

PROPHYLAXIS AGAINST INFECTIVE ENDOCARDITIS draft guideline consultation – stakeholder comments and responses

Order No	Organisation	Document	Page No	Line No	Comments	Response
1.0	Addenbrooke's NHS Trust	Full	General		It is really important for day to day clinical practice to have clear guidance about exactly who does and does not require antibiotic prophylaxis. The current BSG guidelines are very simple to apply and there is a real danger that this new guidance will lead to more confusion. If "invasive lower GI procedures" includes polypectomy we will find ourselves administering a vast increase in antibiotic prophylaxis with associated increase in procedure time, cost and risk of anaphylaxis without any meaningful evidence of benefit.	<p>Thank you. The concerns regarding the importance for clear guidance are noted. The GDG, the NICE editorial team and the NICE implementation team are working together to ensure the maximum clarity of guidance and support for implementation.</p> <p>The GDG has reconsidered the evidence in relation to GI and GU procedures and the guideline now recommends that prophylaxis for GI and GU procedures should not be given.</p>
1.1	Addenbrooke's NHS Trust	Full	26	575-6	It is vital to accurately define "acquired valvular heart disease with stenosis or regurgitation". Does this include patients with a trace of regurgitation on echocardiography.	<p>Thank you.</p> <p>It was beyond the scope of the guideline to address how structural cardiac defects should be diagnosed, including the place of echocardiography.</p>
1.2	Addenbrooke's NHS Trust	Full	44-46	Multiple	The evidence presented suggests that oesophageal dilatation and variceal sclerotherapy are the only 2 procedures associated with a significant increase in bacteraemia. Polypectomy does not increase the risk of bacteraemia with colonoscopy. It is very important to define both "invasive upper GI procedures" and "invasive lower GI procedures". It is not possible to extrapolate from variceal sclerotherapy to, for example, adrenaline injection of a duodenal ulcer or variceal band ligation. Some may consider polypectomy to be "invasive" but there is no evidence that this is a high risk procedure.	<p>Thank you. The GDG has reconsidered the evidence in relation to GI and GU procedures and the guideline now recommends that prophylaxis for GI and GU procedures should not be given.</p>
2	ARHAI				This organisation was approached but did not respond.	

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3	Association of British Academic Oral & Maxillofacial Surgeons				This organisation was approached but did not respond.	
4.0	Association of Medical Microbiologists	Full	1.3.1	144-145	BSAC recommended prophylaxis for dental surgery, but only for very high risk patients; in the long term we agree with the NICE guidance and if taken forward In their current format will bring improvement.	Thank you.
4.1	Association of Medical Microbiologists	Full	1.3.2.2	186-187	BSAC recommended prophylaxis for dental surgery, but only for very high risk patients; in the long term we agree with the NICE guidance and if taken forward In their current format will bring improvement	Thank you.
4.2	Association of Medical Microbiologists	Full	General		The document is very lengthy for a 'short' guideline, and any recommendation about which antibiotic to give, if required, it is not easily found in the document	Thank you. The SCG process refers to the length of the development time of the guideline – short does not refer to the length of document
4.3	Association of Medical Microbiologists	Full	General		The document contains an enormous amount of health economic detail based on current BNF recommendations, not the revised BSAC recommendations. We are unsure whether this makes a difference.	The prophylactic options explored were those set out in BNF 54 as they represent current UK practice at the time the guideline was developed.
4.4	Association of Medical Microbiologists	Full	General		There are some differences between the BSAC guidelines and the NICE recommendations in the procedures that warrant prophylaxis; these are very minor, and if anything the NICE guidance is easier to follow than the BSAC guidance	Thank you
4.5	Association of Medical Microbiologists	Full	1.3.1	144-145	BSAC recommended prophylaxis for dental surgery, but only for very high risk patients; in the long term we agree with the NICE guidance and if taken forward In their current format will bring improvement.	Thank you.
5	Association of the British Pharmaceuticals Industry,(ABPI)				This organisation was approached but did not respond.	
6	Avon, Gloucestershire & Wiltshire Cardiac Network				This organisation was approached but did not respond.	
7	Barnsley Hospital NHS Foundation Trust				This organisation was approached but did not respond.	
8	Berkshire Healthcare NHS Trust				This organisation was approached but did not respond.	
9	Birmingham Women's Hospital				This organisation was approached but did not respond.	
10	Birmingham, Sandwell and Solihull Cardiac Network				This organisation was approached but did not respond.	
11	Bolton Council				This organisation was approached but did not respond.	
12	Bournemouth & Poole PCT				This organisation was approached but did not respond.	
13	Britannia Pharmaceuticals Limited				This organisation was approached but did not respond.	
14	British Association of Oral and Maxillofacial Surgeons				This organisation was approached but did not respond.	

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15.0	British Cardiovascular Society	Full version	General	<p>While accepting that an evidence base is fundamental to any NICE guideline, in this particular subject there will never be the evidence base we need to make a judgement. There will never be a controlled trial of antibiotic prophylaxis in patients with acquired valve disease. We are dealing with a condition which has a high mortality, but which is not notifiable. There is no national record of the condition, and contrary to belief CCAD does not collect data on infective endocarditis. We are not in a position therefore to identify the consequences of the proposed NICE guidance.</p>	<p>Thank you. The concerns regarding the importance for clear guidance are noted. The GDG, the NICE editorial team and the NICE implementation team are working together to ensure the maximum clarity of guidance and support for implementation.</p> <p>The GDG considered the available clinical, cost effectiveness and expert viewpoint evidence to develop the recommendations.</p> <p>It is outside the remit of the NICE Guideline to address issues relating to a national register of IE cases and/or make IE a notifiable disease.</p>
				<p>With the evidence available it is possible to see how the conclusions were derived. However the American College of Cardiology/American Heart Association with the same evidence available to them have come up with different conclusions: ie that high risk patients should receive antibiotic prophylaxis prior to dental work.</p> <p>This disparity in advice will lead to confusion amongst cardiologists in the UK. In high risk groups in particular mortality in infective endocarditis can reach 50%. There will be enormous difficulty implementing the proposed NICE guideline both by cardiologists and their patients who will favour the status quo or the AHA/ACC proposals. The committee seems to be reaching conclusions based on flimsy bacteriological evidence. We must accept that there will never be the evidence we need, and stick to good clinical practice: protecting the high risk group. These are a relatively small group in terms of cost.</p>	<p>The developers consider they offer a clear and detailed explanation as to how their recommendations are derived from the available evidence.</p> <p>As detailed in the relevant evidence to recommendations section in the full guideline [2.2], the GDG considered the potential confusion which can arise from a detailed stratification into different risk groups, and given the difficulties in relative risk definition the GDG decided that a simple classification of conditions into either at risk or not at risk groups is both supported by the</p>

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						available evidence and would help with clarity
16.0	British Dental Association	Full version	General		The BDA welcomes this draft guidance from NICE and is pleased to have the opportunity to comment. The guidance includes detailed analysis of the evidence associating oral status and dental procedures with infective endocarditis (IE) and the BDA agrees with the recommendation that antibiotic prophylaxis against IE is not recommended for patients at risk of IE undergoing dental procedures. The arguments for and against antibiotic cover have been clearly covered, and the argument for continuing antibiotic cover for dental treatment cannot be made in the light of the evidence presented. Research comparing the levels of bacteraemia produced during day-to-day living with those resulting from dental treatment has shown antibiotic prophylaxis to be an unsupportable intervention, and the BDA supports the current proposal to stop its use.	Thank you.
16.1	British Dental Association	Full version	General		The new guidance could cause problems for dentists who need to explain to patients who have previously received antibiotic cover for routine dental work that they no longer need it. Reassuring them that this decision is not related to NHS financial issues could be difficult and, in some cases, patient anxiety will take a while to manage. As such, the BDA feels that it would be of great benefit to produce some guidance for patients in addition to the full guidance, and would be keen to be included in the development of this.	Thank you. The concerns regarding the importance for clear guidance are noted. The GDG, the NICE editorial team, the NICE Patient and Public Involvement Group (PPIP) and the NICE implementation team are working together to ensure the maximum clarity of guidance and support for implementation. The NICE implementation team will produce implementation tools to assist both professionals and patients.
16.2	British Dental Association	Full version	Page 5	Lines 165-167	These lines currently read: "Antimicrobial regimens should be modified to cover endocarditis-causing organisms when procedures are undertaken at a site of infection or potential infection in patients at risk of IE."	Thank you, this wording has been revised to ensure clarity.

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					<p>Please could this be amended to: “Where an antibiotic regime is recommended, antimicrobial regimens should be modified to cover endocarditis-causing organisms when procedures are undertaken at a site of infection or potential infection in patients at risk of IE.”</p> <p>At first glance the current wording may give the impression that antibiotics are required whenever there is or the potential for infection. Later in the document it does clarify that this only applies where an antibiotic regime is recommended. However, some professionals may only read the summary. This organisation was approached but did not respond.</p>	
17	British Dental Health Foundation				This organisation was approached but did not respond.	
18	British Geriatrics Society				This organisation was approached but did not respond.	
19	British Heart Foundation				This organisation was approached but did not respond.	
20	British Infection Society				This organisation was approached but did not respond.	
21.0	British National Formulary (BNF)	Full version	6	172	<p>Patients with a history of endocarditis are included in the category of cardiac conditions that place patients at high-risk of endocarditis in the British Society of Antimicrobial Chemotherapy (<i>J Antimicrob Chemother</i> 2006; 57: 1035–1042) guidelines, American Heart Association (<i>Circulation</i> 2007; 116: 1736–1754) guidelines, and current recommendations in BNF 54. Patients with a history of endocarditis have not been included in the NICE analysis, although this was stipulated in the Scope. The NICE guidance must address this issue.</p>	<p>Thank you. The GDG had considered that those with a previous episode of IE were covered in the groups of patients who are considered to be at risk, however the GDG has considered that for reasons of clarity those with previous IE will be specified as an at risk group</p>
21.1	British National Formulary (BNF)	Full version	6	199	<p>Do lower gastro-intestinal tract procedures also include sigmoidoscopy, colonoscopy, and barium enema?</p>	<p>Thank you. The guideline will address all GI procedures that are defined as interventional procedures.</p>
21.2	British National Formulary (BNF)	Full version	7	206	<p>Should patients undergoing tonsillectomy, adenoidectomy, or nasal packing or intubation receive prophylaxis against endocarditis?</p>	<p>Thank you. Antibiotic prophylaxis to prevent IE is not recommended for ENT procedures, the recommendations have been revised which should assist with clarity</p>
21.3	British National Formulary (BNF)	Full version	7	210	<p>Should patients undergoing caesarean section or hysterectomy receive prophylaxis against endocarditis?</p>	<p>Thank you. Antibiotic prophylaxis to prevent IE is not recommended for obstetric and</p>

