: patients who had taken		Blood samples: baseline (after nasotracheal intubation and before local anaesthetic injection),		Bacteraemia, factors related to the development of bacteraemia Microbiology: Bottles with	Grant from Xunta de Galicia

duration and aetiology of bacteraemia following dental extractions. *ORAL DIS* 2007;**13**:56-62. Ref ID: 27		y Hospital, Spain	antibiotics in the 3mths prior to the study (including antibiotic prophylaxis for the surgical procedure in the present series), routine use of oral antiseptics, patients suffering from any type of congenital or acquired immunodeficiency		30sec after final dental extraction, 15min and 1hr after finishing the surgical procedure[85] Oral health status was graded in each patient using a specifically designed and previously validated scale		aerobic and anaerobic culture media were processed in Bactec 9240, each positive culture was gram stained, Bacteria isolated were identified using biochemical tests provided by the Vitek system	

Effect size:

Oral health scale
N=10 (19%) were grades 0-1, N=21(40%) were grade 2 and N=22(41%) were grade 3

Bacteraemia
At baseline, 9.4% had positive blood cultures, at 30sec 96.2%, at 15min 64.2% and at 1hr 20%
Of the 209 pairs of blood culture bottles were used, N=100 were positive, a single bacterium was identified in N=71 of the positive blood cultures, two bacteria in N=26, three bacteria to N=2 and four in the remaining blood culture
N=133 bacterial strains were isolated of which N=10(7.5%) were aerobes, N=110(82.7%) were facultative and N=13(9.8%) were obligate anaerobes
The most frequent were *Streptococcus* spp. (63.8%), particularly S. viridans, followed by *Staphylococcus* spp. (11.25) and *Neisseria* spp. (7.5%)

Factors related to the development of bacteraemia
Analysis of the factors potentially contributing to bacteraemia at 30sec was not performed as there were only N=2 patients with negative blood cultures
Female gender and gingival inflammation <3 were significantly related to bacteraemia at 15min, the risk of bacteraemia was x5 higher in females than in males (OR 5.385; 1.356 to 21.378, 95%CI), and x5 higher in patients with gingival inflammation <3 compared with those with grade 3 (OR 0.186; 0.047 to 0.737, 95%CI)

At 15min the following were NS related to bacteraemia; age, levels of plaque and calculus, presence of periodontal pockets, dental mobility, number of decayed teeth, presence of submucous abscesses and/or periapical lesions and number of teeth extracted

None of the variables showed significant association with bacteraemia at the 1ht time point								
Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Van der Meer JT TJVHMMF. Epidemiology of bacterial endocarditis in The Netherlands. I. Patient characteristics. *Arch Intern Med.* 1992;**152**:1863-8. Ref ID: 518	Prospective consecutive case series	N=559 reported episodes of suspected endocarditis following, N=438 episodes in N=432 patients Netherlands	All cases of patients in the Netherlands who were suspected of having BE on the basis of blood cultures, reported by microbiologists Exclusion: due to the application of Von Reyn criteria and being denied access Median age was 52yrs (range 2-89yrs) A recurrence was considered to be when there was at least 6-mths between episodes or when a different micro-organism was isolated	Patients were visited for an in-person interview while in hospital and medical records were reviewed	1st November 1986 to 1st Novermber 1988		Patient characteristics, native valve endocarditis, prosthetic valve endocarditis	Netherlands Heart Foundation
Effect size: [86] N=349/438 (79.7%) involved a native valve and N=89 (20.3%) involved a prosthetic valve The crude incidence of BE was 15 per million person-years, adjusted for age and sex was 19 per million person-years								

Native valve
NVE – total N=349, crude incidence of NVE was 12 per million person-years, adjusted for age and sex was 15 per million person-years
N=197 (56.4%) had a previously known cardiac lesion predisposing to BE
N=145 (41.6%) had heart disease at admission that had not been recognised previously
N=7 (2%) had no heart disease

Mitral valvular disease (N=125, 35.8%) and aortic valvular disease (N=110, 31.5%)
Mitral valve prolapse was present in N=29 (8.3%), of these 86% (N=25) were known to have the condition

Underlying heart disease in N=349 NVE

Aorta	**110(31.5%)**	**Mitral**	**125(35.8%)**
Bicuspid valve	2	Prolapse	1
Bicuspid valve & AOI/AOS	3	Prolapse & regurgitation	27
Sclerotic valve	7	Prolapse & stenosis	1
Regurgitation	64	Regurgitation	89
Regurgitation & stenosis	17	Regurgitation & stenosis	4
Stenosis	9	Stenosis	3
Hypertrophic obstructive cardiomyopathy	8	**Right-sided**	**21(6.0%)**
Mitral and Aortic	**36(10.9%)**	Tricuspid regurgitation	19
Regurgitation & stenosis	36	Pulmonary regurgitation	1
Congenital heart disease	**38(10.9%)**	Pulmonary & tricuspid regurgitation	1
ASD	1	**Other**	**19(5.4%)**
VSD	13		
VSD & right sided valvular disease	6		
Patent arterial duct	5		
Fallot's tetralogy	5		
Other	8		

Prosthetic valve
PVE – total N=89, crude incidence of PVE was 3 per million person-years, adjusted for age and sex was 6 per million person-years
N=11 (12.4%) had early PVE (≤60 days after implantation) and N=78 (87.6%) had late PVE (>60 days)

N=39 (43.8%) aortic prosthesis, N=22 (24.7%) mitral prosthesis, N=28 (31.5%) multiple prostheses Previous endocarditis N=50 one or more recurrences, N=6 had 2 episodes during the time of the survey, N=44 previous endocarditis and one episode during the study time N=51 recurrences (N=30 NVE and N=21 PVE)

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of fundin g
van der Meer JT, Thompson J, Valkenburg HA, Michel MF. Epidemiology of bacterial endocarditis in The Netherlands. II. Antecedent procedures and use of prophylaxis. *Arch Intern.Med* 1992;**152**:1869-73. Ref ID: 32	Prospective case series	N=427	Included: late prosthetic or native valve endocarditis	Structured questionnaire to interview patients (pr proxy respondents) about procedures undergone within 180 days of the onset of symptoms, all information was checked with dental and/or medical practitioners If antibiotic prophylaxis had been used the dose and route of administration were checked with the			Antecedent procedures Use of prophylaxis	Netherla nds Heart Foundati on

				presciber and/or pharmacist				

Effect size:

