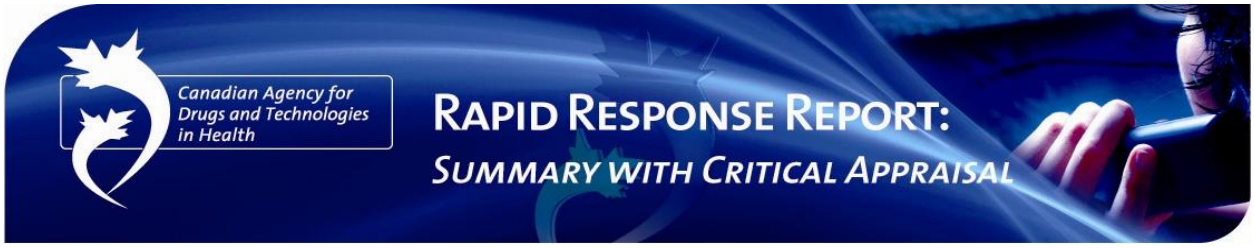


TITLE: Antibiotic Prophylaxis for Patients with Cardiac or Orthopedic Implants undergoing Dental Procedures: A Review of the Clinical Effectiveness and Guidelines

DATE: 11 March 2013

CONTEXT AND POLICY ISSUES:

Oral antibiotics are often used prophylactically in patients undergoing dental procedures, with the aim of preventing oral bacteria from entering the bloodstream, and causing serious complications due to infection among susceptible patients.[1]

Among the conditions for which this measure has been used prophylactically are infective endocarditis in patients who have had cardiac implants,[2] and prosthetic joint infection.[3] While this practice has been commonplace, it has been carried out with little supporting clinical evidence.[2,3] Given the frequency with which dental procedures are performed, the potential for antimicrobial resistance,[4] and potential cost,[5] clinical effectiveness should be demonstrated. However, current practice is largely based on a theoretical basis for prophylaxis, and because some patient groups are considered to be at high risk for serious complications in the event of infection.[2]

The present review was conducted to explore the existence of recent clinical evidence for the prophylactic use of oral antibiotics during dental procedures in patients with cardiac or orthopedic implants, and to review current evidence-based guideline recommendations for these two patient groups.

RESEARCH QUESTIONS

1. What is the evidence for the clinical effectiveness of antibiotic prophylaxis for patients with cardiac or orthopedic implants undergoing dental procedures?

2. What are the evidence-based guidelines for the use of antibiotic prophylaxis for patients with cardiac or orthopedic implants undergoing dental procedures?

KEY FINDINGS

No randomized studies to support the use of oral antibiotic prophylaxis during dental procedures in patients with cardiac and orthopedic prostheses were identified. A single guideline for patients with orthopedic prostheses does not recommend oral antibiotic prophylaxis based on a lack of supportive evidence. Guidelines for cardiac implant patients have recommended both for and against prophylaxis in high risk-patients. While well-designed clinical studies are needed to address this medical issue, evidence may be difficult to obtain as such studies are likely to require very large sample sizes.

METHODS

Literature search strategy

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2013, Issue 1), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials and guidelines. The search was also limited to English language documents published between Jan 1, 2008 and Feb 8, 2013.

Selection criteria and method

The citations identified by this literature search were screened according to the selection criteria provided in Table 1. One reviewer screened the titles and abstracts of the retrieved publications and evaluated the full-text publications of the final article selection.

Table 1: Study Selection Criteria

Population	Any age group of patients undergoing dental procedures who have cardiac implants (e.g., mechanical heart valves) or orthopedic implants (e.g., joint replacement)
Intervention	Any antibiotic used prophylactically
Comparator	No antibiotic prophylaxis
Outcomes	Q1: prevention of implant infection Q2: guidelines
Study designs	Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, guidelines

Exclusion criteria

Articles were excluded if they did not fulfill the study selection criteria described in Table 1, and in the case of guidelines, if they were not evidence based.

Critical appraisal of individual studies

The AMSTAR tool[6] was used to assess the methodological quality of systematic reviews, and the AGREE II instrument[7] was used to evaluate guidelines. A numeric score was not calculated. Instead, each report's fulfillment of the relevant criteria was described and summarized.

SUMMARY OF EVIDENCE

Quantity of research available

The literature search yielded 444 citations. The abstracts for these reports were reviewed and nine studies that could potentially fulfill the study selection criteria were selected for further screening. An additional four references were identified from the grey literature. A total of five reports were selected for inclusion. A summary of the screening results is provided in Appendix 1. Of the five selected reports, one[8] was a systematic review of antibiotic prophylaxis against endocarditis and four[4,9-11] were guidelines that addressed infective endocarditis or infection of orthopedic prostheses. No randomized controlled trials were identified in the screening process.