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21.4	British National Formulary (BNF)	Full version	56	215 - 16	<p>These antibacterial regimens are reasonable for the surgical procedures where endocarditis prophylaxis is recommended in the current draft NICE guidelines, and they are consistent with the British Society of Antimicrobial Chemotherapy (<i>J Antimicrob Chemother</i> 2006; 57: 1035–1042) guidelines which recommend intravenous amoxicillin/ampicillin + intravenous gentamicin <i>or</i> intravenous teicoplanin + intravenous gentamicin for these procedures. However, it is not clear how the NICE guidance derived this recommendation. In addition the economic evaluation in the NICE guidance should also analyse the following antibiotic strategy: intravenous amoxicillin + intravenous gentamicin.</p> <p>Antibacterial prophylaxis is already recommended before certain surgical procedures regardless of whether a patient is at risk of endocarditis or not e.g. open biliary surgery, resection of colon, ERCP, TURP, and transrectal prostatic biopsy (see BNF 54 p280–1); these antibacterial regimens are different to those for endocarditis prophylaxis. In these cases, which antibacterial regimen should be given to patients at high risk of endocarditis?</p>	<p>gynaecological procedures, the recommendations have been revised which should assist with clarity</p> <p>The economic analysis was undertaken with respect to antibiotic prophylaxis in dental procedures. The choice of strategies were those set out in BNF 54 as they represent current UK practice at the time the guideline was developed.</p> <p>Based on GDG opinion regarding the risk of developing IE following a dental procedure, the analysis indicates that <u>all</u> antibiotic strategies are not cost-effective.</p> <p>Recommendation 1.3.2.9 identifies that where antibiotic regimens are being given they should be modified to cover endocarditis causing organisms and therefore should comply with the recommended antibiotic regimen</p> <p>Thank you, the studies which used chlorhexidine as an oral irrigation did show reduction in the level of bacteraemia, but those which used it as an oral rinse did not.</p> <p>Thank you. It is outside the scope of the guideline to consider the invasive nature of specific procedures.</p>
21.5	British National Formulary (BNF)	Full version	67	1488 - 9	<p>Is this interpretation correct? 3 of the 6 studies analysed showed a significant reduction in the level of bacteraemia for chlorhexidine compared to placebo.</p>	<p>Thank you, the studies which used chlorhexidine as an oral irrigation did show reduction in the level of bacteraemia, but those which used it as an oral rinse did not.</p>
21.6	British National Formulary (BNF)	Full version	101	2132 - 5	<p>Should the invasive nature of a procedure also be taken into account when deciding which procedures require endocarditis prophylaxis?</p>	<p>Thank you. It is outside the scope of the guideline to consider the invasive nature of specific procedures.</p>
22	British Nuclear Medicine Society				<p>This organisation was approached but did not respond.</p>	
23	British Society for Antimicrobial Chemotherapy				<p>This organisation was approached but did not respond.</p>	

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24.0	British Society of Disability and Oral Health	Full	116	<p>BSDH welcomes the extensive review of the existing evidence in this area. It is also aware of the significant change to existing guidance that is proposed.</p> <p>BSDH feel that it is important to have well worded Patient Information Sheets, and it would be useful to view and comment on these when they are available. We predict that patients who have had intravenous antibiotics for prophylaxis may well object to having this withdrawn and it would be useful to have a robust information sheet to give to them.</p>	<p>Thank you. The GDG, the NICE editorial team, the NICE Patient and Public Involvement Group (PPIP) and the NICE implementation team are working together to ensure the maximum clarity of guidance and support for implementation.</p>
24.1	British Society of Disability and Oral Health	Full	Section 3.3.11	<p>Audit Methods: It would be helpful to determine the audit criteria commissioned by CASPE / HQS when auditing the implementation of the guidance.</p>	<p>Thank you. The GDG agrees with the need to audit any impact of this guideline, guideline and this is noted in the research recommendations in this guideline. Audit tools will be developed in conjunction CASPE.</p>
24.2	British Society of Disability and Oral Health	Full	107	<p>Disclaimer: The disclaimer section assumes that "healthcare professionals will use general medical knowledge and clinical judgement in applying these recommendations", however for dental practitioners this may not be appropriate.</p> <p>Some advice for practitioners would be appreciated when the patient asks for prophylaxis despite advice to the contrary. The practitioner may well seek advice from a Cardiologist whose views may be at variance with the Guidelines.</p> <p>Overall the Society welcomes this significant move and fully understands the need for the emphasis for these patients to be on the preventive side of dental care.</p>	<p>Thank you. The GDG, the NICE editorial team, the NICE Patient and Public Involvement Group (PPIP) and the NICE implementation team are working together to ensure the maximum clarity of guidance and support for implementation.</p>
25.0	British Society of Echocardiography	Full	General	<p>I suggest we state unequivocally that transoesophageal echocardiography does not require antibiotic prophylaxis. I think that 'invasive oesophageal procedures' implies OGD with biopsy and NOT transoesophageal echocardiography, but it would not harm to make this explicit since the BCS/RCP guidelines included transoesophageal echocardiography as a risk</p>	<p>Thank you</p> <p>The GDG have further considered and discussed the development of the recommendations in relation to GI procedures and these have been updated. The guideline now recommends that prophylaxis for GI and GU procedures should not be given.</p>
25.1	British Society of Echocardiography	Full	General	<p>The definition of acquired valve disease is no longer clear since on echocardiography we now find thickening or regurgitation in many people with no clinical evidence of valve disease. Thus 25% aged</p>	<p>Thank you</p> <p>The developers specifically</p>

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over 65 have aortic valve thickening and 15% have mild or moderate aortic regurgitation. How much MR associated with mitral prolapse qualifies as a risk since we often find trivial jets which are well within normal limits? Equally we often find a little more MR than average in structurally normal mitral valves. These are difficult areas because there is a lack of evidence but they are of great practical importance. This is particularly an issue as more GPs use open access or private echo services and then have to interpret the significance of normal MR or TR entered into the report without an intermediary cardiologist to comment on clinical significance.

I suggest not recommending antibiotic prophylaxis unless there is more than mild regurgitation or stenosis.

looked at the risk of developing IE in those with pre-existing structural cardiac defects. We report evidence from case control studies on an association between mitral prolapse (MVP) and an increased risk of IE relative to controls. We did not identify evidence that specifically looked at “How much MR associated with mitral prolapse qualifies as a risk”.

It was beyond the scope of the guideline to address how structural cardiac defects should be diagnosed, including the place of echocardiography.

26.0	British Society of Oral Medicine	Full	General	The British Society for Oral Medicine welcomes these draft guidelines and applauds the work the committee has undertaken reviewing and presenting the evidence. There is much in current endocarditis prophylaxis practice which is anecdotal or ‘defensive medicine’ and this clarification will be of benefit to both patients and clinicians on a daily basis.	Thank you
26.1	British Society of Oral Medicine	Full	General	In its current form this guidance is clear and concise and the BSOM would support publication without modification.	Thank you
26.2	British Society of Oral Medicine	Full	General	These guidelines will represent a significant change in clinical practice for many patients who have received antibiotic prophylaxis as part of dental care over many years. This sudden change may be very confusing for them and the BSOM would welcome some explanatory comment or summary to be made available to patients explaining the need for this change in appropriate language. This could be presented through the NICE portal or be included as part of the document appendices.	Thank you. The GDG, the NICE editorial team, the NICE Patient and Public Involvement Group (PPIP) and the NICE implementation team are working together to ensure the maximum clarity of guidance and support for implementation. The NICE implementation team will produce implementation tools to assist both professionals and patients.

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26.3	British Society of Oral Medicine	Full	26		The clarification of 'risk groups' is welcome, particularly the omission of patients with a history of rheumatic fever without evidence of subsequent valvular damage	Thank you.
26.4	British Society of Oral Medicine	Full	54-55		The BSOM welcomes the detailed evidence review linking infective endocarditis with oral or dental procedures. We support the committee's view that antibiotic prophylaxis is not justified for 'at risk' patients undergoing oral and dental procedures.	Thank you.
26.5	British Society of Oral Medicine	Full	54-55		The recommendation that the reduction of bacteraemia from an oral source is through the maintenance of high standards of oral health is supported by BSOM. We endorse the view that this is a shared responsibility between the patient and oral healthcare professionals. This organisation was approached but did not respond.	Thank you.
27	British Society of Paediatric Dentistry					
28.0	British Society of Periodontology	Full	General		These new guidelines have the complete support of all members of the British Society of Periodontology who have responded to the consultation. The guidelines should be implemented as soon as possible to prevent the possibility of further fatal anaphylaxis in otherwise healthy dental patients.	Thank you
28.1	British Society of Periodontology	Full	54 and 56	1212 and 1246	There is a concern that the recommendation given in 1.3.2.2 (<i>Antibiotic prophylaxis against IE is not recommended for patients at risk of IE undergoing dental procedures</i>) could be perceived as contradictory to the recommendation given in 1.3.2.9 (<i>Antimicrobial regimes should be modified to cover endocarditis-causing organisms when procedures are undertaken at a site of infection in patients at risk of IE</i>) if, for example, treatment is required of an oral or dental infection. Perhaps further clarity could be provided by amending the recommendation in 1.3.2.2 to read <i>Antibiotic prophylaxis against IE is not recommended for patients at risk of IE undergoing dental procedures, including treatment of any oral, dental or periodontal infections.</i>	Thank you. The GDG considered that if appropriate antibiotics were being prescribed for a spreading infection, then this would cover organisms known to cause IE. The guideline covers prophylaxis and it is not appropriate to add that into the recommendation
					Additionally, it would be helpful to further define what is meant by "infection" in recommendation 1.3.2.9. For example, does this include a dental abscess (which may be endodontic or periodontal in origin)? Some individuals would even consider chronic gingivitis or periodontitis to be an "infection", though this is not a widespread opinion. Therefore, there needs to be greater clarity in recommendations 1.3.2.2 and 1.3.2.9.	

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28.10	British Society of Periodontology	Full	55	1224	"Preventative" should be rewritten as "preventive"	Thank you, this has been revised.
28.11	British Society of Periodontology	Full	69	1552	"Preventative" should be rewritten as "preventive"	Thankyou – the text has been amended
28.12	British Society of Periodontology	Full	100	2099	"Preventative" should be rewritten as "preventive"	Thank you, this has been changed.
28.13	British Society of Periodontology	Full	General		There is a concern that many patients may have become used to, or even expect to have, antibiotic prophylaxis for dental procedures, and may become alarmed when this is no longer offered to them. It is requested that patient leaflets are produced that can be provided to all dentists to give to those patients concerned in which the reasons for the changes in the guidelines are explained.	Thank you. The GDG, the NICE editorial team, the NICE Patient and Public Involvement Group (PPIP) and the NICE implementation team are working together to ensure the maximum clarity of guidance and support for implementation.
28.14	British Society of Periodontology	Full	66	1460	The authors of the guidelines may wish to consider the findings of a recent study in which bacteremia was found to be reduced following oral rinsing with 7.5% povidone-iodine solution compared to rinsing with saline. <i>Cherry M. Daly CG. Mitchell D. Highfield J. Effect of rinsing with povidone-iodine on bacteraemia due to scaling: a randomized-controlled trial. Journal of Clinical Periodontology. 34(2):148-55, 2007.</i> While we do not feel that the findings of this study materially affect the conclusions of the guidelines, they may be of interest for completeness.	Thank you. The scope of this guideline included the use of chlorhexidine compared with other agents, therefore papers which considered povidone-iodine and saline were excluded.
28.15	British Society of Periodontology	Full	50	1096	Grammatical error	Thank you, this has been revised.
28.16	British Society of Periodontology	Full	50	1096	Grammatical error	Thank you, this has been revised.
28.17	British Society of Periodontology	Full	53	1170	Grammatical error	Thank you, this has been revised.
28.18	British Society of Periodontology	Full	53	1170	Grammatical error	Thank you, this has been revised.
28.19	British Society of Periodontology	Full	54	1195	"hydrochloride" is wrong	Thank you, this has been revised.
28.20	British Society of Periodontology	Full	54	1195	"hydrochloride" is wrong	Thank you, this has been revised.
28.21	British Society of Periodontology	Full	56	1251	In recommendation 1.3.2.10 it would be helpful to clarify doses and routes of administration	Thank you. Doses and routes of administration would be as per the BNF, however following reconsideration by the GDG this recommendation has been