Antecedent procedures
N=149/427 (34.9%) had undergone a procedure within 180days of the onset of symptoms, N=31 were excluded as it was unlikely that the agent isolated from the blood was related to the procedure, N=29 excluded as the procedure did not have indications for prophylaxis [87].
Therefore N=89 (20.8%) had undergone a procedure for which prophylaxis was indicated within the previous 180days of the onset of symptoms; N=48 (24.4%) of those with NVE (N=197) who were known to have heart disease, N=25 (16.4%) of those who were not and N=16 (20.5%) of the N=78 with late PVE

Prophylaxis indications
Prophylaxis was definitely indicated in N=55 of the 89, for n=34 of the procedures the indication for prophylaxis was not certain (33 had had dental cleaning and 1 had had a cystoscopy)

Actual prophylaxis
NVE
N=8/48 (16.7%) with NVE who had known heart disease had antibiotics in accordance with guidelines, N=2 received antibiotics not in accordance with guidelines (should have provided adequate protection)
In those cases where endocarditis developed despite prophylaxis, the bacteria never were resistant to the administered antibiotics

For N=25 procedures in patients with native valves without known heart disease, prophylaxis would have been indicated had the cardiac lesion been known

Those known to have heart disease and those not did NS differ in the proportion of dental procedures; 92% (N=44/48) and 76% (N=19/25) respectively

PVE
N=9/16 (56.3%) of those with prosthetic valves had antibiotics, N=8 received antibiotics not in accordance with guidelines (could be considered to offer equivalent protection)
N=5/16 had cardiac surgery, N=8/16 had a dental procedure

Dental status, recent dental procedure
Endocarditis due to α-haemolytic streptococci in those with NVE appeared to be associated with; the presence of known heart disease, natural dentition, the performance of recent dental procedures, with endocarditis occurring x4.9 more often among those with all 3 factors than among those without any (RR 4.9, CI 2.8 to 8.7). For those with 1 or 2 factors the risk was in between (RR 1.9, CI 1.0 to 3.5 and RR 2.9, CI 1.6 to 5.3 respectively).

In those with late PVE; natural dentition, and a recent dental procedure, endocarditis was caused by α-haemolytic streptococci x2 as often as in other patients with late PVE (RR 2.6, CI 1.4 to 4.6)

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
van der Meer JT, van Wijk W, Thompson J, Vandenbroucke JP, Valkenburg HA, Michel MF. Efficacy of antibiotic prophylaxis for prevention of native-valve	Case control	N=48 Netherlands	Cases included: those with known cardiac disease in whom endocarditis developed within 180days of a medical or dental procedure for which prophylaxis was indicated. The diagnostic criteria for endocarditis described by Von Reyn et al was used. Cases excluded: those with prosthetic heart valves, those where a casual relation between the procedure and endocarditis was ruled out because it was unlikely that the agent isolated from the blood originated from the area of the procedure	Subjects were interviewed using a structured questionnaire about recent medical or dental procedures and the use of prophylaxis. Data about previous diagnoses of heart disease, physical	Controls selected from outpatients of the cardiology department of the university hospital and 4 regional hospitals, of N=200 controls included in the analysis, none got endocarditis within 180 days of the procedure		Procedures, interval from procedures to onset, antibiotic prophylaxis	Netherlands Heart foundation

endocarditis. *Lancet* 1992;**339**:135-9.			Controls included: with a cardiac lesion and increased risk of endocarditis, if they were in the same 5-yr age category as a case and had undergone a medical or dental procedure with an indication for prophylaxis within 180days of the interview Cases and potential controls were NS different in the number of procedures they had undergone in the previous 180 days, though there were more men among the cases (p=0.05)	examination and lab results were obtained Cases from Nov 1986 to Nov 1988 who were consecutively admitted to hospital				

Effect size:

Cases
Total number of procedures was N=48, N=44 dental and N=4 other, prophylaxis was definitely indicated in N=28 of the 48 procedures. For the other N=20 the indication for prophylaxis was not certain, all involved the removal of tartar
Median interval between the procedure and onset of symptoms was 72.5 days (range 3-170) for those with a possible indication for prophylaxis and 10 days (range 0-175) for other procedures, p<0.001
Antibiotics were given in N=8/48 (17%) cases[88]
Prophylaxis was given more often to those who had previous IE than those who had not (N=3/9 vs. N=5/39)

Controls
N=181/200 procedures were dental, prophylaxis was indicated in N=96, for N=104 the indication was possible because dental scaling had been done and it was unclear whether subgingival calculus had been removed.
N=26/200 (13%) of controls with a definite indication had received prophylaxis before a procedure, 1/104 (1%) of those with a possible indication[89]

Cases and controls
The interval between procedure and onset of symptoms or interview was significantly shorter for cases (median interval 30, range (0-175) than was the interval between procedure and interview for controls (median interval 75, range (0-179). This difference disappeared for procedures with a possible indication and increased for those with a definite indication when analysed separately
(the authors consider that this difference suggests a causal relationship between endocarditis and procedures with a high risk for bacteraemia, such as dental root work or dental extractions, but not between endocarditis and the scaling of teeth)

The use of prophylaxis was similar between cases (17%) and controls (13%).

For procedures within 180days of onset of symptoms[90], the OR was 1.04 (90%CI, 0.36 to 2.99) for first time episodes and 3.63 (0.98 to 13.4) for recurrent episodes
For procedures within 30days of onset of symptoms[91], the OR was 0.51 (0.11 to 2.29) for first time episodes and 2.13 (0.48 to 9.44) for recurrent episodes
(the authors consider that the stratified OR of 0.51 for cases with first-time endocarditis and a procedure within 30days of onset seems to provide the best estimate of the risk reduction obtained with prophylaxis, since 30days is a more likely incubation period than 180days. On the assumption that the incubation period is 30days, the protective effect of prophylaxis is 49%, this is NS)

Endocarditis developed within 30days of a procedure in N=25/197 (12.7%) of those with a previously diagnosed heart lesion

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Verheul HA, van den Brink RB, van Vreeland T et al. (1993) Effects of changes in management of active infective endocarditis on outcome in a 25-year period. American Journal of Cardiology 72: 682-7	Case series	N=130 (N=141 episodes) Study between 1966 and 1991 The Netherlands	Inclusion: consecutive patients with a diagnosis of active endocarditis at the cardiology department, von Reyn criteria used to define probable and possible episodes of IE Exclusion: endocarditis of a valve prosthesis 59% of patients had a murmur or cardiac lesion was known before admission			The end of the follow-up period was 1st January 1991 (only 1 patient was lost to follow-up), total follow-up 790patient-years, mean follow-up was 8.7yrs (range 0.3 to 23.5)	Early mortality, late mortality and survival, late morbidity	Not stated