Summary of study characteristics

The Cochrane systematic review conducted by Oliver et al.[8] looked at the evidence for prophylaxis against bacterial endocarditis with the use of antibiotics (vs. placebo) prior to invasive dental procedures. The authors considered randomized controlled trials, controlled clinical trials, cohort, and case-control studies that were published between 1950 and 2008 in their search strategy. The authors identified only one case-control study conducted in the Netherlands over a 2-year period. The authors assessed the external validity of the case-control study as good. With regard to the study's internal validity, the validity of the outcome measure and the similarity of timing of the groups were good, the losses to follow-up were moderate, and the similarity of the groups compared was unclear. As this was a case-control study, randomization, blinding, and allocation concealment were not done.

Of the four guidelines, three[4,9,11] were for the prevention of infective endocarditis, and one[10] was for the prevention of infection in orthopedic implants.

The guideline for the prevention of infection in orthopedic implants in patients undergoing dental procedure was published in 2012 by the American Academy of Orthopaedic Surgeons and the American Dental Association.[10] This guideline met all recommended Institute of Medicine standards for the development of systematic reviews and clinical practice guidelines, with the exception of allowing for patient input. The systematic review considered studies published on or after 1960 and included most study types, with the exception of some case series (i.e. retrospective, non-consecutive) and studies of very small sample size (i.e. <10 per group). There was no restriction placed on the age of patients. The strength of recommendations was based on the strength of evidence and had five levels (Strong, moderate, limited, inconclusive, and consensus).

The National Institute for Health and Clinical Excellence (NICE) in the United Kingdom published a guideline for prophylaxis against infective endocarditis in adults and children undergoing interventional procedures in 2008.[9] The guideline was developed in accordance with NICE Short Clinical Guideline methodology and included a systematic review of the literature. The literature search included systematic reviews, randomized controlled trials, and

observational studies published between 1950 and September 7 2007. Evidence was assigned one of eight levels as defined by the Scottish Intercollegiate Guidelines Network. Recommendations were made based on consideration of specific criteria (internal validity, consistency, external validity, clinical impact, cost-effectiveness, ease of implementation, patient's perspective, social value judgment, overall synthesis of evidence).

The American Academy of Pediatric Dentistry's guideline on antibiotic prophylaxis for dental patients at risk for infective endocarditis was published in 2011[4] and was an update of a previous version of the guideline. The method used to update this guideline was a literature search of studies (restrictions on study type not stated) published in the previous 15 years, as well as consideration of the American Heart Association's 2007 guideline on the same topic and expert opinion. A method for grading evidence or recommendations was not provided.

Habib et al. published the European Society of Cardiology guideline for the prevention, diagnosis, and treatment of infective endocarditis in 2009.[11] This guideline was an update of one published in 2004. Recommendations were made based on a review of the literature and expert consensus. It is unclear whether the literature review was conducted in a systematic manner. And included all series (except case reports) published in the previous 10 years. The strength of evidence was assessed using three levels and the strength of recommendations was assigned one of five classes.

A summary of the characteristics of the 4 guidelines included in this review is provided in Table A.1 of Appendix 3.

With regard to the quality of the studies on which the guideline recommendations were based, the main evidence statement made by the NICE guideline[9] was based on studies rated as 1++ (high quality meta-analyses, systematic reviews of randomized controlled trials, or randomized controlled trials with a very low risk of bias), 2+ (Well-conducted case-control or cohort studies with low risk of confounding or bias) and 3 (non-analytic studies). The guideline published by Habib et al.[11] for the European Society of Cardiology based its recommendation on evidence whose strength it rated as C (consensus of opinion of the experts and/or small studies, retrospective studies, registries). The American Academy of Pediatric Dentistry[4] did not provide a rating for the evidence it considered in its guideline. The guideline published by the American Academy of Orthopedic Surgeons and the American Dental Association[10] rated the strength of the evidence on which they based their recommendation as 'limited' (the quality of the supporting evidence that exists is unconvincing, or well-conducted studies show little clear advantage to one approach versus another).

Summary of critical appraisal

The details of the critical appraisal that was conducted using the AMSTAR[6] and AGREE II[7] instruments are given in Table A.2 in Appendix 4.

The systematic review[8] on prophylaxis of bacterial endocarditis was of good quality and fulfilled most of the AMSTAR criteria for methodological quality. Study selection and data extraction was done by two reviewers, and study quality was assessed using the Downs and Black instrument. There was no apparent search of the grey literature conducted for this review, and the authors did not describe an assessment of possible publication bias.