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						changed and the guideline no longer recommends prophylaxis.
28.22	British Society of Periodontology	Full	5	149	"Preventative" should be rewritten as "preventive"	Thank you, this has been revised.
28.23	British Society of Periodontology	Full	6	194	"Preventative" should be rewritten as "preventive"	Thank you, this has been revised.
29	BUPA				This organisation was approached but did not respond.	
30	Calderdale PCT				This organisation was approached but did not respond.	
31.0	CASPE Research	Full version	General		These comments are made from the perspective of drafting audit criteria for NICE guidance. The comments are therefore restricted to considering the key priorities for implementation and whether these are phrased in such a way as to facilitate the development of audit criteria to ascertain if the guidance has been implemented by health service providers.	Thank you.
31.1	CASPE Research	Full version	Page 5	144 - 145	This is auditable against a standard of 0%, as a non-recommended practice.	Thank you.
31.2	CASPE Research	Full version	Page 5	146-149	This recommendation is only partly auditable as it involves seeking information not easily available in the patient record. The audit criterion is likely to be constructed around the advice given to the patient and records of preventive dentistry.	Thank you.
31.3	CASPE Research	Full version	Page 5	150 - 153	This is auditable against a standard of 100% of patients at risk of IE having antibiotic prophylaxis prior to undergoing the stated procedures.	Thank you.
31.4	CASPE Research	Full version	Page 5	154-157	This is auditable against a standard of 100% of patients at risk of IE having antibiotic prophylaxis prior to undergoing the stated procedures, with an exception for patients undergoing urethral catheterisation.	Thank you.
31.5	CASPE Research	Full version	Page 5	158 - 162	This recommendation is auditable against a standard of 0%, as a non-recommended practice.	Thank you.
31.6	CASPE Research	Full version	Page 5	163 - 164	This recommendation is auditable against a standard of 0%, as a non-recommended practice.	Thank you.
31.7	CASPE Research	Full version	Page 5	165 - 167	This recommendation is auditable but through the audit of prescribing records.	Thank you.
32	Coast to Coast Cardiac Network				This organisation was approached but did not respond.	
33	Cochrane Oral Health Group				This organisation was approached but did not respond.	
34	Commission for Social Care Inspection				This organisation was approached but did not respond.	
35	Connecting for Health				This organisation was approached but did not respond.	

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36	Coventry and Warwickshire Cardiac Network		This organisation was approached but did not respond.	
37.0	Department of Health	General	We support the recommendations within the guidance in relation to antibiotic prophylaxis prior to dental procedures to prevent endocarditis (IE). In our view, this will help to reduce the misuse, over-prescription and potential unwanted side effects in relation to antibiotics, and the concurrent increase in antibiotic resistance.	Thank you.
37.1	Department of Health	General	We feel that the guidance, as currently drafted, represents a very significant shift from current practice, particularly with respect to dental prophylaxis. In our opinion therefore, it is very important that an appropriate communication strategy is put in place for cardiologists, dentists, GPs, patients and undergraduate teaching establishments. Unless this happens, we feel that there is a serious risk of confusion, and a lack of compliance. In our view, it is unreasonable to expect a dentist to comply if, for example, the local cardiologist responsible for the patient is either unaware of the revised guidance or has differing views.	Thank you. The GDG, the NICE editorial team, the NICE Patient and Public Involvement Group (PPIP) and the NICE implementation team are working together to ensure the maximum clarity of guidance and support for implementation.
37.2	Department of Health	General	<p>It is widely accepted that the evidence base from which endocarditis prophylaxis recommendations can be made is very weak. Therefore, any guidance is based heavily on expert opinion. We feel that, to some extent, the guidance is based on the premise that lack of evidence equates with lack of indication and/or benefit. While this may be true, there is also the risk that current antibiotic prophylaxis recommendations actually result in some benefit, however difficult that may be to quantify, and a significant shift from current recommendations needs to be carefully monitored.</p> <p>In our view, insufficient emphasis has been given to the need to audit whether the incidence of endocarditis increases following implementation of these guidelines.</p>	<p>Thank you. The evidence base in this area is acknowledged to be weak. The guidance was not based on the premise that a lack of evidence equates a lack of indication/benefit. The GDG considered the clinical and cost effectiveness evidence and expert viewpoints and developed recommendations based on this evidence.</p> <p>The GDG agrees with the need to audit any impact of this guideline and this is noted in the research recommendations in this guideline</p>
37.3	Department of Health	General	In our view, cardiologists may feel very uneasy (and may resist) the GDG's conclusions, because their training has been contrary to the new recommendations for so long. They also see the consequences (and treat cases) of endocarditis, and obviously do not see those who do not get IE; we feel that this will lead them to be concerned that the new guidelines may increase the risk of IE in their patients.	<p>Thank you.</p> <p>The GDG, the NICE editorial team, the NICE Patient and Public Involvement Group (PPIP) and the NICE implementation</p>

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Comment ID	Commenter	Topic	Comment	Response
				team are working together to ensure the maximum clarity of guidance and support for implementation. The NICE implementation team will produce implementation tools to assist both professionals and patients.
37.4	Department of Health	General	<p>Whilst a registry is recommended as something 'for future research', we feel that it should be a minimum requirement of implementing these guidelines, so that any increase in cases of IE can be monitored and compared with historical sources of data. If there is no change in incidence, all can be reassured that the change in practice has not been detrimental. Only in this way can we be confident that the guideline has not placed patients at increased risk (IE has a 20% mortality – please see page 9 of the draft).</p>	<p>Thank you. The GDG agrees with the need to audit any impact of this guideline and this is noted in the research recommendations in this guideline.</p> <p>It is outside the remit of the NICE Guideline to address issues relating to a national register of IE cases and/or make IE a notifiable disease.</p>
37.5	Department of Health	General	<p>Stress is placed on patient information, but in our view, all we can really do is inform patients that there may be a risk of IE following dental procedures (but that this risk is difficult to quantify, is likely to be low, and has been regarded by NICE to be sufficiently low to make recommendation of antibiotic prophylaxis no longer valid).</p> <p>Also, the information given to patients depends on who is giving it. For instance, dental practitioners will understandably refer patients to your new guidance and assure them that antibiotic prophylaxis is not required. We feel that they are perfectly justified in doing this if the conclusions of the current draft are published unchanged. Cardiologists, on the other hand, will acknowledge that you have pronounced that antibiotic prophylaxis is not required, but will acknowledge the lack of evidence either in favour or against such a recommendation.</p> <p>Patients, particularly those who have been having antibiotic</p>	<p>Thank you. The GDG, the NICE editorial team, the NICE Patient and Public Involvement Group (PPIP) and the NICE implementation team are working together to ensure the maximum clarity of guidance and support for implementation.</p>

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37.6	Department of Health	General	<p>prophylaxis for many years, will look to the cardiologist for information and advice and will inevitably sense the concern of at least many cardiologists that they simply do not know whether the change in practice will result in an increase in cases of IE or not. We feel that many patients will therefore conclude that they wish to continue having antibiotic prophylaxis. We would ask if they have the right to request this and if so, does the patient's wish override the dental practitioner's wish, supported by yourselves, that prophylaxis is not given? We believe this sort of situation will arise frequently and would at least be helped if we could legitimately reassure patients that we are collecting data and should know whether the change in practice has altered the risk of IE - and hopefully reassure patients and cardiologists that there has, indeed, been no change.</p> <p>Patients who have already had an episode of IE have, de facto, identified themselves as individuals at highest risk of IE, whatever the complex mechanisms by which the IE occurs. As such, we would have thought that the GDG would have specifically mentioned this group of patients and advised whether they should or should not continue to have antibiotic prophylaxis. Intuitively, we would have thought that they should continue to have antibiotics. But in our opinion, the GDG should specifically address this issue.</p>	<p>Thank you.</p> <p>The GDG had considered that those with a previous episode of IE were covered in the groups of patients who are considered to be at risk, however the GDG has considered that for reasons of clarity those with previous IE should be specified as an at risk group.</p>
37.7	Department of Health	General	<p>There will again be no evidence to support or refute continuing antibiotic prophylaxis. However, if a patient has already had one episode of IE (and given that we do not understand fully the interplay between bacteraemia, underlying cardiac condition, immune status etc. which are likely contributing factors to the development of IE) they would seem to be a group that are flagging themselves up to be at higher than usual risk. We would also ask whether there should be specific mention of what to do in the immunocompromised patient.</p> <p>We have concerns that the cost-effectiveness analysis appears to have been based largely on assumptions, and that the GDG may not have taken sufficient account of it. For instance, amoxycillin or clindamycin can be cost effective (please see page 99) but the GDG concludes that there is no evidence for their use.</p>	<p>Given the paucity of the data it was considered appropriate to develop only a simple economic model. However, it was found that antibiotic prophylaxis is only cost effective if optimistic assumptions (in the view of the GDG) are made.</p>
37.8	Department of Health	General	<p>We are also concerned about the statement (on page 13) that healthcare professionals are expected to use their judgement, but the guideline may prevent them from doing so. For instance,</p>	<p>Thank you. The guideline is there to guide clinical practice and as such it cannot be</p>

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cardiologists may advise that, in their professional opinion and despite your guidance, a certain patient should have antibiotic prophylaxis for dental procedures, but the dental practitioner may quite legitimately decline to give this, citing your guidance as the justification. The GDG could usefully address how these differences of opinion might be resolved, so that patients are not left without a clear and agreed management plan.

We feel that the guidance could more specifically accept that a minority of patients may still be felt by the cardiologist to warrant antibiotic prophylaxis, and that dental practitioners should be sympathetic to this. We realise this is not an evidence-based position, but we feel that it may be helpful if you were able to adopt a clearer statement.

applicable to all clinical situations. Therefore the guideline is not designed to replace expert clinical judgement which should be applied to its usage.

The GDG, the NICE editorial team, the NICE Patient and Public Involvement Group (PPIP) and the NICE implementation team are working together to ensure the maximum clarity of guidance and support for implementation.

37.9 Department of Health

General

In summary, the document is well written and obviously is the result of much detailed professional deliberation. However, the outcomes of implementation of the guidance should be closely audited to detect any rise in cases of IE which could be attributed to dental procedures. We are however concerned that, with such a major change, there may be an increase in IE. As such, we feel that an audit of its prevalence should be a mandatory consequence of the change in guidance. In our opinion, this will help to reassure those patients and cardiologists who may feel that this is a major departure from current practice which could have devastating consequences.