Effect size:

Early mortality
Overall 26%, medically treated was 27% at 1mth and 29% at 3mths [92]
Causes of death (medically treated); severe heart failure and cardiogenic shock (N=13), acute intractable rhythm disturbances (N=6), major cerebral emboli (N=5), ruptured cerebral mycotic aneurysms (N=2), DIC (N=1), bleeding oesophageal varices (N=1)

Logistic regression analysis marked heart failure as an independent determinant of mortality within 3mths after admission
Early mortality with severe heart failure was 68% (RR 21.1; 7.4 to 60.3, 95%CI) compared with those without severe heart failure
High risk for urgent surgery or death, or both; patient with heart failure (RR 47.6; 9.1 to 249.0, 95%CI); those with aortic valve endocarditis (RR 3.0; 1.7 to 14.3, 95%CI)

Late mortality and survival
N=91/101 survived the hospital phase, during follow-up N=19 (29%) died (cardiac cause of death N=13)

Late morbidity
N=60 medically treated patients; valve replacement N=17 (28%), relapsing endocarditis N=1, recurrent endocarditis N=10
N=31 surgically treated patients; recurrent endocarditis N=1
At the end of follow-up N=64 patients were alive, of these N=45 were without recurrent endocarditis or valve replacement, only N=33/45 were without any cardiac complaints

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Wahlmann U, Al Nawas B, Jutte M, Wagner W. Clinical and microbiologi cal efficacy of single dose cefuroxime	RCT [93]	N=59 Germany	Inclusion: patients with multiple tooth extraction in preparation for radiotherapy of oral cancer, N=54 male, mean age 46yrs (range 31 to 81yrs) Exclusion: those with allergy to cephalosporins, had received antibiotics in the past 3wks, those with an absolute indication for perioperative chemoprophylaxis	N=30 1.5g IV cefuroxime 10mins before multiple tooth extractions Blood samples: 10mins and 40mins after the start of the	N=29 placebo (0.9% NaCl)		Bacteraemia Cefuroxime levels were determined by HPLC Blood was inoculated into a Signal System and processed	Not stated

prophylaxis for dental surgical procedures. *International Journal of Antimicrobial Agents* 1999;**12**:253-6				administration of the drug (for cefuroxime levels), at the start of the surgical procedure, 30min later in the control group			according to the manufacturer's recommendations	
Effect size: A mean of 8.8 teeth were extracted in each patient **Bacteraemia** N=54/118 cultures were positive A significantly lower rate of bacteraemia was identified after cefuroxime administration at 10min (cefuroxime N=7/30, 23% vs. control N=23/29, 79%) and 30min (cefuroxime N=6/30, 20% vs. control N=20/29, 69%) after the start of surgery. This was also significant for 10 or 30min (N=10/30, 33% vs. N=25/30, 86%) There was NS difference in the occurrence of bacteraemia and oral hygiene or periodontal status The duration of the surgical procedure had NS effect on bacteraemia rates There was NS difference for <6 or 6-10; for >10 teeth extracted there was a statistically significant difference N=7 (70%) cefuroxime vs. N=8 (89%) control group N=46/53 (87%) strains studies were susceptible to cefuroxime								

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Wang A, Pappas P, Anstrom KJ	Cohort	N=355	Inclusion: PVE from the International Collaboration on Endocarditis Merged Database (ICE-MD), (7sites in 5countries				In-hospital complications	Not stated

et al. (2005) The use and effect of surgical therapy for prosthetic valve infective endocarditis: a propensity analysis of a multicenter, international cohort 728. American Heart Journal 150: 1086-91			contribute), Duke criteria used to determine PVE Exclusion: recent history of IV drug use					
Effect size: N=2212 in the merged database, definite PVE in N=355 **In-hospital complications** Total; CHF 38.6%, systemic embolisation 27.3%, brain embolisation 18.9%, intracardiac abscess 19.4%, inhospital death 24.1% CHF significantly more likely following surgery vs. no surgery (28.0% vs. 53.4%, p<0.001) they were also significantly more likely to have intracardiac abscess (8.2% vs. 35.1%, p<0.001) Logistic regression analysis of variables independently associated with inhospital mortality in patients with PVE and matched propensity for surgical treatment; S aureus infection (OR 3.67, 1.39 to 9.74, P=0.009) and brain embolisation (OR 11.12, 4.16 to 29.73, p<0.001) were independently associated with inhospital mortality Multivariate analysis of N=137 patients who had a high propensity score for surgery similar results were found to be predictive of inhospital death; S aureus (OR 4.28; 1.23 to 14.91), brain embolisation (OR 2.52; 1.02 to 6.21)								

Reference	Study	Number	Patient characteristics	Intervention	Comparison	Length of	Outcome	Source

	type/ Evidence level	of patients				follow-up	measures	of funding
Wang A, Athan E, Pappas PA et al. (2007) Contemporary clinical profile and outcome of prosthetic valve endocarditis 2926. JAMA: Journal of the American Medical Association 297: 1354-61	Observational cohort	N=556	Inclusion: patients with PVE defined by Duke criteria enrolled in the International Collaboration on Endocarditis-Prospective Cohort Study (61 medical centres in 28 countries)			Study from June 2000 to August 2005	In-hospital mortality, complications and outcomes	American Heart Association Grant-in-Aid
Effect size: N=2670 with definite IE, N=556 (20.1%) PVE Those with PVE; aortic valve N=384 (69.1%), mitral valve or ring N=280 (50.4%), prosthetic pulmonic valve N=31 (5.6%) Compared with NVE (N=1895) those with PVE were significantly older; 65.0 (49.9 to 74.3) vs. 56.3 (41.1 to 69.9), p<0.001, less likely to use injection drugs; 10 (1.8) vs. 235 (12.4%), p<0.001, and more likely to have health care associated infection; 203 (36.5%) vs. 587 (31.0%), p=0.01 and previous IE; 112 (20.1%) vs. 91 (4.8%), p<0.001 **Complications and outcomes** Significant difference PVE vs. NVE;								