The guidelines published by NICE[9] and the American Academy of Orthopedic Surgeons and the American Dental Association[10] were well-conducted and of high quality and there were explicit links made between the evidence and the recommendations. It is unclear whether the review of the evidence conducted by Habib et al.[11] was done in a systematic manner, and the link between evidence and recommendations is not clear, given that the authors also stated that recommendations were based largely on expert consensus. The guideline published by the American Academy of Pediatric Dentistry conducted a literature review for its report, however this review was not conducted in a systematic manner (i.e. used only one database, number of reviewers not stated), and it is not clear how the findings of this search were integrated in their final recommendations, which are largely based on expert opinion and the 2007 recommendations of the American Heart Association.

Summary of findings

Clinical Effectiveness

A single study was identified by the systematic review on the prophylaxis of bacterial endocarditis by Olivier et al.[8] This study, by Van der Meer (1992), selected patients based on the following criteria: previous congenital heart disease, coarctation of the aorta, rheumatic or other valvular dysfunction, or mitral valve prolapse with mitral regurgitation. Cases had to have been diagnosed with endocarditis within 180 days of undergoing a medical or dental procedure that required definite antibiotic prophylaxis. Age-matched controls had not had endocarditis but had to have had a medical or dental procedure that required definite prophylaxis in the previous 180 days. The authors reported that seven of the 24 cases (29%) and 16 of the 79 controls (20%) had received appropriate prophylaxis within 180 days of their dental procedure (statistical analysis not provided).

Guidelines

A detailed summary of the recommendations made by the four reviewed guidelines is provided in Table A.3 in Appendix 5.

Based on a lack of definitive evidence, the guideline published by NICE[9] did not recommend the routine use of antibiotic prophylaxis among patients considered to be at high risk for infective endocarditis. The guideline development group not only recommended that at-risk patients should no longer be given antibiotic prophylaxis against infective endocarditis, but based on a *de novo* economic model conducted for this report, concluded that the risk of antibiotic side effects, particularly in the case of amoxicillin, can lead to greater deaths through fatal anaphylaxis, compared with no antibiotic prophylaxis.

The guideline published by Habib et al.[11] for the European Society of Cardiology recommended limiting antibiotic prophylaxis for patients undergoing dental procedures to only those with the highest risk of infective endocarditis, including patients with a prosthetic valve or a prosthetic material used for cardiac valve repair. The authors noted that their current (as well as their past) recommendations are not based on strong or appropriate evidence, but reflect an expert consensus of opinion.

The guideline published by the American Academy of Pediatric Dentistry[4] also recommended limiting antibiotic prophylaxis for patients undergoing dental procedures to only those with the highest risk of infective endocarditis (i.e. including patients with a prosthetic valve or a prosthetic

material used for cardiac valve repair), and its recommendations were largely based on the 2007 guideline published by the American Heart Association.

The American Academy of Orthopedic Surgeons together with the American Dental Association[10] recommended that "The practitioner might consider discontinuing the practice of routinely prescribing prophylactic antibiotics for patients with hip and knee prosthetic joint implants undergoing dental procedures." Their rationale was based on moderate strength evidence that found that dental procedures are unrelated to implant infection and that antibiotic prophylaxis prior to dental procedures did not reduce the risk of implant infection. This evidence was a single prospectively conducted case control study of 339 cases and 339 controls that found no statistically significant difference in the odds of prosthetic hip or knee infection given antibiotic prophylaxis. Because of the limited nature of the evidence, this recommendation related only to patients with hip and knee prostheses and not to patients with other types of orthopedic implants.

Limitations

No randomized studies of antibiotic prophylaxis during dental surgery were identified, and recent evidence for the clinical effectiveness of antibiotic prophylaxis is lacking.

Evidence (a case-control study) from a systematic review is not specific to heart valve patients only, or patients undergoing dental procedures only.

Few guidelines were identified. Those that were identified differed in their recommendations for antibiotic prophylaxis. Recommendations for prophylaxis in high risk patients are not based on high-level evidence but are largely based on expert consensus.

No recent Canadian guidelines were identified.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING:

Infections of cardiac and orthopedic prostheses are rare events and as such it is difficult to determine if dental procedures are associated with their incidence. Sexton et al.[2] have noted that because of the low incidence of these infective events following dental procedure, well designed prospective randomized controlled studies would require at least 6000 patients per group, and are therefore unlikely to be undertaken.