In our view, it is important that patients who had previously had IE should be addressed specifically as a group.

Thank you. The GDG agrees with the need to audit any impact of this guideline and this is noted in the research recommendations in this guideline.

It is outside the remit of the NICE Guideline to propose that “an audit of its prevalence [IE] should be a mandatory consequence of the change in guidance”.

The GDG had considered that those with a previous episode of IE were covered in the groups of patients who are considered to be at risk, however the GDG has considered that for reasons of clarity those with previous IE should be specified as an at risk group

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					<p>We would be interested to know the experience of those in the USA following the ACC/AHA revised guidelines which appeared earlier this year (and were similar to the GDG's draft guidance). Was there any difficulty in persuading patients and cardiologists of the validity of the changed recommendations, and were the guidelines actually followed (or did patients push to carry on doing what they had been advised to do in the past)?</p>	<p>It is outside the remit of the NICE guideline to report this.</p>
					<p>We feel that the consequences of these changed recommendations are difficult to estimate. If we had some idea how they had been taken up in the USA, we may be more prepared for patients' and cardiologists' feedback following implementation of your own recommendations.</p>	<p>Thank you, the consequences are difficult to estimate, however the implementation team will be working with the guidelines team, the GDG and PPIP on implementation issues</p>
38	Department of Health, Social Security and Public Safety of Northern Ireland				<p>This organisation was approached but did not respond.</p>	
39	Dudley Group of Hospitals NHS Trust				<p>This organisation was approached but did not respond.</p>	
40	East & North Herts PCT & West Herts PCT				<p>This organisation was approached but did not respond.</p>	
41.0	Eastman Dental Institute	full	Summary etc		<p>The ADA has just issued guidelines suggesting cover for HIGH risk groups only. Are you ABSOLUTELY sure and can defend robustly in a court of law, that NICE guidelines are not just a "step too far".</p>	<p>Thank you. This is a short clinical guideline and provides guidance on clinical practice, this does not represent a core clinical standard in the NHS. As everyday bacteraemias are as high risk as dental procedures we would consider this would make causation from a dental procedure impossible to prove in law</p>
42.0	Faculty of Dental Surgery	Full version	5	146	<p>We have great concerns regarding patients who need special care dentistry who rely heavily on others to maintain their oral hygiene and/or those who lack knowledge and skill to maintain a high standard of OH.</p>	<p>Thank you. This guideline has acknowledged the need for high standards of oral health with both personal responsibility and</p>

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42.1	Faculty of Dental Surgery	Full version	5	165	We would be interested to know the recommendations.	professional facilitation highlighted Thank you.
42.2	Faculty of Dental Surgery	Full version	general		There has been no randomised controlled trial to show if AB prophylaxis works on IE so we should not throw away the baby with the bath water.	Thank you. The lack of RCTs in this area has been specifically discussed in this guideline.
42.3	Faculty of Dental Surgery	Full version	general		A reminder that we need very clear, concise evidence-based <u>information</u> to give to our patients who have required Antibiotic Prophylaxis in the past. They will need to be reassured about the safety and risks of the new guidance that is being recommended.	Thank you. The GDG, the NICE editorial team, the NICE Patient and Public Involvement Group (PPIP) and the NICE implementation team are working together to ensure the maximum clarity of guidance and support for implementation.
43	Faculty of General Dental Practice				This organisation was approached but did not respond.	
44	Greater Manchester and Cheshire Cardiac Network				This organisation was approached but did not respond.	
45	Health Commission Wales				This organisation was approached but did not respond.	
46	Healthcare Commission				This organisation was approached but did not respond.	
47	Heatherwood and Wexham Park Hospitals Trust				This organisation was approached but did not respond.	
48	Home Office				This organisation was approached but did not respond.	
49	Institute of biomedical Science				This organisation was approached but did not respond.	
50	Leeds PCT				This organisation was approached but did not respond.	
51.0	Liverpool Women's NHS Trust	FULL	general		It is clear that the evidence does not support prophylaxis in O & G patients but the scope of the guideline does not cover special case such as those who are immunocompromised eg HIV. We have patients from Africa with acquired valvular disease and HIV and would welcome guidance on such cases.	Thank you. Those who are immuno-compromised are outside the scope of this guideline.
52	LNR Cardiac Network				This organisation was approached but did not respond.	
53	Medicines and Healthcare Products Regulatory Agency (MHRA)				This organisation was approached but did not respond.	
54	Mid Essex Hospitals NHS Trust				This organisation was approached but did not respond.	
55	National Patient Safety Agency				This organisation was approached but did not respond.	

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56.0	National Public Health Service - Wales	Full	5	114-5	Reword for clarity "For those patients who are at risk of infective endocarditis (IE) and who are undergoing dental procedures antibiotic prophylaxis is not recommended"	Thank you. This has been re-worded to assist with clarity
56.1	National Public Health Service - Wales		7	211-213	Potential conflict where a patient has infection and is undergoing dental treatment (e.g. drainage of abscess). In this case I assume prophylaxis for the dental procedure is still not routinely advised, however if an antibiotic regime is being utilised (e.g. for management of spreading infection) then it should be modified to cover endocarditis causing organisms.	Thank you. The GDG considered that if appropriate antibiotics were being prescribed for a spreading infection, then this would cover organisms known to cause IE
57	National Treatment Agency for Substance Misuse				This organisation was approached but did not respond.	
58.0	NCCHTA				2.1 Please comment on the validity of the work i.e. the quality of the methods and their application- Please see comments on health economics in 2.2	See response below
58.1	NCCHTA				2.2 Please comment on the health economics and/or statistical issues depending on your area of expertise. - I have some potentially serious reservations about the way the economic analysis has been conducted. I would like to make three general points before going on to make some more specific comments.	See response below
58.2	NCCHTA				3.1 How far are the recommendations based on the findings? Are they a) justified i.e. not overstated or understated given the evidence? b) Complete? i.e. are all the important aspects of the evidence reflected? - Please see 2.2	See response below
58.3	NCCHTA				4.1 Is the whole report readable and well presented? Please comment on the overall style and whether, for example, it is easy to understand how the recommendations have been reached from the evidence. - Presentation is fine.	Thank you.
58.4	NCCHTA		100	2010	Delete 'there'.	Thank you, this has been corrected (s/b line 2101)
58.5	NCCHTA		226		The formatting in the 'cost-effectiveness results' needs attention.	Thank you. This section will be reformatted as necessary.
58.6	NCCHTA		68	1504	It would be helpful to mention here which databases.	Please see appendices 5.3
58.7	NCCHTA		70	1571	\$199,000 should be £200,000 if consistent rounding is applied.	Thank you – the text has been amended
58.8	NCCHTA		70	1576	\$500,000 should be \$498,000 if consistent rounding is applied.	Thankyou – the text has been amended
58.9	NCCHTA		71	1590-1591	The corresponding figure in appendix 6 on page 228 is \$1.3 million per <i>spared year of life</i> .	Thankyou, the Appendix was correct. The relevant text has been amended accordingly.

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58.10	NCCHTA	71	1602	\$20,000 should be £18,000 if consistent rounding is applied.	Thankyou – the text has been amended
58.11	NCCHTA	72	1624	What is the Years of Healthy Life Measure? Please explain and supply a reference.	Thankyou – The “Years of Healthy Life measure” was developed to monitor the health (longevity and health-related quality of life) of US citizens. A reference has now been included. Toward Consistency in Cost-Utility Analyses: Using National Measures to Create Condition-Specific Values Marthe R. Gold, Peter Franks, Kristine I. McCoy, Dennis G. Fryback <i>Medical Care</i> , Vol. 36, No. 6 (Jun., 1998), pp. 778-792 The choice of utilities for the present analysis were obtained elsewhere and are fully referenced in the text.
58.12	NCCHTA	72	1650-1652	Reiterate here why no model was developed for other interventional procedures.	There is a much greater paucity of data in relation to the use of antimicrobial prophylaxis for individuals undergoing other interventional procedures, and it was not considered feasible to undertake a separate analysis in this case.
58.13	NCCHTA	75	1660	What is the justification for basing the analysis on Agha et al.?	See above. That analysis in common with others included relevant health states accepted by the GDG. The Agha et al approach was a useful starting point, but was not necessarily slavishly adhered to.
58.14	NCCHTA	77	1694-	Given that ‘the cost-effectiveness of antibiotic prophylaxis appears to	The base case risk estimate of

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			1695	also critically depend on the baseline risk of developing IE' (page 72, lines 1638-1640), please justify why this estimate has been chosen.	developing IE following a dental procedure has now been substantially reduced. The estimates derived from the work of Duval et al have been explored in sensitivity analyses. It remains useful to explore these alternate 'optimistic' estimates, given that firstly they have been published, secondly are based on a European population, and thirdly, there are scenarios where even under these risk assumptions, antibiotic prophylaxis appears not to be cost effective.
58.15	NCCHTA	80	1730-1731	Why was the starting age set at 50 years? Does a 55 year time horizon make sense here?	The aim was to follow the hypothetical cohort until the overwhelming majority of individuals are dead. A 50 year time horizon admittedly involves making some heroic assumptions, which was why an analysis based on a 10 year follow-up was also included. However, given the available data, cut off has been reduced to 50 years.
58.16	NCCHTA	98	2026-2039	Why choose to run the model with such a high risk in light of the view expressed by the GDG on page 99, lines 2075-2079?	Thankyou. The response above should address this question.
58.17	NCCHTA	General point 1		My first general point concerns the terminology used in the cost-effectiveness analysis (CEA) and the presentation of the CEA results.	See below.
58.18	NCCHTA	General point 1		Does it make sense to compare strategies for local or no anaesthetic with those for general anaesthetic? If it does not, then Tables 18a, 18b, 19a and 19b should be split into 2, in which strategies 1, 2 and 5 are compared with each other and no antibiotic, and strategies 3-8 are compared to each other and no antibiotic.	As you correctly allude to, different subgroups of patients would be selected for different strategies. For example, those patients with a known allergy to penicillin undergoing a dental procedure requiring only local anaesthesia would receive oral clindamycin, according to the