- other systemic embolisation higher with NVE; 83 (14.9%) vs. 468 (24.7%), p<0.001
- in-hospital death higher with NVE; 127 (22.8%) vs. 310 (16.4%), p<0.001

NS difference between PVE and NVE;

- heart failure, stroke, surgery during admission, persistent bacteria

Regional comparison – mortality

In-hospital mortality rates were NS different between the regions

PVE in-hospital death N=127 (22.8%) was predicted by age,

- healthcare associated infection N=62 (30.5%), adjusted OR 1.62 (1.08 to 2.44), p=0.02
- S aureus infection N=44 (34.4%), adjusted OR 1.73 (1.01 to 2.95), p=0.05
- heart failure N=60 (32.8%), adjusted OR 2.33 (1.62 to 3.34), p<0.001
- stroke N=34 (33.7%), adjusted OR 2.25 (1.25 to 4.03), p=0.007
- intracardiac abscess N=47 (32.6%), adjusted OR 1.86 (1.10 to 3.15), p=0.02
- persistent bacteraemia N=27 (55.1%), adjusted OR 4.29 (1.99 to 9.22), p<0.001

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding

Weickert U, Vetter S, Burkhardt U, Eickhoff A, Buhl A, Riemann JF. Bacteremia after diagnostic conventional laparoscopy and minilaparoscopy: a prospective study in 100 patients. *Journal of Clinical Gastroenterology* 2006;**40**:701-4. Ref ID: 42	Consecutive case series	N=100	Inclusion: patients having undergone diagnostic laparoscopy, mean age 53.5yrs(range 19 to 81yrs), N=59 male, N=41 female Exclusion: <18yrs, fever or other signs of infection with 14days before laparoscopy, antibiotics within 14days before laparoscopy, conditions for which current guidelines recommend antibiotic prophylaxis, immunosuppressant therapy	N=50 group I convention laparoscopy	N=50 minilaproscopy Blood samples: immediately before laproscopy and within 5mins after the procedure		Blood cultures Microbiology: 20ml sample, kept in commercially available aerobic/anaerobic blood culture bottles (BD Bactec 9000 system), blood cultures were incubated at 35˚C for 7days	Not stated
Effect size: **Blood cultures** There was no bacterial growth in 100 blood cultures drawn before laparoscopy, bacterial growth occurred in N=4 blood cultures taken immediately after laparoscopy, all bacteria found were gram-positive No difference was found between patients with and without positive blood cultures, none of the patients developed fever or other signs of infection in the follow-up, N=1 patient received oral antibiotics for 5 days								
Reference	Study	Number	Patient characteristics	Intervention	Comparison	Length of	Outcome	Source

	type/ Evidence level	of patients				follow-up	measures	of funding
Yigla M, Oren I, Bentur L, Solomonov A, Elias N, Altshuler R *et al*. Incidence of bacteraemia following fibreoptic bronchoscopy. *European Respiratory Journal* 1999;**14**:789-91. Ref ID: 5944	Consecutive case series	N=200 Rambam Medical Centre, Israel	Inclusion: underwent fibreoptic bronchoscopy during the study period. Mean age 54±24yrs (range 6mths to 94yrs), N=29 (14.5%) were <18yrs and N-171 (85.5%) adults, N=152 (76%) males, N=48 (24%) females. N=119 (59.5%) bronchoscopy for suspected malignant tumours, N=20 for recurrent pneumonia, N=14 for haemoptysis, N=13 for stridor, N=8 diffuse lung infiltrates, N=6 bronchiectasis, N=8 other Exclusion: patients with current respiratory tract infection or febrile illnesses and those receiving antibiotic therapy within a week prior to the bronchoscopy	Procedures were performed transnasally using flexible, fibreoptic bronchoscopes (size 3.6-6mm) N=90 (45%) bronchial biopsy, brushing and lavage N=57 (28.5%) brushing and lavage N=39 (19.5%) lavage N=11 (5.5%) transbronchial biopsy, brushing and lavage N=3 bronchoscopy solely for observation, no specimens obtained	Blood samples: immediately following the bronchoscopy, 10 to 20mins later (prebronchoscopy blood cultures from the first 100 patients were negative, excluding transient incidental bacteraemia)		Bronchoscopy findings, bacteriological findings Microbiology: aerobic and anaerobic blood culture bottles, incubated in a Bac-T-Alert incubator for a period of ≤5days at 37˚C	Not stated

Effect size:

Fibreoptic bronchoscopy findings
N=70 had a normal study and N=130 showed abnormalities (N=50 inflamed bronchial mucosa, N=49 endobronchial lesions, N=31 signs of external pressure on major bronchi)

Bacteriological findings
Blood cultures
N=26 (13%) had positive blood cultures following fibreoptic bronchoscopy, these were N=13 at 0 and 20min; N=13 at 20min+ (organisms identified were Staphylococcus coagulase negative (N=18), Staphylococcus coagulase positive (N=3), Nonhaemolytic streptococci (N=2), Beta haemolytic streptococci (N=1), Kledsiella rhinoscleromatis (N=1), Klebsiella species (N=1)
Defining true bacteraemia as episodes in which two postbronchoscopy positive blood cultures yielded the same organism decreased the bacteraemia rate to 6.5% (N=13/200)

Lavage fluid
Cultures from lavage fluid yielded normal flora in N=120 patients and potentially pathogenic bacteria in N=80

Procedures
For the N=13 with true bacteraemia showed that bronchial biopsy, brushing and lavage were performed in N=5; brushing and lavage in N=4; lavage only in N=2 (the remaining N=2 had no specimens obtained with bronchoscopy solely for observation)

Indications for fibreoptic bronchoscopy, macroscopic findings, size of bronchoscope used, and rate of invasive procedures performed during bronschocopy did not differ significantly between the N=13 patients with true bacteraemia and the N=187 without bacteraemia

