

# Impact of the NICE guideline recommending cessation of antibiotic prophylaxis for prevention of infective endocarditis: before and after study

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## ABSTRACT

**Objective** To quantify the change in prescribing of antibiotic prophylaxis before invasive dental procedures for patients at risk of infective endocarditis, and any concurrent change in the incidence of infective endocarditis, following introduction of a clinical guideline from the National Institute for Health and Clinical Excellence (NICE) in March 2008 recommending the cessation of antibiotic prophylaxis in the United Kingdom.

**Design** Before and after study.

**Setting** England.

**Population** All patients admitted to hospital in England with a primary or secondary discharge diagnosis of acute or subacute infective endocarditis.

**Main outcome measures** Monthly number of prescriptions for antibiotic prophylaxis consisting of a single 3 g oral dose of amoxicillin or a single 600 mg oral dose of clindamycin, and monthly number of cases of infective endocarditis, infective endocarditis related deaths in hospital, or cases of infective endocarditis with a possible oral origin for streptococci.

**Results** After the introduction of the NICE guideline there was a highly significant 78.6% reduction ( $P<0.001$ ) in prescribing of antibiotic prophylaxis, from a mean 10 277 (SD 1068) prescriptions per month to 2292 (SD 176). Evidence that the general upward trend in cases of infective endocarditis before the guideline was significantly altered after the guideline was lacking ( $P=0.61$ ). Using a non-inferiority test, an increase in the number of cases of 9.3% or more could be excluded after the introduction of the guideline. Similarly an increase in infective endocarditis related deaths in hospital of 12.3% or more could also be excluded.

**Conclusion** Despite a 78.6% reduction in prescribing of antibiotic prophylaxis after the introduction of the NICE guideline, this study excluded any large increase in the incidence of cases of or deaths from infective endocarditis in the two years after the guideline. Although this lends support to the guideline, ongoing data monitoring is needed to confirm this, and further clinical trials should determine if antibiotic prophylaxis still has a role in protecting some patients at particularly high risk.

## INTRODUCTION

Infective endocarditis is a rare disease with a high morbidity and mortality.<sup>1</sup> For more than 50 years antibiotic prophylaxis before invasive procedures has been the primary focus for preventing infective endocarditis and remains the standard of care for patients with the disease in most parts of the world.<sup>2,3</sup> The rationale for such treatment is to reduce or eliminate the bacteraemia that may result from such procedures.<sup>4</sup> A particular focus is on antibiotic prophylaxis before dental procedures, as oral streptococci have been implicated in between 18% and 65% of cases of infective endocarditis, although most studies suggest the proportion is closer to 35-45%.<sup>5-9</sup> Regardless, little or no firm scientific evidence supports the effectiveness of antibiotic prophylaxis in preventing infective endocarditis,<sup>4</sup> and two case-control studies provide evidence that dental treatment is unlikely to be a risk factor.<sup>8,9</sup> Some authors therefore suggest that the current focus on antibiotic prophylaxis is an unproved, expensive, and potentially harmful standard of care, whereas others argue that it prevents cases of infective endocarditis.<sup>2,10-13</sup> Owing to ethical and medicolegal issues, cost, and the large number of patients necessary to achieve statistically significant results, a randomised placebo controlled trial of antibiotic prophylaxis has never been attempted.<sup>14</sup>

In March 2008, the National Institute for Health and Clinical Excellence (NICE) in the United Kingdom produced controversial new guidance recommending the cessation of antibiotic prophylaxis for all patients at risk of infective endocarditis undergoing dental and a wide range of other invasive procedures.<sup>15-17</sup> Although the American Heart Association<sup>2</sup> and the European Society for Cardiology<sup>3</sup> changed their guidelines around the same time, they did not recommend the complete cessation of antibiotic prophylaxis. Both continued to recommend antibiotic prophylaxis for patients with prosthetic heart valves undergoing invasive dental procedures, patients with cardiac valves repaired using prosthetic material, and patients with significant congenital heart lesions, a heart transplant with valvular lesions, or a history of endocarditis.