The results of this review have found the evidence for antibiotic prophylaxis during dental procedures for patients with cardiac and orthopedic prostheses to be lacking. Guidelines for patients with orthopedic prostheses are very limited. Furthermore, the recommendations for antibiotic prophylaxis for the prevention of infective endocarditis differ between guidelines.

Of note, while recent Canadian evidence-based guidelines were not identified, the Canadian Dental Association,[12] the Canadian Pediatric Society,[13] and the Institut National d'Excellence en Santé et en Services Sociaux (INESS),[14] all support or endorse the 2007 American Heart Association guideline[15] for the prevention of infective endocarditis.

A recent Canadian paper that researched and discussed the controversy surrounding antibiotic prophylaxis and dental treatment[1] found that the papers they reviewed showed that antibiotic prophylaxis has been used without a clear and full understanding of its benefits. The authors concluded that “any perceived potential benefit from administering antibiotic prophylaxis before dental procedures must be weighed against the known risks of lethal toxicity, allergy, and development, selection, and transmission of microbial resistance”.

PREPARED BY:
Canadian Agency for Drugs and Technologies in Health
Tel: 1-866-898-8439
www.cadth.ca

REFERENCES

1. Brondani MA. Health technology assessment fireside: antibiotic prophylaxis and dental treatment in Canada. Journal of Pharmaceutics [Internet]. 2013 [cited 2013 Mar 6];2013(article ID 365635). Available from: http://www.hindawi.com/journals/jph/2013/365635/

2. Sexton DJ. Antimicrobial prophylaxis for bacterial endocarditis. 2012 Oct 18 [cited 2013 Feb 22]. In: UpToDate [Internet]. Version 20.4. Waltham (MA): UpToDate; 1992 - . Available from: www.uptodate.com Subscription required.

3. Barbari E, Baddour LM. Prevention of prosthetic joint infections. 2012 Jan 9 [cited 2013 Feb 22]. In: UpToDate [Internet]. Version 20.4. Waltham (MA): UpToDate; 1992 - . Available from: www.uptodate.com Subscription required.

4. Guideline on antibiotic prophylaxis for dental patients at risk for infection [Internet]. Chicago: The American Academy of Pediatric Dentistry; 2011. [cited 2013 Feb 22]. Available from: http://www.aapd.org/media/Policies_Guidelines/G_AntibioticProphylaxis.pdf

5. Little JW, Jacobson JJ, Lockhart PB, American Academy of Oral Medicine. The dental treatment of patients with joint replacements: a position paper from the American Academy of Oral Medicine. J Am Dent Assoc. 2010 Jun;141(6):667-71.

6. Shea BJ, Hamel C, Wells GA, Bouter LM, Kristjansson E, Grimshaw J, et al. AMSTAR is a reliable and valid measurement tool to assess the methodological quality of systematic reviews. J Clin Epidemiol. 2009 Oct;62(10):1013-20.

7. The AGREE Next Steps Consortium. Appraisal of guidelines for research and evaluation II [Internet]. London: The AGREE Research Trust; 2009 May. [cited 2013 Feb 28]. Available from: www.agreetrust.org/?o=1397

8. Oliver R, Roberts GJ, Hooper L, Worthington HV. Antibiotics for the prophylaxis of bacterial endocarditis in dentistry. Cochrane Database Syst Rev. 2008;(4):CD003813.

9. Prophylaxis against infective endocarditis [Internet]. NICE clinical guideline 64. London: National Institute for Health and Clinical Excellence; 2008 Mar. [cited 2013 Feb 22]. Available from: http://www.nice.org.uk/nicemedia/live/11938/40039/40039.pdf

10. Prevention of orthopaedic implant infection in patients undergoing dental procedures. Evidence-based guideline and evidence report [Internet]. Rosemont (IL): American Academy of Orthopaedic Surgeons; 2012. [cited 2013 Feb 28]. Available from: http://www.aaos.org/research/guidelines/PUDP/PUDP_guideline.pdf

11. National Guideline Clearinghouse [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (AHRQ); 1997 - . Guideline summary: Guidelines on the prevention, diagnosis, and treatment of infective endocarditis (new version 2009); 2009 [cited 2013 Feb 22]. Available from: http://guidelines.gov/content.aspx?f=rss&id=15947