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Yildirim I, Okur E, Ciragil P, Aral M, Kilic MA, Gul M. Bacteraemia	Consecutive case series	N=64	Inclusion: patients with a history of recurrent episodes of acute tonsillitis or obstructive symptoms due to tonsillar hypertrophy who had been admitted for elective tonsillectomy, randomly classified into two groups, N=28 male, N=36 female	N=33, group I Blood samples: pre-operative (after intubation),	N=31, group II Blood samples: pre-operative (after intubation),		Blood cultures Microbiology: 6ml (those under 10yrs), 16-18ml)those >10yrs),	Kahramanmaras Sutcu University Research

during tonsillectomy. *Journal of Laryngology & Otology* 2003;**117**:619-23. Ref ID: 238			Exclusion: any cardiovascular risk factors, had received antibiotic therapy for at least 20days before the operation	early post-operative (within 2mins after tonsillectomy) and post-operative (60mins after tonsillectomy) Tonsillar surface and deep tissue cultures were taken	post-operative (15 and 60mins after tonsillectomy) Tonsillar surface and deep tissue cultures were taken		half of the samples inoculated into an aerobic culture bottle, half into an anaerobic culture bottle, blood culture bottles were incubated within the Bactec 9050 automatic blood culture system, routine bacteriological inoculations were performed from the bottles in which bacterial growth took place, aerobic microorganisms were identified by standard lab methods, anaerobic were identified by using OXOID An-identdiscs	Fund
Effect size: **Blood cultures** All of the pre-operative blood cultures were negative Group I, bacterial growth was observed in N=9/33 (27.3%) blood cultures taken within 2mins of tonsillectomy Group II, bacterial growth was observed in N=2/31 (6.5%) blood cultures taken within 15mins after tonsillectomy, the difference between the two groups was significant, p=0.027 (organisms identified both groups; E. coli, Staph sureus, H. influenzae, unclassified streptococci, GABHS[94], Streph viridans, Strep pneumoniae								

The organisms isolated from the tonsillar surface did not always correspond with the organisms isolated from the deep tissue specimens. Staphylococcus aureus was the most commonly grown organism in the core of the tonsillar tissue and/or surface culture (N=18), followed by GABHS (N=14), Haemophilus influenzae (N=11) and Streptococcus pneumoniae (N=10) The patients with bacteraemia did not have any clinical signs and/or symptoms of a serious infection and were discharged without hospitals

Reference	Study type/ Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Zuccaro G, Jr., Richter JE, Rice TW, Achkar E, Easley K, Lewis J *et al*. Viridans streptococcal bacteremia after esophageal stricture dilation.[see comment]. *Gastrointestinal Endoscopy* 1998;**48**:568-73. Ref ID: 5981	Controlled trial	N=153 USA	Inclusion: consecutive patients with dysphagia presenting for upper endoscopy and stricture dilation, without valvular disease[95]. Patients, N=73 male, N=30 female; controls, N=32 male, N=18 female Exclusion: <18yrs old, received antibiotics within 2wks before the procedure, anaemic	N=103 with dysphagia having upper endoscopy and stricture dilation Blood samples: pre-procedure, 5, 20 and 30mins after the procedure	N=50 control, without dysphagia or oesophageal disease undergoing upper endoscopy for reasons unrelated to swallowing disorders	9mth study period	Blood cultures Microbiology: 20ml sample, 10ml inoculated into commercially prepared blood culture bottles, the bottles were then incubated for 5days ion the BacT/Alert instrument, when a blood culture bottle became positive by the BacT/Alert signal or growth on the subculture plate it was removed from the BacT/Alert and a gram stain performed	Not stated

Effect size:

Benign strictures were dilated in N=80 and malignant in N=15, of the N=103 patients N=96 underwent endoscopy immediately before dilation
Time after dilation:
1min; N=81 blood cultures obtained; N=24 positive cultures; organisms cultured, viridans streptococcus (N=19), coagulase negative staph (N=3), neisseria species (N=3), diptheroids (N=2), other (N=3)
5min; N=96 blood cultures obtained; N=17 positive cultures; organisms cultured, viridans streptococcus (N=16), coagulase negative staph (N=3), neisseria species (N=1), diptheroids (N=1)
20to30min; N=63 blood cultures obtained; N=4 positive cultures; organisms cultured, viridans streptococcus (N=3), coagulase negative staph (N=1)

Blood cultures
All blood cultures performed before the procedure were negative. Viridans streptococcal bacteraemia occurred in N=22/103 (21.4%; 13.4 to 29.3%, 95%CI)after stricture dilation, compared with N=1/50 (2%; 0.06 to 10.7%, 95%CI) control patients, p=0.001

N=19/81 (23%) blood cultures obtained 1min after stricture dilation were positive for viridans streptococcus, compared with N=16/96 (17%) obtained 5min after dilation, and N=3/63 (5%) obtained 20 to 30min after dilation

Of the N=19 bacteraemic patients at 1min, N=14/19 (74%) were still bacteraemic at 5min and N=2/19 were still bacteraemic at 20 to 30mins

Stricture diameter
Stricture diameter before dilation appeared to be the single most predictive factor for viridans streptococcal bacteraemia, N=13/96 had strictures which precluded passage of the endoscope before dilation of these bacteraemia occurred in N/13 (62%), the other N=83/96 had strictures which allowed the passage of the endoscope before dilation of these N=12/83 (14%); p=0.001, OR 9.5 (2.7 to 33.8, 95%CI)

There was NS difference in the rate of viridans streptococcal bacteraemia among patients with benign versus malignant strictures, passage of single versus multiple dilators, presence or absence of oesophagitis, use of antisecretory therapy, or the presence or absence of periodontal disease

No patients experienced fever, chills, or other symptoms/signs of clinically significant bacteraemia in the recovery room. All those with bacteraemia were follow-up by telephone and no adverse events related to transient bacteraemia were reported

5.5 Appendix 5 – References

Reference List – Prophylaxis against Infective Endocarditis

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5.6 Appendix 6 – Health Economics Evidence Tables

This section provides evidence tables that summarise the data provided in the published economic evaluations identified for the purpose of this guideline. Two modelling studies (Bor and Himmelstein, 1984 and Tzukert et al, 1986) were also reviewed but since they did not consider costs, no further details are presented here.

Note: Economic evaluations that examined antibiotic prophylaxis for indivudials with joint disease/ prosthetic joints undergoing dental procedures were excluded from detailed consideration since they do not consider the relevent patient population covered by this guideline.

Published economic evaluations were quality assessed using methods as described in the current Guidelines methods manual.