We hypothesised that by studying national prescribing data as well as data recorded for all inpatient hospital activity in the United Kingdom, we would be able to quantify the effect of the new NICE guideline on prescribing of antibiotic prophylaxis and the incidence of infective endocarditis. We describe the effect of the guideline on the prescribing of antibiotic prophylaxis in England and the changes in the incidence of cases of infective endocarditis and deaths from the disease in hospital over that period.

## METHODS

Prior to the introduction of the NICE guideline in March 2008 a single 3 g oral dose of amoxicillin or a 600 mg oral dose of clindamycin was used as antibiotic prophylaxis to prevent infective endocarditis in people at risk undergoing invasive dental procedures. We obtained national monthly prescribing data for all such prescriptions issued in England between January 2004 and April 2010 (25 months after the introduction of the guideline), from the prescription pricing division of the NHS Business Services Authority ([www.ppa.org.uk/ppa/ppa\\_main.htm](http://www.ppa.org.uk/ppa/ppa_main.htm)).

Figures on the incidence of infective endocarditis in England were obtained from national data on inpatient hospital activity from January 2000 until April 2010. All patients admitted to hospitals in the United Kingdom have standard data recorded, including their primary discharge diagnosis and up to 12 secondary diagnoses, using the ICD-10 coding system (<http://apps.who.int/classifications/apps/icd/icd10online>). These anonymised data are reported to the data warehouse of the Secondary Uses Service ([www.connectingforhealth.nhs.uk/systemsandservices/sus](http://www.connectingforhealth.nhs.uk/systemsandservices/sus)). We used Dr Foster Intelligence ([www.drfoosterintelligence.co.uk](http://www.drfoosterintelligence.co.uk)), a public-private partnership health service information and intelligence organisation, to access and assess the data from the Secondary Uses Service. The data presented are for England only.

We identified all patients, including those who died in hospital, with a primary or secondary discharge diagnosis of “acute or subacute infectious endocarditis” (ICD-10 I33.0). We also identified patients with such a diagnosis where a streptococcal or staphylococcal cause was also recorded (ICD-10 A40, A41 codes for septicaemia or B95 supplementary causal organism codes). Codes A40.0 to A40.3 and B95.0 to B95.3, respectively, identify group A, B, and D streptococci and *Streptococcus pneumoniae* as causal organisms. Codes A40.4, A40.5, B95.4, and B95.5 identify other streptococci or unspecified streptococci as the cause of disease. For analysis purposes we grouped cases of infective endocarditis with an A40.4, A40.5, B95.4, or B95.5 code as cases with a possible oral streptococcal cause. For comparison we also identified cases with a staphylococcal cause by grouping cases with codes A41.0 to A41.2 or B95.6 to B95.8.

By searching individual patient level data we were able to identify when patients admitted to one hospital were transferred to another as part of their

management. We counted such continuous periods of illness, known as “superspells,” only once.

## Statistical analysis

We plotted graphically data on monthly prescribing and incidence of infective endocarditis. In each case we also plotted the moving average figure for every three months and, for the incidence data on infective endocarditis, the linear trend lines and lines representing 2 standard deviations either side of the trend line for the periods before and after the introduction of the guideline.

The biostatistician (DJC) analysed data up to March 2008 and prepared the plan for testing the subsequent data before being given access to such data.

We used a Poisson regression model to investigate the monthly trends in cases of infective endocarditis and deaths in hospital. This assumed a proportional change and allowed control for population size. Population data for England were obtained from [www.statistics.gov.uk/hub/population/index.html](http://www.statistics.gov.uk/hub/population/index.html) and we fitted a cubic spline function to obtain monthly estimates of population size. We investigated non-linear trends by adding a quadratic term in the Poisson regression model, but as this term was not statistically significant for any of the outcomes it was dropped from the models. To test for over-dispersion we carried out likelihood ratio tests between “standard” Poisson regressions and negative binomial regressions, with all other settings equal. The log likelihood ratios reported for the negative binomial regressions were lower than those reported for the standard Poisson regressions, which indicated (without the need for a likelihood ratio test) that negative binomial regressions did not offer an improvement over Poisson regressions.

For the primary analysis of cases of infective endocarditis and deaths we used a “non-inferiority” test. This requires specification of a margin of indifference. We determined this by examining the number of cases and variability in the data before March 2008—that is, the limitations of the data. It was not determined by deciding what might be a clinically meaningful margin of indifference.