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				<p>recommendations in BNF 54. Dental procedures may need to be undertaken under general anaesthesia, for example due to severe disability: under these circumstances, strategies 3 to 8 become relevant. For these reasons therefore, all strategies will be compared to a no prophylaxis option.</p>
58.19	NCCHTA	General point 1	<p>Despite labelling the cost-effective ratios as average, they would appear to be incremental cost-effectiveness ratios (ICERs) calculated relative to no antibiotic. A correctly performed incremental analysis would present ICERs for interventions compared to the next most efficient intervention (as indicated by the authors themselves on page 73 lines 1653-1654 where it is stated that the antibiotic prophylaxis strategies were compared with each other). Restricting the comparisons to those indicated above, strategies 6 and 7 in Tables 18a, 18b 19a and 19b are dominated by strategy 8 (both more costly, but no more effective). There may also be implications for the cost-effectiveness ratios presented in tables 20 and 21, although I cannot check this due to a lack of detail presented.</p>	<p>Thankyou, an error in terminology was made and this has now been corrected.</p>
58.20	NCCHTA	General point 1	<p>If it does make sense to compare all 8 strategies with one another, then all antibiotic strategies except strategy 2 are dominated. The misuse of terminology would seem to stem from Agha et al.. This raises questions (at least to me) regarding the competence of the evaluation performed by Agha et al. (this may be particularly relevant as the model used by the authors in this report is taken from Agha et al.).</p>	<p>See response above</p> <p>The error in terminology was ours. The Agha et al evaluation provided a useful starting point, for the present analysis.</p>
58.21	NCCHTA	General point 1		
58.22	NCCHTA	General point 1	<p>A further point on incremental analysis concerns the authors' claims to have performed such an analysis (page 118), the results of which are reported Tables 22 and 23 on pages 95 and 96. I'm afraid I cannot follow what they have done here.</p>	<p>See above response – the terminology has now been corrects.</p>
58.23	NCCHTA	General point 2	<p>My second general point concerns the sensitivity analysis conducted by the authors. It appears that only univariate analysis has been conducted. The accepted norm for sensitivity analyses in CEAs such as that reported here is probabilistic sensitivity analysis (PSA). In view of this, the authors should provide a justification of why they have not performed a PSA and why they believe a univariate analysis</p>	<p>The aim of the modelling work was to do something very simple and yet potentially informative. Given the paucity of data it's not clear that anything more sophisticated than deterministic</p>

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		<p>will suffice. The authors should also provide stronger justification for which variables they have chosen to include in the sensitivity analysis. In particular, why have the health state utility weights not been varied and why have so many of the cost parameters remained fixed? The reason I have singled these out for comment is that the results of the ICER analysis suggest that the ICERs are very sensitive to changes in these parameters. The differences in QALYs (ΔE) are very small. Taking as an example the results in Table 17, ΔE is occurring at the 5th decimal place. For a ΔE of 0.00002406 (the actual ΔE in this case), a change in the cost difference (ΔC) of £1 has a £41,563 impact on the ICER. Surely, these parameters should be subjected to sensitivity analysis (and ideally a PSA).</p>	<p>sensitivity analyses are necessary, notwithstanding their limitations. However, the revised text will include more extensive sensitivity analyses. The most important parameters seem to be the risk of developing IE, antibiotic efficacy, the level of antibiotic side effects (non fatal and fatal), and the probability of death following acute IE.</p>
<p>58.24 NCCHTA</p>	<p>General point 2</p>	<p>Another parameter around which there would seem to be considerable uncertainty (page 80, lines 1732-1744) and which seems to be a potentially important factor in determining cost-effectiveness is the effectiveness of the antibiotic strategies. I would like to see the effects of differing assumptions on the <i>relative</i> effectiveness of the antibiotics on the results.</p>	<p>There was no evidence to suggest that antibiotic efficacy/effectiveness would differ between the strategies and it is therefore unclear how exploring differing assumption on their relative effects would inform decision making.</p>
<p>58.25 NCCHTA</p>	<p>General point 3</p>	<p>My third general point concerns the strategies included in the modelling. The authors state the strategies are from the BNF 54 (page 73) which is fine. However, I am unconvinced it makes sense to compare all 8 strategies against each as if they are substitutes for one another, which is what I think the authors have done. In an attempt to illustrate my point, let us consider strategies 1, 2 and 5 for dental procedures under local or no anaesthesia. As set out on page 76 (lines 1681-1683) for each strategy the authors model 10 million patients. My understanding of what the authors have done is that for each strategy they have modelled the impact of 10 million patients having that strategy – so for example, with strategy 1, all 10 million patients receive oral amoxicillin 3g 1 hour before the procedure. The cost and QALY impacts of this are then estimated from the model to produce a baseline estimate of the cost-effectiveness ratio for strategy 1. This procedure is then repeated for strategies 2 and 5. If this is indeed what the authors have done, then I have reservations about it reflecting the reality of prophylaxis treatment decisions. Rather than treat strategies 1, 2 and 5 as independent, I believe it would make more sense to merge them into a single strategy for procedures under local or no anaesthetic. In a cohort of 10 million people, we would know something about these people which would allow us to determine which strategy we believe</p>	<p>See response above. For simplicity it was not considered necessary to explore combined strategies. In addition, the revised base case analysis now assumes that the risk of antibiotic side effects (fatal and non fatal) is zero in all cases. It is not clear how many individuals would have an unknown allergy to penicillin, and consequently the risk of fatal anaphylaxis was varied between 0.9 and 40 per million in sensitivity analyses. The impact of non-fatal allergic reactions was also explored in sensitivity analyses.</p>

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					is most appropriate. The combined strategy would be something like: default to strategy 1 unless the patient: has a known allergy to penicillin in which case they would follow strategy 2; or the patient has previous endocarditis, in which case they would follow strategy 5. The cost-effectiveness of this combined strategy would then be estimated relative to no antibiotic. One potentially significant impact of this would be to reduce the incidence of anaphylaxis by virtue of the fact we are able to select out those patient who have a known allergy to penicillin (which is surely what happens in the real world).	
58.26	NCCHTA		General point 3		A similar combined strategy for dental procedures under general anaesthesia should be developed from strategies 3-8, which should then be compared with no antibiotic.	See above
58.27	NCCHTA		General point 3		Another possibility that has come to mind is a strategy involving penicillin allergy tests. Is this feasible (or at least feasible enough to be considered in the modelling)?	Ideally, the impact of relevant diagnostic technologies should be explored in any analysis, but in this instance it was not considered necessary or feasible. Thank you.
58.28	NCCHTA	Full			1.1 Are there any important ways in which the work has not fulfilled the declared intentions of the NICE guideline (compared to its scope – attached) - Seems fine.	
59.0	Neonatal & Paediatric Pharmacists Group (NPPG)	Full	General		These guidelines are a logical and well thought out move forward. The use of prophylaxis for dental cases has been questioned for years. This brings together the evidence and makes the approach to endocarditis more logical.	Thank you.
60	Newcastle upon Tyne NHS Hospitals Trust				This organisation was approached but did not respond.	
61	NHS Plus				This organisation was approached but did not respond.	
62	NHS Quality Improvement Scotland				This organisation was approached but did not respond.	
63	NHS South Central vascular Network				This organisation was approached but did not respond.	
64	North and East Yorkshire & Northern Lincolnshire Cardiac Network				This organisation was approached but did not respond.	
65	North Tees PCT				This organisation was approached but did not respond.	
66.0	North West London Cardiac Network	Full	General		Excellent document overall but see specific comments from clinical cardiology and cardiac surgery colleagues below.	Thank you.
66.1	North West London Cardiac Network	Full	P5 P6	144 181	It feels wrong to stop advising antibiotic prophylaxis in high risk groups undergoing invasive dental procedures, even when the evidence of benefit is equivocal. Successful surgical repair or	Thank you. The GDG reconsidered and defined the cardiac conditions

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66.2	North West London Cardiac Network	P5	144	percutaneous closure of PDA (patent ductus arteriosus) may leave a residual shunt and thus a continuing risk of IE Patients at high risk of IE should have prophylaxis for dental procedures. Recently saw a large vegetation on a device 3 months after “successful” ASD (atrial septal defect) closure.	which should assist with the clarity Thank you.
66.3	North West London Cardiac Network	P5 P6	144 178	Patients at high risk of IE (especially prosthetic valve patients) should have prophylaxis for dental procedures on a precautionary principle because of the high mortality if they get IE.	Thank you. The high mortality rate with IE has been acknowledged in this guideline however the risk of anaphylaxis due to antibiotic use must also be noted. The GDG considered the clinical and cost effectiveness evidence and expert viewpoints and developed the recommendations.
66.4	North West London Cardiac Network	P5 P6	144 178	A new guideline has just been published in AHA. Prophylaxis is required for prosthetic valve patients. The NICE panel should have a further look at it (mentioned but differences in this recommendation not explained).	Thank you. We have reviewed the AHA guideline in the guideline and explain in the relevant evidence to recommendations section why the guideline does not stratify cardiac risk into high, medium and low.
66.5	North West London Cardiac Network	P5	144	Unhappy about not recommending prophylaxis for high risk patients undergoing dental procedures. Infective endocarditis is such a dangerous condition with high mortality and morbidity that unless the evidence is CONCLUSIVE that antibiotic prophylaxis is ineffective we should continue to use it.	Thank you. The high mortality rate with IE has been acknowledged in this guideline; however the risk of anaphylaxis due to antibiotic use must also be considered in assessing both benefit and risk. The GDG explicitly considered the clinical and cost effectiveness evidence and expert viewpoints and developed the recommendations based on this evidence.
66.6	North West London Cardiac Network	P5 P7	163 210	There is also the possibility that the guideline as written suggests there are a whole raft of investigations and operations that do not need antibiotic cover regardless of the underlying pathology (ie whether it is infective or not). Thus any gynae procedure is thought to be low risk but it is not low risk if there is infection involved. The	Thank you. We have now addressed this issue in the revised recommendations – the use of prophylaxis for GI and GU (including gynaecological)

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				wording ought to make that clear by saying “any non-infected gynae procedure”.	procedures is not recommended.
67	OCD-Today			This organisation was approached but did not respond.	
68.0	Papworth Hospital NHS Trust	full	general	The guideline fails to mention other types of surgery, and this will be questioned and may make implementation in practice very difficult. It should mention abdominal surgery (prophylaxis required), thoracic surgery (required), orthopaedic surgery (?required), ophthalmic surgery etc. THIS IS VERY IMPORTANT	Thank you. The guideline scope clearly sets out which sites for interventional procedures are, and are not, included in the guideline. Thoracic, orthopaedic and ophthalmic surgeries are outside the scope of this guideline.
69	Peninsula Clinical Managed Cardiac Network			This organisation was approached but did not respond.	
70	PERIGON Healthcare Ltd			This organisation was approached but did not respond.	
71	PRIMIS+			This organisation was approached but did not respond.	
72	Royal Brompton & Harefield NHS Trust			This organisation was approached but did not respond.	
73	Royal College of General Practitioners			This organisation was approached but did not respond.	
74	Royal College of Midwives			This organisation was approached but did not respond.	
75.0	Royal College of Nursing		General	The RCN welcomes this guideline. It will help clarify aspects of treatment for health professionals.	Thank you.
76	Royal College of Obstetricians and Gynaecologists			This organisation was approached but did not respond.	
77.0	Royal College of Paediatrics and Child Health	Full	General	We believe that the guidelines present a well argued and balanced overview of the need (or otherwise) for antibiotic prophylaxis against infective endocarditis, and have defined carefully the circumstances in which it should, or need not, be used. We think the guideline presents a cogent argument after painstaking analysis of numerous sources of data. We believe the recommendations will come as a surprise to many, if not most health professionals, as they fly in the face of the perceived truth which has been prevalent for many years. It will take a great deal to change the beliefs and behaviours of parents and doctors, for example to not prescribe antibiotics for a child with a VSD having dental extractions, and to overcome fears and concerns from both	Thank you. The GDG, the NICE editorial team, the NICE Patient and Public Involvement Group (PPIP) and the NICE implementation team are working together to ensure the maximum clarity of guidance and support for