Data extraction tables for included studies – Dental procedures

Primary Source	Clemens JD, Ransohoff DF. A quantitative assessment of pre-dental antibiotic prophylaxis for patients with mitral-valve prolapse. J Chronic Dis. 1984;37(7):531-44
Author	Clemens
Date	1984
Type of economic evaluation	Cost effectiveness analysis
Currency used	US dollars
Year to which costs apply	1981
Perspective used	Third party payer
Timeframe	<1 year / Lifetime
Comparators	No antibiotic prophylaxis Two prophylaxis regimens ("oral" versus "parenteral" penicillin) and no prophylaxis. Authors argued that streptomycin not relevant for MVP population, although it might be used for patients with prosthetic valves.
Source(s) of effectiveness data	Efficacy estimated on the basis of expert opinion. In base case it was assumed that antibiotics were 70% effective. A range of 10 - 100% was tested
Source(s) of resource use data	Published sources and authors assumptions
Source(s) of unit cost data	Bacterial endocarditis costs: Maryland Health Services Cost Review Commission (MHSCRC) [1979] Antibiotic costs: fee schedule of the Yale-New Haven Hospital. Costs of providing antibiotic prophylaxis included not only the direct costs of the drugs but also the costs for 'drug handling' and administration where relevant. Penicillin reaction costs: fee schedule of the Yale-New Haven Hospital and MHSCRC
Modelling approach used	Simple decision tree
Summary of effectiveness results	Cases of IE / spared years of life. Not clearly reported Cases of IE No prophylaxis: 4.1 per million Parenteral penicillin 1.8 per million Oral pencillin 1.8 per million

	Spared years of life (discounted at 5%): Oral penicillin – varied from -9.2 (age at dental procedure = 10) to +2.3 (age at dental procedure = 70)	
Summary of cost results	Per million procedures (discounted at 5% for 'cost per spared year of life model') No prophylaxis Parenteral penicillin Oral pencillin	 $54,703 $35,903,191 $3,748,886
Summary of cost-effectiveness results	Cost per prevented case and cost per spared year of life In base case the parenteral prophylaxis strategy caused a net loss of life at higher cost when estimating cost per prevented case and cost per life year saved. Cost per prevented case: Oral penicillin In cost per spared year of life model, life is only spared after the age of 50 at a cost of $1.3 million per spared year of life.	 $2,638,702
Sensitivity analysis	Discount rate varied between 0 and 10% in sensitivity analysis; varied antibiotic efficacy and relative risk of endocarditis in MVP (according to ranges cited in text). Results sensitive to absolute risk of post dental endocarditis in MVP and to the annual discount rate. At an endocarditis risk of 18.7 cases per million procedures (an "extremely high value"), the cost per spared year of life would range from $72,000 to $190,000, varying inversely with age. At a discount rate of 0%, the cost per spared year of life would extend from $269,000 to $718,000, varying directly with age.	
Main Conclusions	Authors concluded that their results are only applicable to 'ordinary' dental procedures in persons with 'reasonably good' oral hygiene. Authors also stated that the suffering caused by adverse events plus the wider societal impacts (e.g. loss of productivity) must be factored into clinical decision making. The authors note that at the individual level, the choice is whether to spend a small sum of money to reduce the risk of IE from one improbable level to another while at the same time incurring a risk of a fatal penicillin reaction which appears to be of the same order of improbability as the risk of endocarditis.	

Primary Source	Gould, IM and Buckingham, JK. Cost-effectiveness of prophylaxis in dental practice to prevent infective endocarditis. Br Heart J 1993; 70: 79-83
Author	Gould
Date	1993
Type of economic evaluation	Cost cosequence analysis
Currency used	UK pounds
Year to which costs apply	1991/92
Perspective used	Third party payer (NHS)
Timeframe	Unclear – Lifetime?
Comparators	No prophylaxis versus penicillin
Source(s) of effectiveness data	It was assumed that penicillin was 100% effective. Explored impact of halving effectiveness by 50% in sensitivity analyses. No clear basis for this base case estimate, although it was commented that a "lack of case reports of failed prophylaxis where currently recommended regimes are used does suggest that [penicillin] is very effective."
Source(s) of resource use data	Resource use was based on an inspection of the notes of 63 patients who had had IE in Grampian over the decade 1980-90. Few details given, although data is presented on relation between cost of care and survival after infective endocarditis (Cost = £1923 + £620/yr).
Source(s) of unit cost data	Costs of a stay in hospital, valve replacement operations and outpatient visits were supplied by the health authority.
Modelling approach used	Not clear, but appears to be a simple decision analysis

Summary of effectiveness results	Not clearly reported. (1) High risk patients after all at risk dental procedures It was noted that the risk of death for at risk individuals undergoing high risk dental procedures is about 0.65 / 10,000 procedures. As the mortality is about 20%, the risk of non-fatal IE is 2.6 cases / 10,000 procedures (2) Restricting prophylaxis for high risk patients to dental extractions It was assumed that 95% of cases of IE associated with dental procedures are attributable to dental extractions. The risk of death in this group is 5.7 deaths for 10,000 procedures (3) Propviding prophylaxis to high risk patients after high risk procedures other than extractions. Providing prophylaxis will save only three lives in a million procedures.
Summary of cost results	Not clearly reported. Discounted at 6% (1) High risk patients after all at risk dental procedures Cost saving of approximately £7750 (2) Restricting prophylaxis for high risk patients to dental extractions Cost saving of approximately £264,000 (3) Providing prophylaxis to high risk patients after high risk procedures other than extractions. Costs of providing antibiotics exceed savings. Costs of providing antibiotics = £23,727 per 10,000 procedures
Summary of cost-effectiveness results	Saving / cost per life saved Restricting prophylaxis for high risk patients to dental extractions Cost saving of approximately £264,000 Propviding prophylaxis to high risk patients after high risk procedures other than extractions. £1 million per life saved
Sensitivity analysis	Limited analyses. Undertook sensitivity analysis on antibiotic efficacy and mortality after IE. Sensitivity analyses did not alter conclusion that prophylaxis is cost effective for at risk patients undergoing extraction.
Main Conclusions	Study concluded that prophylaxis should be limited to patients undergoing extractions. The authors noted that prophylaxis was (at that time) currently provided to only about 50% of patients thought to be at high risk - "savings might be achieved by extending antibiotic cover for dental extractions and reducing such cover for other high risk procedures".