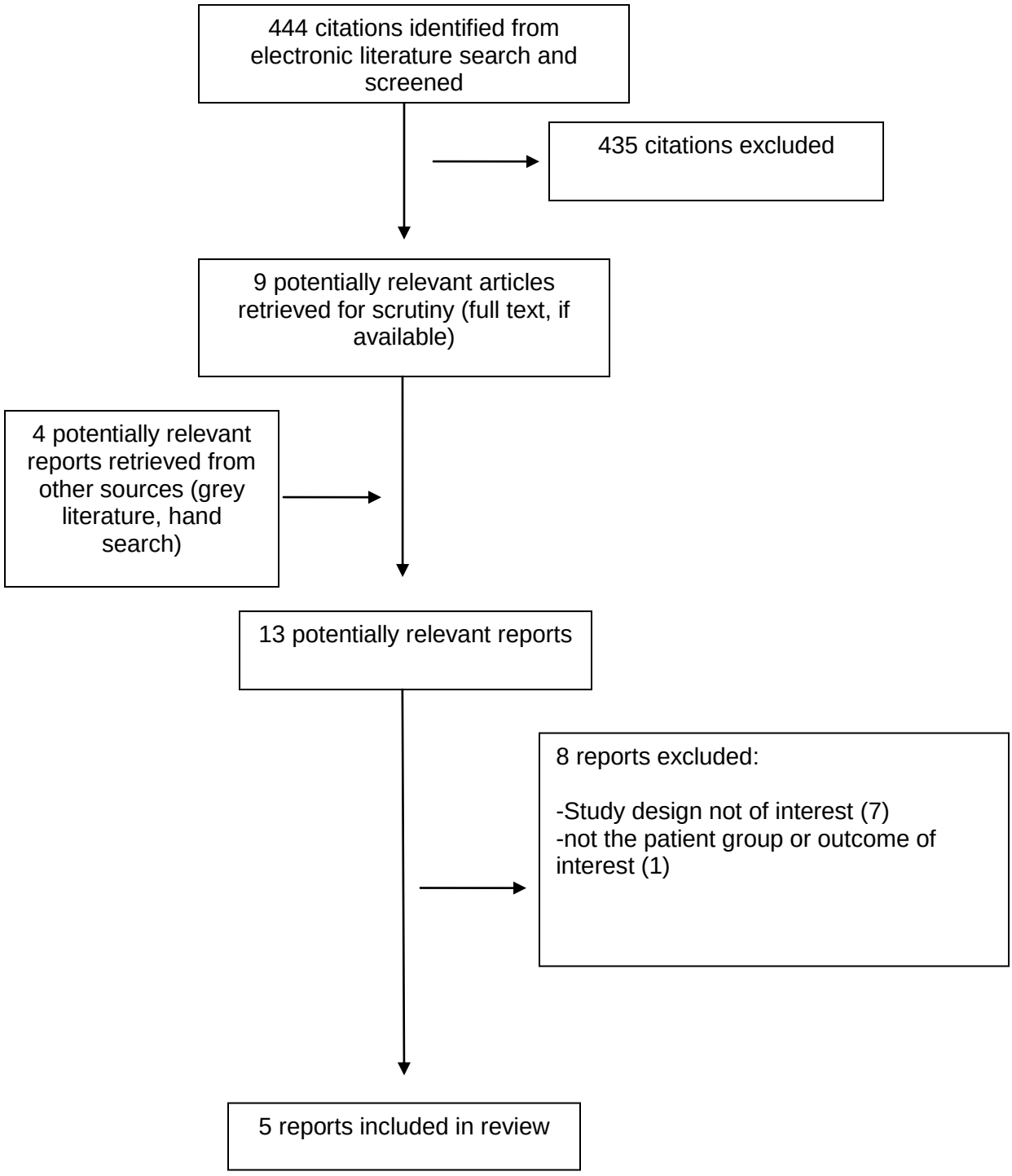
12. CDA position on prevention of infective endocarditis [Internet]. Ottawa: Canadian Dental Association; 2007 Nov. [cited 2013 Mar 8]. Available from: http://www.cda-adc.ca/_files/position_statements/infectiousEndocarditis.pdf

13. Allen U. Infective endocarditis: updated guidelines. Can J Infect Dis Med Microbiol [Internet]. 2010 [cited 2013 Feb 11];21(2):74-7. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2912107

14. Antibiotic prophylaxis for infective endocarditis [Internet]. Québec (QC): Institut national d'excellence en santé et en services sociaux; 2012 Jun. [cited 2013 Feb 22]. Available from: http://www.inesss.qc.ca/fileadmin/doc/INESSS/Outils/Guides_antibio_II/endocardite_2012_web_EN.pdf

15. Wilson W, Taubert KA, Gewitz M, Lockhart PB, Baddour LM, Levison M, et al. Prevention of infective endocarditis: guidelines from the American Heart Association: a guideline from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. Circulation. 2007 Oct 9;116(15):1736-54.