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					groups. There will need to be a strong campaign of information and reassurance when the guidelines are introduced that it is safe and acceptable not to give antibiotics. Is it possible that, if IE prophylaxis is only used in a small group of conditions, we will see an increase in the number of cases of IE? We would urge a programme of surveillance to ensure that there is no increase in cases of IE compared to the current standard where prophylaxis is widely undertaken. This will clearly not be the remit of NICE. This organisation was approached but did not respond.	implementation. The GDG agrees with the need to audit any impact of this guideline.
78	Royal College of Pathologists				This organisation was approached but did not respond.	
79	Royal College of Physicians of London				This organisation was approached but did not respond.	
80	Royal Pharmaceutical Society of Great Britain				This organisation was approached but did not respond.	
81	SACAR				This organisation was approached but did not respond.	
82	Sandwell PCT				This organisation was approached but did not respond.	
83	Scottish Intercollegiate Guidelines Network (SIGN)				This organisation was approached but did not respond.	
84	Scottish Oral Health Group				This organisation was approached but did not respond.	
85	Sheffield PCT				This organisation was approached but did not respond.	
86	Sheffield Teaching Hospitals NHS Foundation Trust				This organisation was approached but did not respond.	
87	Social Care Institute for Excellence (SCIE)				This organisation was approached but did not respond.	
88	Stockport PCT				This organisation was approached but did not respond.	
89	Sussex Heart Network				This organisation was approached but did not respond.	
90	The British Society Of Paediatric Dentistry	Full version	General		Comments from members of the Society have been favourable. Only concerns expressed are around the maintenance and achievement of good oral health in the light of an apparent lack of availability of good preventive care in the modern NHS. Patient and professional education is likely to need time and financial resources.	Thank you. The GDG, the NICE editorial team, the NICE Patient and Public Involvement Group (PPIP) and the NICE implementation team are working together to ensure the maximum clarity of guidance and support for implementation.
91	The Phoenix Partnership				This organisation was approached but did not respond.	
92	UK Clinical Pharmacy Association				This organisation was approached but did not respond.	
93	University Hospital Birmingham				This organisation was approached but did not respond.	
94.0	University Hospital Birmingham NHS Foundation Trust	Full	55	1229	Barium enemas are generally and outpatient procedure and IV antibiotics are impractical routinely. This is reflected by the	Thank you.

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				withdrawal in 2001 of the Royal College of Radiologist’s advisory document BFCR(99)7 which had recommended antibiotics should be used. This was supported by the British Society for Antimicrobial Chemotherapy and the Royal College of Pathologists.	The GDG has reconsidered the evidence in relation to GI procedures which clarifies this point. GI and GU procedures do not require AB prophylaxis solely to prevent IE.
95	University of North Tees and Hartlepool NHS Trust			This organisation was approached but did not respond.	
96	Welsh Assembly Government			This organisation was approached but did not respond.	
97	Welsh Scientific Advisory Committee (WSAC)			This organisation was approached but did not respond.	
98	West Yorkshire Cardiac Network			This organisation was approached but did not respond.	
99	Western Cheshire Primary Care Trust			This organisation was approached but did not respond.	
100	WhippsCross Hospital NHS Trust			This organisation was approached but did not respond.	
101	Wiltshire PCT			This organisation was approached but did not respond.	
102	York NHS Trust			This organisation was approached but did not respond.	
105	Guys and St Thomas’ Hospital	Full version	General	<p>Do these guidelines suggest that all patients undergoing ERCP, flexible sigmoidoscopy, colonoscopy and oesophageal endotherapy should undergo echocardiography prior to the procedure?</p> <p>Clinical examination alone is insensitive in the detection of acquired valvular heart disease, and in many patients the clinical urgency of the procedure does not allow any time for the echocardiogram to be performed.</p> <p>If an echocardiogram is required 1-2% of the population have endoscopic procedures per year- which will increase with colorectal cancer screening. All these patients will require echocardiography</p>	<p>Thank you.</p> <p>The GDG has reconsidered the evidence in relation to GI and GU procedures and the guideline now recommends that prophylaxis for GI and GU procedures should not be given.</p> <p>The guideline scope covers those with known cardiac lesions. It is outside the scope of the guideline to advise or review the evidence on work up of patients prior to the procedure to screen for heart lesions using echocardiography.</p>
106	Southport and Ormskirk NHS Trust	Full	General	I feel that in the absence of evidence to the contrary (RCTs) antibiotic prophylaxis should be maintained for traditionally considered at risk cardiac conditions. The British Cardiac Society are	Thank you. The lack of RCT evidence in this area is acknowledged; however, the

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					not at all supportive of these new guidelines and as a practicing clinician Having seen one very serious endocarditis case from failed antibiotic prophylaxis I remain of the opinion that the simple preventative measures that we all widely practice should be maintained. I feel that NICE have exposed clinicians and patients to the risks of endocarditis by rather blindly applying opinion rather than evidence. If these guidelines are widely adopted perhaps the only true proof of effect will be acquired by rising or falling incidence and mortality rates.	GDG considered the clinical and cost effectiveness evidence and expert viewpoints and developed the recommendations based on the evidence. The GDG agrees with the need to audit any impact of this guideline
107.0	Manchester Heart Centre, Manchester Royal Infirmary	Full Version	Page7	232-237	The draft groups all structural congenital heart patients apart from 3 simple conditions (two of them treated) as a single entity. While the simplicity of this approach is quite understandable it does not take cognizance of the fact that is a very varied group of patients ranging from patients having very complex conditions who have undergone multiple surgeries to patients with simple conditions under clinical monitoring only. The more complex patients are likely to have a higher risk of endocarditis. One simple classification of higher risk congenital patients could be as follows: 1. Patients with cyanotic congenital heart disease with or without palliative shunts 2. Patients with single ventricular physiology and/or with a Fontan type of circulation 2. Patients with prosthetic heart valves or valved conduits and patients with aortic valve disease 3. All patients with unrepaired structural heart disease (albeit haemodynamically insignificant) excluding isolated secundum atrial septal defect and pulmonary stenosis. The uses of such a classification are detailed in the next section.	Thank you. As detailed in the relevant evidence to recommendations section in the full guideline [insert numbering], the GDG considered the potential confusion which can arise from a detailed stratification into different risk groups, and given the difficulties in relative risk definition the GDG decided that a simple classification of conditions into either at risk or not at risk groups is both supported by the available evidence and would help with clarity.
107.1	Manchester Heart Centre, Manchester Royal Infirmary	Full version	54	1212-4	There is no class 1 evidence (double blind, placebo controlled, RCT data) to show that antibiotic prophylaxis is of no value in patients at risk for IE undergoing dental procedures. Much of the evidence recorded in the guideline uses bactremia as a surrogate for potential endocarditis. While bactremia is an important contributor the reaction of the host endothelium is also an important factor in the establishment of infection. Adult patients with congenital heart disease may have potential endothelial dysfunction. Until further audit data is available that there is no increased incidence of IE in the non higher risk group, the higher risk patients identified in the previous comment should receive antibiotic prophylaxis for dental procedures since IE can be potentially life threatening in this group with a high morbidity.	Thank you. The GDG considered the clinical and cost effectiveness evidence and expert viewpoints and developed the recommendations based on the evidence.

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107.2	Manchester Heart Centre, Manchester Royal Infirmary	Full version	70	1576-80	<p>While there is no accurate data to show NNT to prevent an episode of endocarditis following dental treatment the study by Agha et.al suggests it may be cost-effective for persons with moderate or high risk of developing endocarditis. In keeping with this it would be prudent to continue prophylaxis for dental procedures for this high risk group until further data is available.</p>	<p>Based on GDG opinion regarding the risk of developing IE following a dental procedure, the analysis indicates that all antibiotic strategies are not cost-effective. This GDG considered it biologically implausible that a single dental procedure would lead to a greater risk of IE than regular tooth-brushing. The economic analysis has been revised so that the base case estimate of risk is substantially less than that used by Agha et al. The estimates derived from the work of Duval et al (and Agha et al) have, however, been explored in sensitivity analyses</p>
109	The Cardiothoracic Centre Liverpool	Full and appendices	General		<p>Response to Draft Document by NICE on “Antimicrobial prophylaxis against infective endocarditis in adults and children undergoing interventional procedures”</p> <p>This document is so extremely unwieldy and voluminous that it is virtually unreadable. As a draft guideline it is very disorganised and unclear and should be an embarrassment to those associated with it. The Appendices unbelievably total 228 pages and the whole document consists of almost 350 pages. It is pretty unlikely that it has been written by anyone with any clinical experience of managing patients with infective endocarditis (IE) or with experience of writing papers for publication.</p> <p>There are numerous summaries of data from the literature presented which associate IE with various dental, surgical and interventional procedures but conclusions are then illogically drawn that patients “at risk” do not need to receive antibiotic prophylaxis (ABP). The conclusions are not supported by evidence from the literature but are simply the opinion of those responsible for this misleading document. The authors try to justify their conclusions by quoting estimates of risk for patients with particular cardiac defects, and estimates of risk for certain procedures. This is a meaningless exercise and such estimates cannot be accepted as the science on which to base advice which is illogical.</p>	<p>Thank you.</p> <p>This guideline follows the accepted format for NICE short clinical guidelines. The attachment of the appendices allows for clarity of the evidence considered by the GDG.</p> <p>The linking evidence to recommendations sections of this guideline describe the means by which the evidence presented and the expert viewpoints were developed into the recommendations which were agreed by the GDG. With regard to this specific point on cardiac risk, we clearly set out why this is an appropriate approach.</p>

Pathology has taught us that IE cannot occur without bacteraemia and a susceptible endocardial lesion or intravascular foreign body in-situ. The consequences of this are ignored by the authors because randomised clinical trials do not exist to support the case for antibiotic prophylaxis (ABP). I agree that the conditions that need to exist for an endocardial vegetation to develop in a patient include a susceptible cardiac lesion with endocardium that is in such a state to enable bacteria to adhere to it, bacteraemia itself sufficient to allow seeding of the endocardium and the ability of the bacteria to resist the body's immune defense mechanisms to eradicate the infection. This understanding explains why not every patient "at risk" who undergoes a bacteraemia-producing procedure goes on to develop IE and why those who do, present at various intervals from the interventional procedure. Indeed, cardiac surgeons and pathologists notice areas of healed infected areas on the endocardium of patients with cardiac structural disease who have not had a clinical presentation of acute IE. To recommend not trying to eradicate or minimise bacteraemia associated with these procedures in patients "at-risk", especially when thousands of case reports have been published in the literature linking them with IE is in my view illogical and perverse. The authors have chosen to ignore such reports and their significance. In the UK, 83.3% of cardiac specialists believe that case reports of bacteraemia associated with invasive procedures constitute "evidence" to support the need to try and prevent IE associated with those procedures in cardiac patients at risk. Moreover, 74.6% felt that case reports of IE associated with invasive/interventional procedures constituted "evidence" sufficient enough to warrant ABP for those patients at risk who were undergoing those procedures.¹ The value and importance of case reports in helping us to understand disease mechanisms, pathogenesis and treatment strategies should not be underestimated and thankfully most editors of peer-review journals still take this view. There is also evidence in the literature that bacteraemia may persist for > 1 hour after procedures.² Although I accept that ABP will not be successful all the time there is evidence that bacteraemia can be abolished or minimised by ABP³ - but this too has been conveniently ignored. We all have to accept that although day-to-day tasks such as eating and tooth brushing are associated with bacteraemia, it is impractical to use ABP for these events even though occasionally these episodes may indeed be responsible for IE in patients at risk. We must therefore strongly support the need for

In the introduction section to the guideline we discuss current thinking on the pathogenesis of IE. Underlying these principles is the assumption that antibiotic prophylaxis is effective in humans for the prevention of IE in dental and non-dental procedures. However, this assumption is now considered by many researchers in the field to be not proven (Prendergast, 2006 54 /id) and this has led to calls to significantly reduce the use of antibiotic prophylaxis in this setting. This shift in opinion is reflected in national and international clinical guidelines for prophylaxis against infective endocarditis.