Primary Source	Devereux, Frary, Kramer-Fox et al. Cost-effectiveness of infective endocarditis prophylaxis for mitral valve prolapse with or without a mitral regurgitant murmur. Am J Cardiol, 1994;74:1024-1029.
Author	Devereux
Date	1994
Type of economic evaluation	Cost effectiveness analysis
Currency used	US dollars
Year to which costs apply	1990
Perspective used	Third party payer Costs included direct costs of antibiotic prophylaxis, costs of anaphylaxis, and costs relating to IE.
Timeframe	Lifetime
Comparators	No antibiotic prophylaxis Three antibiotic regimens considered: (A) oral amoxicillin; (B) oral erythromycin; (C) IV ampicillin.
Source(s) of effectiveness data	Estimates of antibiotic efficacy were based on ones used in anayses by previous authors (Clemens and Ransohoff, 1984 and Bor and Himmelstein, 1984). The efficacy of antibiotic prophylaxis was assumed to be 80% for amoxicillin and ampicillin and 60% for erythromycin.
Source(s) of resource use data	Published estimates and authors assumptions.
Source(s) of unit cost data	Antibiotics - patient charges sourced from several pharmacies in the vicinity of The New York Hospital Medicare fee schedules.
Modelling approach used	Simple decision tree
Summary of effectiveness results	Cases of IE prevented / Net years of life saved All patients with mitral valve prolapse (per 1 million dental procedures) — Cases prevented / net years of lfe saved

	No prophylaxis	0 / 0
	Amoxicillin	32. / 176.0
	Erythromycin	24.0 / 136.0
	Ampicillin	17.0 (-243.0)
	Patients with Mitral prolapse wuth a systolic murmur	
	No prophylaxis	0 / 0
	Amoxicillin	80.0 / 450.0
	Erythromycin	60.0 / 341.0
	Ampicillin	65.0 / 29.0
	(discounting does not appear to have been applied)	
Summary of cost results	All patients with mitral valve prolapse (per 1 million dental procedures)	US $
	No prophylaxis	1,831,000
	Amoxicillin	5,502,000
	Erythromycin	4,234,000
	Ampicillin	27,161,000
	Patients with Mitral prolapse wuth a systolic murmur	
	No prophylaxis	4,595,000
	Amoxicillin	6,056,000
	Erythromycin	5,336,000
	Ampicillin	27,701,000
	(discounting does not appear to have been applied)	
Summary of cost-effectiveness results	Cost per IE case prevented / cost per year of life saved All patients with mitral valve prolapse (per 1 million dental procedures)	Cost per IE case prevented / cost per year of life saved
	Amoxicillin	118,803 / 20,846
	Erythromycin	100,926 / 17,708
	Ampicillin	1,507,738 / Life lost
	Patients with Mitral prolapse wuth a systolic murmur	
	Amoxicillin	18,540 / 3,254
	Erythromycin	12,396 / 2,714
	Ampicillin	357,125 / 791,301
Sensitivity analysis	Limited sensitivity analyses Explored impact on costs by using a higher risk subgroup (MVP patients with a mitral systolic murmur - result: lower costs). Also explored impact of changing population prevalence of MVP, % of IE post dental, efficacy of prophylaxis, costs of IE, costs of antibiotics, years of life lost (increased from 5.7 years to 7.5 years). Sensitivity analysis suggested that erythromycin prophylaxis might be cost saving under some scenarios.	
Main Conclusions	The authors concluded that prevention with oral antibiotics of the cumulative morbidity and incremental health care costs due to IE in MVP patients is reasonably cost-effective for MVP patients with mitral murmurs. It was noted that the present results suggest better cost effectiveness for MVP patients than previous analyses published in 1984. This difference, according to the authors, is largely due to the subsequent recognition that the risk of IE is strongly concentrated in MVP patients with a mitral regurgitant murmur.	

Primary Source	Agha Z, Lofgren RP, VanRuiswyk JV. Is antibiotic prophylaxis for bacterial endocarditis cost-effective? Med Decis Making. 2005 May-Jun;25(3):308-20.
Author	Agha
Date	2005

Type of economic evaluation	Cost-effectiveness analysis and cost-utility analysis.
Currency used	US dollars
Year to which costs apply	The price year was 2003. All cost data were adjusted to 2003 based on the medical care component of the Consumer Price Index.
Perspective used	Societal
Timeframe	Lifetime (55 years)
Comparators	Eight management strategies (including no prophylaxis) for IE in patients undergoing dental procedures who have underlying cardiac conditions. The strategies were: no antibiotics; oral amoxicillin 2 g, administered 1 hour before the procedure; oral clarithromycin 500 mg, administered 1 hour before the procedure; oral clindamycin 600 mg, administered 1 hour before the procedure; oral cephalexin 2 g, administered 1 hour before the procedure; intravenous or intramuscular ampicillin 2 g, administered 30 minutes before the procedure; intravenous or intramuscular cefazolin 1 g, administered 30 minutes before the procedure; and intravenous clindamycin 600 mg, administered 30 minutes before the procedure.
Source(s) of effectiveness data	Pooled analysis of four case control studies examining the effectiveness of antibiotic prophylaxis. Pooled odds ratios with 95% confidence intervals were calculated, after testing for heterogeneity, using the Mantel-Haenszel procedure.
Source(s) of resource use data	Resource use based on published estimates referenced by the authors.
Source(s) of unit cost data	Medicare fee schedules (1997) for hospitalisation costs Drug Topics Red Book (antibiotic acquisition costs). Comprised the average wholesale price of the drug, plus an average dispensing cost based on published data. The indirect costs of patient or caregiver time lost were estimated. The value assigned to a lost workday was the amount for a fulltime wage earner, and the value assigned to a lost "no work" day was the amount as reported by the Bureau of Labor Statistics. Patients requiring intravenous antibiotic administration were estimated to have lost the productivity equivalent of a 0.5 workday
Modelling approach used	Simple decision tree for short term outcomes and Markov process for long term costs and effects
Summary of effectiveness results	Cases of IE prevented /QALYs Under the base-case assumptions, if 10 million patients underwent prophylaxis compared with the no-prophylaxis strategy, the outcomes would be: Amoxicillin / ampicillin: 119 cases of BE prevented but a net loss of 181 lives (-30,311 QALYs) secondary to anaphylaxis Clarithromycin: 119 prevented cases of BE, 19 prevented deaths from BE, and 1,125 QALYs saved Oral cephalexin / IV cefazolin: 119 prevented cases of BE, 9 prevented deaths from BE, and 827 QALYs saved Oral clindamycin / IV clindamycin: 119 prevented cases of BE, 19 prevented deaths from BE, and 1,118 QALYs saved Secondary analyses were reported for patients with high-risk cardiac conditions only and with prior beta-lactam antibiotic use. In the high-risk group, if 10 million patients underwent prophylaxis with any of the seven prophylaxis strategies, there would be 237 endocarditis cases prevented for patients with prior BE and 475 cases prevented for patients with prosthetic heart valves. (QALYs discounted at 3%)
Summary of cost results	The total intervention costs for the 55-year horizon time strategies were not reported. Costs discounted at 3%
Summary of	Annual cost per QALY (US$)