APPENDIX 1: Selection of Included Studies



APPENDIX 2: Excluded Guidelines

Antibiotic prophylaxis for infective endocarditis [Internet]. Québec (QC): Institut national d'excellence en santé et en services sociaux (INESSS).; 2012 Jun. [cited 2013 Feb 22]. Available from: http://www.inesss.qc.ca/fileadmin/doc/INESSS/Outils/Guides_antibio_II/endocardite_2012_web_EN.pdf

This guideline was excluded because it is not an original evidence-based guideline, but an endorsement of the American Heart Association guideline for infective endocarditis prophylaxis published in 2007.

APPENDIX 3: Characteristics of Included Studies

Table A.1: Characteristics of Included Studies

First author/ organization, publication year	Study objectives	Research approach, basis of recommendations / rating of evidence and recommendations	Studies considered in literature/systematic review
Infective Endocarditis			
Oliver et al.[8] (2008)	"To determine whether prophylactic antibiotic administration compared to no such administration or placebo before invasive dental procedures in people at increased risk of BE influences mortality, serious illness or endocarditis incidence." (p. 3)	Systematic review. Included studies ranked according to study design and quality assessed using Downs and Black instrument.	RCT, CCT, cohort, and case-control studies published between 1950 and June 2008
National Institute for Health and Clinical Excellence (NICE)[9] (2008), United Kingdom	To provide "…best practice advice on antimicrobial prophylaxis against infective endocarditis before an interventional procedure for adults and children in primary dental care, primary medical care, secondary care and care in community settings." (p. 6)	Systematic review Evidence levels for interventional studies from Scottish Intercollegiate Guidelines Network (SIGN) (eight levels with range of 1+++ for high quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias, to 4 for expert opinion)	Systematic reviews, randomized controlled trials, observational studies published between 1950 and September 7th 2007
Habib et al.[11] for the European Society of Cardiology (2009)	"To provide recommendations regarding adequate diagnosis, treatment, and prevention of infective endocarditis." "To provide clear and simple recommendations, assisting health care providers in clinical decision making."	Literature review, expert opinion Strength of evidence assessed using three levels; A: data derived from multiple RCTs or meta-analyses, B: data derived from single RCT or large non-randomized study; and C: consensus of opinion of the experts and/or small studies, retrospective studies, registries.	All series (except case reports) published in previous 10 years. Update of previous guideline published in 2004.

Table A.1: Characteristics of Included Studies			
First author/ organization, publication year	**Study objectives**	**Research approach, basis of recommendations / rating of evidence and recommendations**	**Studies considered in literature/systematic review**
		Strength of recommendations assigned one of five classes (I, II, IIa, IIb, III)	
American Academy of Pediatric Dentistry[4] (2011)	"…to help practitioners make decisions regarding antibiotic prophylaxis for dental patients at risk." (p. 275)	Systematic literature search, expert opinion, American Heart Association Guideline (2007) Rating of evidence not provided.	Literature search considered clinical trials published in previous 15 years. Update of a guideline adopted in 1990 and last revised in 2008.
Orthopedic Implant Infection			
American Academy of Orthopedic Surgeons and the American Dental Association[10] (2012)	``The purpose of this clinical practice guideline is to help improve prevention and treatment based on the current best evidence.'' (p. 1)	Systematic review, expert opinion Strength of recommendation based on strength of evidence and had five levels: Strong, moderate, limited, inconclusive, and consensus.	Published in or after 1960. Some case series were excluded (i.e. retrospective, non-consecutive) and studies with small sample size excluded (n<10 per group)

IE: infective endocarditis; CCT: controlled clinical trial; RCT: randomized controlled trial

APPENDIX 4: Summary of Critical Appraisal

Table A.2: Summary of Critical Appraisal of Included Studies

First author/ organization, publication year	Strengths	Limitations
Oliver et al.[8] (2008)	• A priori design • Duplicate study selection and data extraction • Comprehensive literature search • Excluded studies list provided • Characteristics of included studies and quality assessment provided • Scientific quality of included study used appropriately in formulating conclusion • Declarations of interest made	• Grey literature not included • Publication bias not assessed
National Institute for Health and Clinical Excellence[9] (2008)	• Overall objectives described • Health questions covered by guideline specifically described • Relevant population clearly described • Target users of guideline clearly defined • The recommendations are specific and unambiguous • Systematic methods used to search for evidence • Strengths and limitations of evidence clearly described	• Unclear whether patients' views and preferences were sought • Unclear if guideline was piloted among users
Habib et al.[11] for the European Society of Cardiology (2009)	• Overall objectives described • Relevant population clearly described • Target users of guideline clearly defined • The recommendations are specific and unambiguous • Systematic methods used to search for evidence • Strengths and limitations of evidence clearly described	• Recommendation based in part on expert consensus due to lack of evidence • Unclear whether patients' views and preferences were sought • Unclear if guideline was piloted among users • Potential cost implications of applying the recommendation were not included in the recommendation • Competing interests disclosed

