Supplemental Material

THE COST-EFFECTIVENESS OF ANTIBIOTIC PROPHYLAXIS FOR PATIENTS AT-RISK OF INFECTIVE ENDOCARDITIS

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1. Supplementary Methods

Calculation for risk of IE following an (un)protected high-risk (invasive) dental procedure

A similar method for calculating risk of IE following a dental procedure for patients with a predisposing cardiac condition (PCC) was incorporated in the NICE 2008 model[1, 2] and by three other studies.[3-5] This calculation was:

Risk of IE following an unprotected dental procedure =

("Incidence of IE" **multiplied by** *"proportion of incident cases that would have occurred with a PCC"* **multiplied by** *"proportion of PCC IE cases attributed to dental procedures")* **divided by** *("number of dental procedures per patient per year"* **multiplied by** *"prevalence of PCC")*

Equation 1: Equation to calculate the risk of IE following an unprotected dental procedure

A slightly different and simpler way of presenting Equation 1 is presented as part of Equation 2, where people with a PCC are now defined as people "at-risk" of IE, of which people with PCC are the majority. The steps used to get to the point of estimating Equation 2 are described in this Appendix.

Risk of IE following an (un)protected dental procedure =
"The risk of IE in an at-risk population per year **multiplied by**
"*Number of dental procedures/patient/year for at-risk patients*"

Equation 2: Alternative equation to calculate the risk of IE following an unprotected dental procedure

It is information provided by Dayer, *et al* (2015)[6] and Duval, *et al* (2006)[5], supplemented with data obtained from HES and ONS[7] which provides the basis for calculating the risk of IE following an unprotected dental procedure for this study. The logic for this calculation using the figures presented in Table 1 are now presented in Table A1 and Table A2 for four hypothetical patient groups:

1) **All-at-risk** patients undergoing a **protected** dental procedure (**AP is used**), Table S1;
2) **All-at-risk** patients undergoing an **unprotected** dental procedure (**AP *not* used**), Table S1;
3) **High-risk** patients undergoing a **protected** dental procedure (**AP is used**), Table S2;
4) **High-risk** patients undergoing an **unprotected** dental procedure (**AP *not* used**), Table S2.

In order to describe the calculation used to estimate the risk of IE following a protected dental procedure, consider the calculation for the first hypothetical patient group (All-at-risk patients undergoing a protected dental procedure (AP is used))

using the figures presented in Table 1 (presented here in *Italic* font) and calculations presented in Table S1 (presented here in **Bold** font).

Step 1 – estimate "Number of IE cases in all-at-risk group": The "Number of IE cases per year" (*1486*) is multiplied by the "Incident cases that would have occurred for at risk-patients" (*0.0521*) which estimates the "Number of IE cases in all-at-risk group" (*1486*0.0521* = **774.46**).

Step 2 – estimate "Number of IE cases due to dental work for all-at-risk": The "Number of IE cases in all-at-risk group" (**774.46**) is multiplied by "IE cases attributed to dental procedures in at-risk group" (*0.052*) which estimates the "Number of IE cases due to dental work for all-at-risk" (**774.46****0.052* = **40.13**).

Step 3 – estimate "Size of the population of all-at-risk patients": The size of the population of interest (for the purpose of this analysis, "Population of England (year 2012)": *51.4 million people*) multiplied by the "Prevalence of all-at-risk group" (*0.033*) estimates the "Size of the population of all-at-risk patients" (*51.4 mil * 0.033* = **1,696,590**).

Step 4 – estimate "Risk of IE in this all-at-risk population per year": The "Number of IE cases due to dental work for all-at-risk" (**40.13**) multiplied by "Size of the population of all-at-risk patients" (**1,696,590**) estimates the "The risk of IE in this all-at-risk population per year" (**40.13 * 1,696,590** = **0.000024**).