We recognise that this guideline represents a significant shift in current UK practice. The GDG, the NICE editorial team, the NICE Patient and Public Involvement Group (PPIP) and the NICE implementation team are working together to ensure the maximum clarity of guidance and support for implementation.

We note in the evidence reviews that the evidence base is often limited but we have always used the highest level of available evidence. Thus we have placed appropriate emphasis on the small number of applicable controlled observational studies

good dental hygiene and regular dental care for such patients in order to try and minimise their risk of IE.

In my opinion, patients will be harmed if these guidelines are taken up by dental, medical and surgical colleagues on recommendations from NICE. Moreover, such advice would be against the views of the majority of practising cardiologists and cardiac surgeons in the UK who are responsible for managing those unfortunate enough to develop IE as a result of failed preventative measures in patients who are particularly susceptible. In a survey of cardiologists and cardiac surgeons in the UK, 94.2% felt that patients “at risk” of IE should receive ABP prior to dental procedures in an attempt to try and prevent IE.

Sadly, there is no mention in this draft document of the devastating consequences of IE – the serious systemic upset, the devastating vasculitic and embolic extracardiac complications and the destructive cardiac effects that result in the need for urgent or emergency cardiac surgery in patients who are very sick. The prolonged in-hospital stay – much of which will be in intensive care, the prolonged need for high-dose, expensive parenteral antibiotics, serial haematological, biochemical, microbiological and cardiac investigations and the input required from other specialists to deal with the complications of IE are also ignored. The long-lasting devastating effects of the embolic complications particularly those associated with the CNS such as embolic/haemorrhagic stroke and cerebral abscess including hemiplegia, paraplegia, aphasia and visual loss are disastrous in patients of any age but particularly in the younger patient who has a career and family responsibilities which are wiped out in an instance.

The opening sentence of the document “This guideline offers best practice advice on antimicrobial prophylaxis against infective endocarditis before an interventional procedure” cannot be further from the truth.

References

1. Ramsdale DR. Against the motion: “Prophylactic antibiotic therapy to prevent endocarditis after dental procedures is unnecessary and inappropriate”. BCS Annual Scientific Conference, Glasgow. June 6th 2007.
2. Tomas I, Alvarez M, Limeres J, Potel C, Medina J, Diz P. Prevalence, duration and aetiology of bacteraemia following dental

and large case series.

In the introduction and section of adverse outcomes of people with IE we clearly document the consequences of IE and the considerable rates of mortality and morbidity associated with this condition.

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					extractions. Oral Dis 2007;13:56-62.	
112.0	British Association for the Study of Community Dentistry	Full	General		3. 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. BASCD welcomes the work undertaken by NICE in producing guidelines in this controversial area. We accept the evidence-based recommendation against the routine use of antibiotics or chlorhexidine in people considered at risk for IE. We are particularly pleased that there is now a clear and consistent message, as previously there was discrepancy between the scientific literature and official guidance.	Thank you.
112.1	British Association for the Study of Community Dentistry	Full	7	218	The public are likely to be concerned and/or confused by changes to the regimes they may have followed for many years. There is a need for a publicity campaign to explain the new guidelines. This would be particularly effective if the changes were endorsed by cardiologists and/or their representative body	Thank you. The GDG, the NICE editorial team and the NICE implementation team are working together to ensure the maximum clarity of guidance and support for implementation. The NICE implementation team will produce implementation tools to assist both professionals and patients.
112.2	British Association for the Study of Community Dentistry	Full	13	365	When healthcare professionals wish to apply their own judgement in individual cases, and this judgement is to vary from the NICE recommendations, they need to give very clear reasons why antibiotic cover has to be given, or people will become confused and uncertain again. 3As dentists, we are particularly concerned that some cardiologists will inform their patients that they should continue to receive AB cover for dental treatment without giving any evidenced reasons.	Thank you. The GDG, the NICE editorial team and the NICE implementation team are working together to ensure the maximum clarity of guidance and support for implementation.
112.3	British Association for the Study of Community Dentistry	Full	16	451	Repaired patent ductus arteriosus is listed as a condition regarded as being at increased risk of a person developing IE. This is incorrect, this condition does not give rise to increased risk, as shown in Table 1 page 18.	Thank you. The GDG have reconsidered the evidence and re-defined the cardiac conditions which should assist with the clarity and corrects this point.
112.4	British Association for the Study of Community Dentistry	Full	49	1068	We accept the evidence that using an electric toothbrush does double the bacteraemia compared with using a manual toothbrush. However, we question the significance of separating the two techniques (especially as the recommendation is not to use AB cover in either case). We have concerns that in the public domain this	Thank you. It should be noted that the relevant recommendation does not advocate a particular method for toothbrushing.

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112.5	British Association for the Study of Community Dentistry	Full	81	1762	<p>difference would give rise to concern, and lead to people with reduced manual dexterity to desist from using an electric brush, reverting to using a manual one. This would be likely to lead to a reduction in their oral hygiene, and a consequent increase in risk. The drug named is Ampicillin. However, in line 1865 the drug named is Amoxicillin, and Amoxicillin is also the name given in Table 16 on page 87, Table 17 on page 88, and many other lines and tables subsequently. It requires clarification which drug is being considered.</p>	<p>Based on the recommendations in BNF 54, the relevant antibiotic for the economic analysis is amoxicillin (a derivative of ampicillin).</p>
113.0	Children’s Heart Foundation	Full Version	General	<p>The Children’s Heart Federation (CHF) welcomes the Guidelines. We hope their publication will address the confusion currently being experienced by some parents/carers of children with congenital heart disease who are being given conflicting advice by their cardiologist and dentist.</p>	<p>Thank you. The GDG, the NICE editorial team, the NICE Patient and Public Involvement Group (PPIP) and the NICE implementation team are working together to ensure the maximum clarity of guidance and support for implementation.</p>	
113.1	Children’s Heart Foundation	Full Version	General	<p>We appreciate that the full guidelines are written for clinicians and have therefore not been drafted with patients/parents/carers in mind. However, we understand that an explanation of the new guidelines will be written specifically for patients. We hope that information will:</p> <ul style="list-style-type: none"> o Clarify the groups of patients who have the greatest risk of developing infective endocarditis (IE). o Clearly specify which medical procedures may cause IE. o Explain why dental treatment is no longer considered to be a cause of IE. o Explain what actions patients/parents/carers can take to minimise the risk of developing IE. o Outline the symptoms of IE, so that patients/parents/carers experiencing or noticing such symptoms can alert their healthcare workers – particularly those working in a primary care setting who, because of the rarity IE, may not consider such a diagnosis. o Explain the difference between prescribing antibiotics for prophylaxis and for dealing with an actual infection or with a patient who has neutropaenia. 	<p>Thank you. We have revised the relevant recommendations to better address these issues.</p> <p>The GDG, the NICE editorial team, the NICE Patient and Public Involvement Group (PPIP) and the NICE implementation team are working together to ensure the maximum clarity of guidance and support for implementation.</p> <p>NICE also produces an ‘Understanding NICE Guidance’ and a ‘Quick Reference Guide’ to assist with the clarity and ease of use of NICE guidelines.</p>	
113.2	Children’s Heart Foundation	Full Version	General	<p>Children’s Heart Federation also urges NICE to work closely with the relevant professional disciplines, particularly congenital cardiology and dentistry to ensure that, without compromising clinical</p>	<p>Thank you. The GDG, the NICE editorial team, the NICE Patient and Public Involvement Group</p>	

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				judgement, they provide patients/parents/carers with non-conflicting advice.	(PPIP) and the NICE implementation team are working together to ensure the maximum clarity of guidance and support for implementation. Thank you. The GDG agrees with the need to audit any impact of this guideline and this is noted in the research recommendations in this guideline.
113.3	Children’s Heart Foundation	Full Version	General	We are aware that IE is a rare condition but it is potentially devastating for anyone contracting it. We would therefore urge NICE to recommend that IE becomes a notifiable disease. This would enable an accurate register of case numbers to be maintained which could be monitored to see whether, following the implantation of these guidelines, there is an increase in the number of cases of IE. If such an increase did occur, it would obviously trigger an early review of the guidelines. If it is not possible to make IE a notifiable disease, we would urge that NICE find an alternative mechanism such as an additional question within the data collection process for the Central Cardiac Audit Database for the National Heart Disease Audits.	
113.4	Children’s Heart Foundation	Full Version	General	The Children’s Heart Federation (CHF) welcomes the Guidelines. We hope their publication will address the confusion currently being experienced by some parents/carers of children with congenital heart disease who are being given conflicting advice by their cardiologist and dentist.	Thank you. The GDG, the NICE editorial team, the NICE Patient and Public Involvement Group (PPIP) and the NICE implementation team are working together to ensure the maximum clarity of guidance and support for implementation. Thank you. We have revised the relevant recommendations to better address these issues.
113.5	Children’s Heart Foundation	Full Version	General	We appreciate that the full guidelines are written for clinicians and have therefore not been drafted with patients/parents/carers in mind. However, we understand that an explanation of the new guidelines will be written specifically for patients. We hope that information will: <ul style="list-style-type: none"> ○ Clarify the groups of patients who have the greatest risk of developing infective endocarditis (IE). ○ Clearly specify which medical procedures may cause IE. ○ Explain why dental treatment is no longer considered to be a cause of IE. ○ Explain what actions patients/parents/carers can take to minimise the risk of developing IE. ○ Outline the symptoms of IE, so that patients/parents/carers experiencing or noticing such symptoms can alert their healthcare workers – particularly those working in a primary care setting who, because of the rarity IE, may not consider such a 	The GDG, the NICE editorial team, the NICE Patient and Public Involvement Group (PPIP) and the NICE implementation team are working together to ensure the maximum clarity of guidance and support for implementation. NICE also produces an ‘Understanding NICE Guidance’ and a ‘Quick Reference Guide’ to assist with the clarity and ease of