American Academy of Pediatric Dentistry[4] (2011)	• Overall objectives described • Relevant population clearly described • Target users of guideline clearly defined • The recommendations are specific and unambiguous • Systematic methods used to search for evidence • Strengths and limitations of evidence clearly described	• Unclear whether patients' views and preferences were sought • Unclear if systematic methods were used, or how the results of the search impacted the decision to endorse the 2007 American Heart Association Guidelines • Unclear if guideline was piloted among users • Potential cost implications of applying the recommendation were not included in the recommendation • Competing interests not noted
American Academy of Orthopedic Surgeons and the American Dental Association[10] (2012)	• Overall objectives described • Relevant population clearly described • Target users of guideline clearly defined • Systematic methods used to search for evidence • Strengths and limitations of evidence clearly described • Guideline provides tools on how the recommendations can be put into practice • Competing interests noted	• Unclear whether patients' views and preferences were sought • Recommendation somewhat ambiguous • Unclear if guideline was piloted among users

APPENDIX 5: Summary of Findings

Table A.3: Findings and Recommendations of Included Studies

First author/ organization, publication year, and country	Conclusions / Evidence Statements	Recommendations
Infective Endocarditis		
Oliver et al.[8] (2008)	"There remains no evidence about whether penicillin prophylaxis is effective or ineffective against bacterial endocarditis in people at risk who are about to undergo an invasive dental procedure. There is a lack of evidence to support previously published guidelines in this area. It is not clear whether the potential harms and costs of antibiotic administration outweigh any beneficial effect. Ethically practitioners need to discuss the potential benefits and harms of antibiotic prophylaxis with their patients before a decision is made about administration." (pg.2)	Not applicable
National Institute for Health and Clinical Excellence (NICE)[9] (2008), United Kingdom	"There is insufficient evidence to determine whether or not antibiotic prophylaxis in those at risk of developing infective endocarditis reduces the incidence of IE when given before a defined interventional procedure (both dental and non-dental)." (based on evidence rated as 1++, 2+, 3) (pg. 66) "Antibiotic prophylaxis does not eliminate bacteraemia following dental procedures but some studies show that it does reduce the frequency of detection of bacteraemia	"1**. Healthcare professionals should regard people with the following cardiac conditions as being at risk of developing infective endocarditis:** • acquired valvular heart disease with stenosis or regurgitation • valve replacement • structural congenital heart disease, including surgically corrected or palliated structural conditions, but excluding isolated atrial septal defect, fully repaired ventricular septal defect or fully repaired patent ductus arteriosus, and closure devices that are judged to be endothelialised • previous infective endocarditis • hypertrophic cardiomyopathy. 2. **Healthcare professionals should offer people at risk of infective**

Table A.3: Findings and Recommendations of Included Studies		
First author/ organization, publication year, and country	**Conclusions / Evidence Statements**	**Recommendations**
	post procedure. It is not possible to determine the effect of antibiotic prophylaxis on the duration of bacteraemia." (based on evidence rated as 1+, 2+) (pg. 70)	**endocarditis clear and consistent information about prevention, including:** • the benefits and risks of antibiotic prophylaxis, and an explanation of why antibiotic prophylaxis is no longer routinely recommended • the importance of maintaining good oral health • symptoms that may indicate infective endocarditis and when to seek expert advice • the risks of undergoing invasive procedures, including non-medical procedures such as body piercing or tattooing. 3. **Antibiotic prophylaxis against infective endocarditis is not recommended:** • for people undergoing dental procedures" (pgs. 8-9)
Habib et al.[11] for the European Society of Cardiology (2009)	"…the Task Force proposes limitation of antibiotic prophylaxis to patients with the highest risk of IE undergoing the highest risk dental procedures." (p.2378)	**"Antibiotic prophylaxis should only be considered for patients at highest risk of IE (Class IIa, Level C)** 1. Patients with a prosthetic valve or a prosthetic material used for cardiac valve repair 2. Patients with previous IE 3. Patients with congenital heart disease a. Cyanotic congenital heart disease, without surgical repair, or with residual effects, palliative shunts or conduits b. Congenital heart disease with complete repair with prosthetic material whether placed by surgery or by percutaneous technique, up to 6 months after the procedure c. When a residual defect persists at the site of implantation of a prosthetic material or device by cardiac surgery or percutaneous technique **Antibiotic prophylaxis is no longer recommended in other forms of valvular or congenital heart disease (Class III, Level C)**