Step 5 – estimate "Risk per protected dental procedure for all-at-risk" (Equation 2): "Risk of IE in this all-at-risk population per year" (**0.000024**) multiplied by "Number of dental procedures/patient/year for at-risk patients" (*1.32*) estimates "Risk per protected dental procedure for all-at-risk" (**0.000024** * *1.32* = **0.000018**)

Step 6 – estimate "Risk per million per protected dental procedure for all-at-risk": "Risk per protected dental procedure for all-at-risk" (**0.000018**) multiplied by one million people estimates "Risk per million per protected dental procedure for high-risk" (**0.000018** * 1 million people = **17.87**)

When accounting for the increase in cases of IE due to the cessation of AP (unprotected dental procedures), these same steps are taken; however, steps 1 and 2 are replaced by one step which involves adding the "Yearly increase in IE due to no AP for all-at-risk" (**418.8**) to the "Number of IE cases due to dental work for all-at-risk" before the cessation of AP (**40.13**), which now estimates the "Number of IE cases due to dental work for all-at-risk" without the use of AP (**418.8** + **40.13** = **458.93**). These estimated figures are all presented in Table S1 for all-at-risk patients (as described in this example) and Table S2 for high-risk patients.

2. Supplementary Tables

Table S1. Logic behind the risk per protected and unprotected dental procedure for all-at-risk patients calculation

Description of estimate	Estimate	Calculation	Description of calculation
Protected dental procedure (AP is used) – all figures for this calculation are presented in Table 1			
Number of IE cases per year	1486	-	-
Number of IE cases in all-at-risk group	774.46	1486 * 0.0521	Number of IE cases per year * Incident cases that would have occurred for all-at-risk patients
Number of IE cases due to dental work for all-at-risk	40.13	774.46 * 0.052	Number of IE cases in all-at-risk group * IE cases attributed to dental procedures in all-at-risk group
Size of the population of all-at-risk patients	1,696,590	51.4mil * 0.033	Population of England (year 2012) * Prevalence of all-at-risk group
Risk of IE in this all-at-risk population per year	0.000024	40.13 / 1,696,590	Number of IE cases due to dental work * Size of the population of all-at-risk patients
Risk per protected dental procedure for all-at-risk	**0.000018**	**0.000024 * 1.32**	**Risk of IE in this all-at-risk population per year * Number of dental procedures/patient/year for all-at-risk patients**
Risk per million per protected dental procedure for high-risk	**17.87**	0.000018 * 1mil	Risk per unprotected dental procedure for all-at-risk * One million people
Unprotected dental procedure (AP *not* used) – all figures for this calculation are presented in Table 1			
Monthly increase in IE due to no AP for all-at-risk	34.9	-	-
Yearly increase in IE due to no AP for all-at-risk	418.8	34.9 * 12	Monthly increase in IE due to no AP for all-at-risk * 12 months in a year
Number of cases due to dental work for all-at-risk	458.93	40.13 + 418.8	Number of IE cases due to dental work + Yearly increase in IE due to no AP for all-at-risk

Size of the population of all-at-risk patients	1,696,590	51.4mil * 0.033	Population of England (year 2012) * Prevalence of all-at-risk group
The risk of IE in this population per year	0.000271	458.93 / 1,696,590	Number of cases due to dental work for all-at-risk * Size of the population of all-at-risk patients
Risk per unprotected dental procedure for all-at-risk	**0.000204**	**0.000271 * 1.32**	**The risk of IE in this all-at-risk population per year * Number of dental procedures/patient/year for all-at-risk patients**
Risk per million per unprotected dental procedure for all-at-risk	**204.33**	0·000204 * 1mil	Risk per unprotected dental procedure for all-at-risk * One million people

AP: Antibiotic Prophylaxis; IE: Infective Endocarditis.