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					<ul style="list-style-type: none"> ○ Explain the difference between prescribing antibiotics for prophylaxis and for dealing with an actual infection or with a patient who has neutropaenia. 	use of NICE guidelines.
115.0	King's College London Dental Institute at Guys, Kings and St Thomas' Hospital	Full	General		<p>The comments have been provided by members of the Working Group on the Dental Aspects of Infective Endocarditis Prophylaxis at King's College London Dental Institute.</p> <p>This Group was formed in 2004 as a response to the BCS/RCP guidelines 2004.</p> <p>It consists of senior clinicians from the four academic groupings of Clinical and Diagnostic Sciences, Craniofacial Development, Orthodontics & Microbiology, Dental Practice and Policy, and Restorative Dentistry.</p> <p>A consensus could not be reached on the draft guidelines. The following comments are representative of the Group.</p>	Thank you.
115.1	King's College London Dental Institute at Guys, Kings and St Thomas' Hospital	Full	General		Three members supported the draft guidelines	Thank you.
115.2	King's College London Dental Institute at Guys, Kings and St Thomas' Hospital	Full	General		One member supported the draft guideline , but would accept a reduction on the conditions requiring prophylaxis along the lines of the BSAC 2006 and AHA 2007 guidelines	Thank you. Previous guidelines have been acknowledged; the GDG considered the clinical and cost effectiveness evidence and expert viewpoints and developed the recommendations based on this evidence..
115.3	King's College London Dental Institute at Guys, Kings and St Thomas' Hospital	Full	7	211	<p>One member was concerned about:</p> <p>1.3.2.9 Antimicrobial regimens should be modified to cover endocarditis-causing organisms when procedures are undertaken at a site of infection or potential infection in patients at risk of IE.</p> <p>Viridans group streptococci are one of the commonest bacteria to cause IE (line 707) and found in great numbers within the oral cavity. Infection involving <i>Streptococci sp.</i> is common so is there a threshold of infection where prophylaxis is indicated? Should the recommendation specifically exclude dentally related infections?</p>	<p>Thank you.</p> <p>There is no evidence relating to there being a threshold of infection. The GDG considered that if appropriate antibiotics were being prescribed for a spreading infection, then this would cover organisms known to cause IE</p>
115.4	King's College London Dental Institute at Guys, Kings and St	Full	General		Two members were concerned that prosthetic heart valves, previous history of IE, and surgically constructed conduits and shunts were	Thank you. The GDG had considered that those with a

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	Thomas' Hospital				excluded from antibiotic prophylaxis for dental procedures. Antibiotic prophylaxis would be provided for the above patients undergoing dental procedures likely to cause a bacteraemia as outlined in the RSC/RCP 2004 guidelines. One member would also include biopsy.	previous episode of IE were covered in the groups of patients who are considered to be at risk, however the GDG has considered that for reasons of clarity those with previous IE should be specified as an at risk group The GDG considered the clinical and cost effectiveness evidence and expert viewpoints and developed recommendations based on this evidence.
115.5	King's College London Dental Institute at Guys, Kings and St Thomas' Hospital	Full	97	1992	<p>“Taking into account recurring costs of antibiotic prophylaxis, as well as its potential benefits, the model developed for this guideline appears to indicate that oral amoxicillin (strategy 1) can be highly cost effective when the risk of developing IE following a dental procedure was set at 93 per million (the Duval et al [2006] estimated risk for an individual with a prosthetic valve).”</p> <p>The risk of IE for those with a prosthetic heart valve was found to be higher (Line 532 and 1707). It also appears within the guidelines of a tacit agreement with Duval, 2006, of the increased risk of IE for unprotected at-risk dental procedures in those with a prosthetic heart valve (Line 853). If this is accepted then the sentence at Line 1992 contradicts the Recommendation number 1.3.2.2</p>	<p>Thankyou. Any contradiction has now been</p> <p>The base case risk estimate of developing IE following a dental procedure has now been substantially reduced. The estimates derived from the work of Duval et al have been explored in sensitivity analyses. . Based on GDG opinion regarding the risk of developing IE following a dental procedure, the analysis indicates that all antibiotic strategies are not cost-effective.</p>
115.6	King's College London Dental Institute at Guys, Kings and St Thomas' Hospital		7	217	<p>“Patient information and support.”</p> <p>There is a general concern that the clear and consistent information should come from one informed source. This is to avoid anxiety to patients from poor and unclear information.</p>	<p>Thank you. The GDG, the NICE editorial team and the NICE implementation team are working together to ensure the maximum clarity of guidance and support for implementation.</p>
115.7	King's College London Dental Institute at Guys, Kings and St Thomas' Hospital		7	214	<p>“1.3.2.10 The following antibiotic regime should be used as prophylaxis against IE: amoxicillin plus gentamicin or for penicillin allergic patients teicoplanin plus gentamicin.”</p>	<p>Thank you. This has been reconsidered by the GDG and with the changes developed this should be clarified</p>

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				<p>This contradicts line 1997</p> <p>“The present modelling also shows that IV administered antibiotics are not cost effective under any of the scenarios explored in the model.”</p> <p>Surely, 1.3.2.10 should be clarified to “...where oral administration is contra-indicated”?</p>	<p>The economic analysis was undertaken with respect to antibiotic prophylaxis in dental procedures. Based on GDG opinion regarding the risk of developing IE following a dental procedure, <u>all</u> antibiotic strategies are not cost-effective.</p>	
115.8	King's College London Dental Institute at Guys, Kings and St Thomas' Hospital		36	788	There is a typo in the statistics “n = 8 (51.5%)” should read “n=88 (51.5%)”	Thank you, this has been revised.
116.0	British Society of Gastroenterology	Full	14	409	This should refer to the “American Heart Association ”	Thank you, this has been revised.
116.1	British Society of Gastroenterology	Full	55	1226	<p>The Endoscopy Committee of the BSG, and several members of the society who have since commented to us, wish to challenge the specific recommendation that antibiotic prophylaxis should be administered to patients at moderate cardiac risk undergoing lower GI procedures for the following reasons:</p> <ol style="list-style-type: none"> 1) The incidence of bacteraemia following diagnostic lower GI endoscopy (for which your draft recommends prophylaxis) is no higher than that for diagnostic gastroscopy (for which prophylaxis is not recommended). Nelson (Gastrointest Endosc 2003; 57: 546) quotes a mean bacteraemia rate following colonoscopy of only 4.4%. Lower GI procedures are being unfairly targeted, based on a perception of their being “dirty” rather than an evidence base. 2) “Lower GI procedures” are not defined. By implication the guideline applies not only to colonoscopy and flexible sigmoidoscopy, but also to barium enema X ray (BE), rigid sigmoidoscopy and rectal examinations. Logic would suggest that healthcare professionals would be discouraged from performing rigid sigmoidoscopy, rectal examination and suppository or enema administration without having listened to the heart sounds first. 3) Thousands of lower GI procedures are performed per year in a direct access setting by nurse endoscopists. Whilst patients with a history of heart valve replacement are readily identified in a pre-assessment interview, those without documentation of 	<p>Thank you.</p> <p>The GDG has reconsidered the evidence in relation to GI and GU procedures and the guideline now recommends that prophylaxis solely to prevent IE, for GI and GU procedures should not be given.</p> <p>We therefore agree with the BSG endoscopy committee’s specific point.</p> <p>We would also note that the revised recommendations on GI and GU procedures are now consistent with the American Heart Association (2007) guideline.</p>

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- 4) The guideline, despite its poor evidence base, will open the way for litigation by patients with IE.
- 5) The variation in the literature between time from lower GI procedure to IE diagnosis often means that the cause and effect relationship is unclear.
- 6) In our recent review of the cases reported in the literature for the BSG we identified just 13 cases of IE linked to lower GI procedures, only one of which was due to enterococcus (Postgrad Med J 2004; 80: 619-20).
- 7) The risk/benefit equation clearly undermines the case in favour of IE prophylaxis for lower GI procedures. Given that 2% of the population undergo colonoscopy or sigmoidoscopy per year, and that 10% of these potentially have a cardiac risk factor for IE, 120,000 patients in the UK will need IE prophylaxis for this indication each year. Given the working hypothesis in the guideline that 1 patient in 50,000 will die from anaphylaxis from IV amoxicillin, implementation of the guideline would result in 11 patients dying every 5 years.
- 8) If they were linked, parallel exponential rises in both lower GI procedures and the incidence of related cases of IE would have been expected. This has not occurred, even with the wide use of bowel screening by means of lower GI endoscopy in the USA and elsewhere.
- 9) This particular recommendation is so radically different from that of the American Heart Association that its credibility in the international community will be lacking.

116.2	British Society of Gastroenterology	Full	108	2322	Spelling - Dr Miles Allison	Thank you, this has been corrected.
116.3	British Society of Gastroenterology	Full	General		This guidance predominantly focuses on IE following dental procedures - an association that has been recognized for over 70 years. The Guideline Development Group (GDG) has considered the evidence and proposes that the lifetime risk of IE from everyday living (toothbrushing, etc) far outweighs the lifetime risk for dental procedures. The committee therefore recommends that antibiotic prophylaxis before dental procedures in at risk people is illogical and should be abandoned.	Thank you.

In contrast, the GDG proposes an extension in the guidance for antibiotic prophylaxis before a number of endoscopic procedures, through the inclusion of other groups in the at risk population, including those with acquired valvular disease. To those from the endoscopy community, this extension seems illogical and is contrary to the view taken in America after consideration of the same evidence base.

The argument suggested by the GDG is that enterococcal bacteraemia has not been shown to occur from everyday living activities, though there have been no studies addressing this. Enterococcal endocarditis accounts for 10% of cases of IE, and in some surveys this may be as high as 40% (personal communication at NICE implementation meeting). There is no suggestion that these cases arise from procedural interventions, indicating that enterococcal endocarditis and bacteraemia do occur spontaneously – it is presumed from bacteria translocating across the GI or GU tracts. Strom et al (2000) reviewed 379 cases of IE and found no association with GI endoscopic procedures. A small but statistically significant number of patients had undergone a prior BE. Case note review indicated that the BE examinations were performed to investigate a non-specific illness which was later found to be IE and the authors concluded that BE was not causally related. Furthermore, only 3 out of 38 cases of IE following BE were related to GI organisms.

McDonald et al (2005) reviewed 107 cases of enterococcal endocarditis and found no association with GI procedures – and similar results were found in studies from France and the Netherlands (ref NICE draft).

The rate of bacteraemia following colonoscopy is only 4%, contrasting with a reported rate of 78% following toothbrushing with an electric toothbrush.

We are not aware of any reports of IE following ERCP.

The BSG endoscopy committee believe that there is no good evidence supporting the administration of antibiotics before endoscopic procedures solely to prevent IE, even in at risk patients. The same logic applied to dental procedures should also be applied to endoscopic procedures. We would recommend that the

The GDG has reconsidered the evidence in relation to GI and GU procedures and the guideline now recommends that prophylaxis solely to prevent IE for GI and GU procedures should not be given.

We note these points relating to enterococcal bacteraemia and have re-written the relevant evidence to recommendations section.

We therefore agree with the BSG endoscopy committee that **“there is no good evidence supporting the administration of antibiotics before endoscopic procedures solely to prevent IE, even in at risk patients.”**

We would note that the revised recommendations on GI and GU procedures are now consistent with the American Heart Association (2007) guideline.

PROPHYLAXIS AGAINST INFECTIVE ENDOCARDITIS draft guideline consultation – stakeholder comments and responses

NICE PIE Guideline Development Group follows the lead of the American Heart Association, soon to be endorsed by the American Society for Gastrointestinal Endoscopy. We would also request that the British Society of Gastroenterology, as the major representative body for professional gastroenterologists in the UK, be formally consulted to provide professional expertise to any guidelines involving the 1 million GI endoscopic procedures that are performed in the UK each year.