Cost-effectiveness results	Average cost effective ratios presented for each prophylaxis option. Base case: Oral clarithromycin Oral cephalexin Oral clindamycin IV cefazolin IV clindamycin For the base-case analysis, clarithromycin prophylaxis was the most cost-effective strategy and cephalexin was second best. All other antibiotic regimens were eliminated based on simple dominance (i.e. they were more costly and less effective than clarithromycin). Amoxicillin and ampicillin were eliminated from consideration as they resulted in a net loss of lives For high-risk patients, in patients with prior endocarditis: Oral clarithromycin Oral cephalexin Oral clindamycin IV cefazolin IV clindamycin The strategy was not effective for oral amoxicillin or for ampicillin (intravenous). In patients with prosthetic valve: Oral clarithromycin Oral cephalexin Oral clindamycin IV cefazolin IV clindamycin Oral amoxicillin IV ampicillin	 $88,007 per QALY gained $99,373 per QALY gained $101,142 per QALY (eliminated) $199,430 per QALY gained (eliminated) $411,093 per QALY gained (eliminated) $40,334 $37,916 $46,678 $79,886 $199,783 (as reported in the text) $16,818 $14,060 $19,936 $33,480 $96,029 $160,871 $498,488
Sensitivity analysis	To test the influence of all variables on the model results, one-way sensitivity analyses were conducted. The values of each model estimate for epidemiological parameters and health outcomes, health state utility values and costs were varied across the ranges in the paper. The base-case findings were sensitive to changes in the risk of antibiotic fatal side effects, the incidence of bacterial endocarditis, potentially preventable cases, the cost of antibiotics, the incidence of dental visits requiring prophylaxis, age of the target population, and the discount rate. One-way sensitivity analyses of all other variables did not result in any of the antibiotic prophylaxis strategies achieving the predefined threshold of $50,000 or $100,000 per QALY gained.	
Main Conclusions	Authors concluded that: Routine use of amoxicillin and ampicillin for endocarditis prophylaxis is not safe. Predental antibiotic prophylaxis is cost-effective only for persons with moderate or high risk of developing endocarditis Clarithromycin should be considered the drug of choice and cephalexin (a cephalosporin) as an alternative drug of choice	

Data extraction tables for included studies - non dental procedures (urinary catheterisation in the Emergency department)

Primary Source	Caviness AC, Cantor SB, Allen CH, Ward MA. A cost-effectiveness analysis of bacterial endocarditis prophylaxis for febrile children who have cardiac lesions and undergo urinary catheterization in the emergency department. Pediatrics. 2004 May;113(5):1291-6.
Author	Caviness
Date	2004
Type of economic	Cost effectiveness analysis

evaluation	
Currency used	US dollars
Year to which costs apply	2000
Perspective used	Third party payer Costs included direct costs of antibiotic prophylaxis, costs of anaphylaxis, and costs relating to IE.
Timeframe	Lifetime
Comparators	The strategies were: no antibiotics; oral amoxicillin 50 mg/kg 1 hour before; vancomycin 20 mg/kg IV over 1-2 hours completed within 30 mins of strting the procedure
Source(s) of effectiveness data	Prophylactic efficacy of antibiotics in preventing BE after genitourinary procedures was determined from "1 clinical trial and 2 decision analyses". The RCT examined efficacy of mezlocillin for transurethral prostatectomy. Decision analyses were: Bor & Himmelstein, Clemens and Ransohoff. Antibiotic efficacy was estimated to be 89%, with a range of 0% - 100%.
Source(s) of resource use data	Antibiotic regimens based on AHA guidelines (1997). Also author assumptions and published sources.
Source(s) of unit cost data	Healthcare Cost and Utilization Project data for 2000 (for hospital costs for endocarditis and mitral valve replacement) Medicaid charges for 2000 (outpatient visit costs) Drug Topics Red Book 2001 (antibiotic acquisition costs). Opportunity cost to the parent was taken as the number of hours of work missed while waiting for antibiotic delivery. An average hourly earning of $15.80 was taken from the US Department of Labor Bureau of Labor Statistics for 2000
Modelling approach used	Simple decision tree
Summary of effectiveness results	Excluding antibiotic deaths: The antibiotic strategy would prevent 7 cases of BE per 1 million children treated, with an incremental effectiveness of only 0.00005 QALYs. QALYs discounted at 3% Including antibiotic deaths: Not adjusted for BE incidence Amoxicillin & vancomycin 24.91079 QALYs No propylaxis 24.91124 QALYs Excluding antibiotic deaths: Amoxicillin & vancomycin 24.91129 QALYs No prophylaxis 24.91124 QALYs In terms of BE incidence, incremental effectiveness = 0.000007
Summary of cost results	No prophylaxis $1.47 Amoxicillin $495.30 Vancomycin $667.63 (Costs discounted at 3%)
Summary of cost-effectiveness results	Cost per QALY / cost per case prevented Excluding antibiotic deaths: Amoxicillin: $10 million per QALY gained / $70 million per BE case prevented Vancomycin: $13 million per QALY gained / $95 million per BE case averted Including antibiotic related deaths – antibiotic strategy less effective (net loss of life) and more costly.
Sensitivity analysis	The authors state that sensitivity analysis was conducted by varying study costs and probabilities. Uncertain probabilities that were varied in the sensitivity analysis include the prevalence of bacteria causing UTI and BE, the prophylactic efficacy of antibiotics in preventing bacteremia, the incidence of bacteremia after UC, and the incidence of BE after bacteremia. All costs were varied from $0 to twice the point estimate for sensitivity analysis. Uncertain costs that were varied included the ED opportunity costs; the parental opportunity costs; and the cost of endocarditis hospitalization, endocarditis surgery, and caring for CHF. QALE was varied for BE, no BE, and CHF. The discount rate was also varied between 0% and 5% for both costs and clinical outcomes. (The results of these analyses were not fully reported). Below a threshold value of 0.0000023 for anaphylactic death, the use of antibiotics would be more effective than no antibiotics.
Main Conclusions	In the emergency department, BE prophylaxis before UC in febrile children who are aged 0 to 24 months and have moderate-risk cardiac lesions is not a cost-effective use of health care resources.