Table S2. Logic behind the risk per protected and unprotected dental procedure for high-risk patients calculation

Description of estimate	Estimate	Calculation	Description of calculation
Protected dental procedure (AP is used) – all figures for this calculation are presented in Table 1			
Number of IE cases per year	1486	-	-
Number of IE cases in high-risk group	428	1486 * 0.288	Number of IE cases per year * Incident cases that would have occurred for high-risk patients
Number of IE cases due to dental work for high-risk	13.38	428* 0.031	Number of IE cases in high-risk group * IE cases attributed to dental procedures in high-risk group
Size of the population of high-risk patients	301,244	51.4mil * 0.0059	Population of England (year 2012) * Prevalence of high-risk group
The risk of IE in this population per year	0.000044	13.38 / 301,244	Number of IE cases due to dental work * Size of the population of high-risk patients
Risk per protected dental procedure for high-risk	**0.000135**	**0.000044 * 0.33**	**The risk of IE in this high-risk population per year * Number of dental procedures/patient/year for high-risk patients**
Risk per million per protected dental procedure for high-risk	**134.58**	0.000135 * 1mil	Risk per protected dental procedure for high-risk * One million people
Unprotected dental procedure (AP *not* used) – all figures for this calculation are presented in Table 1			
Monthly increase in IE due to no AP for high-risk	13.7	-	-
Yearly increase in IE due to no AP for high-risk	164.0	13.67 * 12	Monthly increase in IE due to no AP for high-risk * 12 months in a year
Number of cases due to dental work for high-risk	177.42	13.38 + 164.04	Number of IE cases due to dental work + Yearly increase in IE due to no AP for high-risk
Size of the population of high-risk patients	301,244	51.4mil * 0.0059	Population of England (year 2012) *

			Prevalence of high-risk group
The risk of IE in this population per year	0.000271	177.42 / 301,244	Number of cases due to dental work for high-risk * Size of the population of high-risk patients
Risk per unprotected dental procedure for high-risk	**0.001785**	**0.000271 * 0.33**	**The risk of IE in this high-risk population per year * Number of dental procedures/patient/year for high-risk patients**
Risk per million per unprotected dental procedure for high-risk	**1785.13**	0.001785 * 1mil	Risk per unprotected dental procedure for high-risk * One million people

AP: Antibiotic Prophylaxis; IE: Infective Endocarditis.

3. Supplementary References:

1. National Institute for Health and Care Excellence (NICE). Prophylaxis against infective endocarditis. 2008:NICE Clinical Guideline No 64. http://www.nice.org.uk/guidance/cg64 Accessed: June 23rd, 2015
2. National Institute for Health and Care Excellence (NICE). Prophylaxis against infective endocarditis - Appendix 6. de novo economic analysis. 2008:NICE Clinical Guideline No 64 - Appendix 6. http://www.nice.org.uk/guidance/cg64 Accessed: June 23rd, 2015
3. Agha Z, Lofgren RP and VanRuiswyk JV. Is antibiotic prophylaxis for bacterial endocarditis cost-effective? *Medical decision making*. 2005;25:308-20.
4. Clemens JD and Ransohoff DF. A quantitative assessment of pre-dental antibiotic prophylaxis for patients with mitral-valve prolapse. *JChronic Dis*. 1984;37:531-544.
5. Duval X, Alla F, Hoen B, Danielou F, Larrieu S, Delahaye F, Leport C and Briancon S. Estimated risk of endocarditis in adults with predisposing cardiac conditions undergoing dental procedures with or without antibiotic prophylaxis. *Clinical infectious diseases.* 2006;42:e102-7.
6. Dayer MJ, Jones S, Prendergast B, Baddour LM, Lockhart PB and Thornhill MH. Incidence of infective endocarditis in England, 2000-13: a secular trend, interrupted time-series analysis. *Lancet*. 2015;385:1219-28.
7. Office of National Statistics (ONS). Population prediction statistics for 2012/2013. 2013. http://www.ons.gov.uk/ons/rel/pop-estimate/population-estimates-for-uk--england-and-wales--scotland-and-northern-ireland/2013/stb---mid-2013-uk-population-estimates.html Accessed: January 11th, 2016