An upper limit for the acceptable increase in the number of cases was therefore specified based on the quality of the data. For the non-inferiority test we regarded the counts of cases and deaths as continuous variables. Because of the upward trend in the outcomes before the guideline change, we based the limits on the number of cases or deaths in March 2008 estimated from our fitted Poisson regression model. We used the monthly data before the guideline change to set the margin for the mean of the 25 months of data since the change.

Based on the variability of the monthly data before the change we set as the margin a 15% increase over the fitted number for cases and deaths. To carry out the test we constructed a 95% confidence interval for the monthly mean number of cases or deaths for the 25 months after the guideline change. If the upper

limit of the confidence interval corresponded to an increase of less than 15% over the model's estimate for the number of cases or deaths for March 2008 (that is, <139.8 or <22.4, respectively) we considered that the number of cases or deaths had not increased significantly.

Prespecified secondary tests of whether cases of infective endocarditis or deaths had increased since the introduction of the guideline were: testing whether there was an increase in the time trend in the Poisson regression models, and noting whether in 17 or more months from April 2008 to April 2010 the number of cases or deaths exceeded the fitted value for March 2008 (121.6 cases or 19.5 deaths). The probability of 25 independent counts of 17 exceeding this level was 0.22 (that is, <5%) and so we set 17 as the test statistic.

## RESULTS

From mid-2000 to mid-2009, the population of England increased at an annual rate of 0.57%, from 49 233 300 to 51 809 700 (Office for National Statistics).

### Changes in prescribing of antibiotic prophylaxis

In the 12 months after the introduction of NICE clinical guideline No 64, the prescribing of antibiotic prophylaxis for infective endocarditis declined rapidly (fig 1). To compare more stable periods of prescribing for antibiotic prophylaxis, the 12 months before the introduction of the guideline was compared with the most recent 12 months of prescribing data for 14 to 25 months inclusive after the introduction of the guideline. This comparison provided a 78.6% reduction in prescribing, from a mean 10 727 (SD 1068) before the introduction of the guideline to 2292 (SD 176) after. In the 12 months before the guideline, prescribing of antibiotic prophylaxis by dentists accounted for 91.9% of prescriptions for antibiotic prophylaxis, with other prescribers accounting for the remaining 8.1% (general medical practitioners 7.8%, hospitals 0.2%, and nurses 0.1%). However, 14-25 months after the introduction of the guideline, the number of prescriptions issued by dentists decreased significantly, from a mean 9859 per month to 1977 (a decrease of 79.9%,  $P<0.001$ ). Over the same period the number of prescriptions issued by other prescribers significantly decreased, from a mean 868 per month to 315 (a decrease of 63.7%,  $P<0.001$ ).

### Number of cases and in-hospital deaths

#### Before guideline change

The table gives estimated annual percentage changes in the number of cases and number of deaths. From January 2000 to March 2008, there was an increasing trend in the number of cases of infective endocarditis ( $P<0.001$ ), cases possibly attributable to oral streptococci ( $P<0.001$ ), and deaths from infective endocarditis ( $P=0.008$ ). The number of cases was significantly correlated with the number of deaths (Spearman correlation coefficient 0.46,  $P=0.001$ ).

#### After guideline change

Evidence was lacking that the upward trend in cases of infective endocarditis had changed ( $P=0.61$  for the difference between the trend before and after the guideline change, table and fig 2) since the introduction of the guidelines and the precipitous decrease in prescribing of antibiotic prophylaxis.

The average monthly number of cases of infective endocarditis for the 25 months from April 2008 was 125.5 (SD 17.59). The upper limit for the 95% confidence interval for the mean was 132.9. As this is less than the prespecified limit of 139.8, the possibility of a 15% increase in cases can be excluded. More precisely, the possibility of a 9.3% increase can be excluded. The number of cases of infective endocarditis was greater than the fitted number for March 2008 in just 13 of the 25 subsequent months and did not exceed the preset value of 17.