Table A.3: Findings and Recommendations of Included Studies		
First author/ organization, publication year, and country	**Conclusions / Evidence Statements**	**Recommendations**
		Antibiotic prophylaxis should only be considered for dental procedures requiring manipulation of the gingival or periapical region of the teeth or perforation of the oral mucosa **(Class IIa, Level C)** **Antibiotic prophylaxis is not recommended for** local anesthetic injections or non-infected tissue, removal of sutures, dental x-rays, placement o adjustment of removable prosthodontics or orthodontic appliances or braces. Prophylaxis is also not recommended following the shedding of deciduous teeth or trauma to the lips or oral mucosa **(Class III, Level C)** **Recommended prophylaxis for dental procedures at risk** is penicillin or ampicillin (2 g p.o. or i.v. for adults or 50mg/kg p.o. or i.v. for children) 30 to 60 minutes before the procedure. For patients who are allergic to penicillin or ampicillin, clindamycin (600mg p.o. or i.v. for adults and 20 mg/kg p.o. or i.v. for children) 30-60 minutes before the procedure is recommended." (pgs. 2376-2378)
American Academy of Pediatric Dentistry[4] (2011)	"The conservative use of antibiotics is indicated to minimize the risk of developing resistance to current antibiotic regimens. Given the increasing number of organisms that have developed resistance to current antibiotic regimens, as well as the potential for an adverse anaphylactic reaction to the drug administered, it is best to be judicious in the use of antibiotics for the prevention of IE and other distant site infections." (pg. 2)	Endorsement of the AHA (2007) guidelines for the prevention of IE, specifically: **(1) Cardiac conditions associated with the highest risk of adverse outcome from endocarditis for which prophylaxis with dental procedures is reasonable**: - Prosthetic cardiac valve or a prosthetic material used for cardiac valve repair - Previous IE - Congenital heart disease 1. Unrepaired cyanotic congenital heart disease, including palliative shunts or conduits 2. Completely repaired congenital heart defect with prosthetic material or device, whether placed by surgery or by catheter

Table A.3: Findings and Recommendations of Included Studies		
First author/ organization, publication year, and country	**Conclusions / Evidence Statements**	**Recommendations**
		intervention, during the first 6 months after the procedure 3. Repaired congenital heart disease with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device (which inhibit endothelialization). - Cardiac transplant recipients who develop cardiac valvulopathy. **(2) Dental procedures for which endocarditis prophylaxis is reasonable for patients described in (1):** all dental procedures that involve manipulation of gingival tissue or the periapical region of teeth or perforation of the oral mucosa. **(3) Regimens for a dental procedure:** All recommended regimens to be taken 30-60 minutes before a procedure. Oral: Amoxicillin (2 g for adults or 50mg/kg for children); i.m. or i.v.: Ampicillin (2 g for adults and 50 mg/kg for children) or cefazolin or ceftriaxone (1 g for adults and 50mg/kg for children). For persons allergic to penicillin or ampicillin recommend to take orally: cephalexin or clindamycin or azithromycin, or clarithromycin; i.m. or i.v.: cefalozin or ceftriaxone or clindamycin. (guideline details provided in tables on page 3 of guideline)
Orthopedic Implant Infection		
American Academy of Orthopedic Surgeons and the American Dental Association[10] (2012)	"Moderate strength evidence finds that dental procedures are unrelated to implant infection and that antibiotic prophylaxis prior to dental procedures does not reduce the risk of subsequent implant infection. There is no direct evidence to support otherwise. High strength evidence suggests that antibiotic prophylaxis reduces the incidence of post-dental	"The practitioner might consider discontinuing the practice of routinely prescribing prophylactic antibiotics for patients with hip and knee prosthetic joint implants undergoing dental procedures. Grade of Recommendation: Limited"(pg. 75)

Table A.3: Findings and Recommendations of Included Studies		
First author/ organization, publication year, and country	**Conclusions / Evidence Statements**	**Recommendations**
	procedure related bacteremia, but there is no evidence that these bacteremias are related to prosthetic joint infections." (pg. 75)	

AHA: American Heart Association; g: gram; IE: infective endocarditis; i.m.: intramuscular; i.v: intravenous; kg:kilogram; mg:milligram; p.o.:taken orally.