Evidence is lacking that the upward trend in deaths changed after the introduction of the guideline ( $P=0.45$ , table). The average number of deaths from infective endocarditis per month for the 25 months from April 2008 was 20.0 (SD 4.62). The upper limit for the 95% confidence interval for the mean was 21.9. As this is less than the prespecified limit of 22.4, the possibility of a 15% increase in deaths from infective endocarditis can be excluded. More precisely, the possibility of a 12.3% increase in deaths can be excluded. The number of deaths was greater than the fitted number for March 2008 in just 13 of the 25 subsequent months and did not exceed the preset value of 17.

There was also no evidence of a significant change in the upward trend in the number of cases possibly attributable to oral streptococci ( $P=0.66$ ), whereas the rate

Estimated annual percentage change in cases of infective endocarditis before and after the introduction of the National Institute for Health and Clinical Excellence guideline recommending cessation of antibiotic prophylaxis

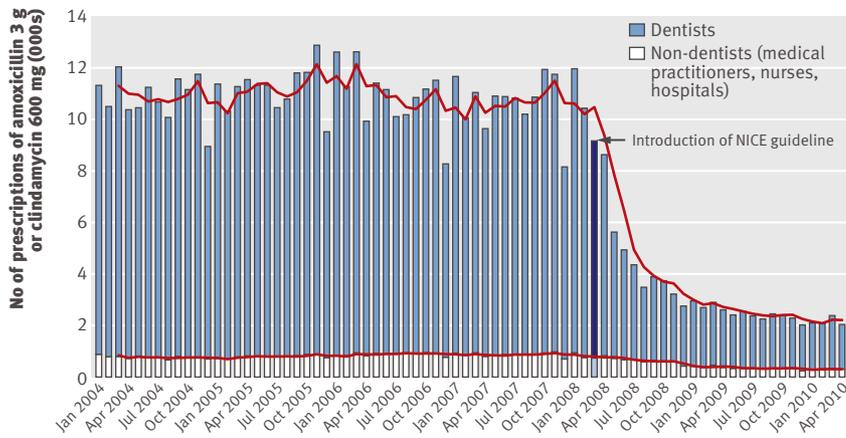
Variables	Before guideline change (95% CI)	P value*	After guideline change (95% CI)	P value†	Difference (95% CI)‡
All infective endocarditis cases	3.82 (3.04 to 4.61)	<0.001	2.72 (-0.94 to 6.52)	0.61	-1.1 (-3.98 to 1.91)
Oral streptococcal cases	8.41 (6.66 to 10.19)	<0.001	10.38 (2.93 to 18.36)	0.66	1.97 (-3.73 to 8.17)
Staphylococcal cases	9.24 (7.45 to 11.06)	<0.001	1.49 (-5.66 to 9.19)	0.08	-7.75 (-13.11 to -1.87)
Deaths from infective endocarditis	2.55 (0.65 to 4.48)	0.008	6.64 (-2.50 to 16.64)	0.45	4.09 (-3.15 to 12.16)

All estimates in a row are from a single Poisson regression model, adjusting for population size, and with one term for months since January 2000 and another for months since guideline change.

\*P value for test of term for change before introduction of guideline.

†P value for test of whether term after guideline change is 0—that is, whether annual percentage change differs between before and after the guideline was introduced.

‡Percentage difference in annual percentage increase in cases before and after guideline was introduced.



**Fig 1 |** Total number of prescriptions for antibiotic prophylaxis (amoxicillin 3 g or clindamycin 600 mg) dispensed each month by type of prescriber. Red lines represent moving average figure for prescriptions every three months

of increase in cases due to staphylococci slowed non-significantly ( $P=0.08$ ; table and fig 3).

**DISCUSSION**

Antibiotic prophylaxis prescribing for infective endocarditis in the United Kingdom stayed relatively constant until the introduction of the NICE guideline in March 2008; most (91.9%) prescribing was by dental practitioners. After the introduction of the guideline a large (78.6%) and rapid decrease occurred in prescribing of antibiotic prophylaxis. However, we did not detect a significant increase in the number of infective endocarditis cases above the long term baseline trend over this period. Neither was there a significant increase in the rate of infective endocarditis related deaths in hospital nor a significant increase in the number of cases due to streptococci of possible oral origin.

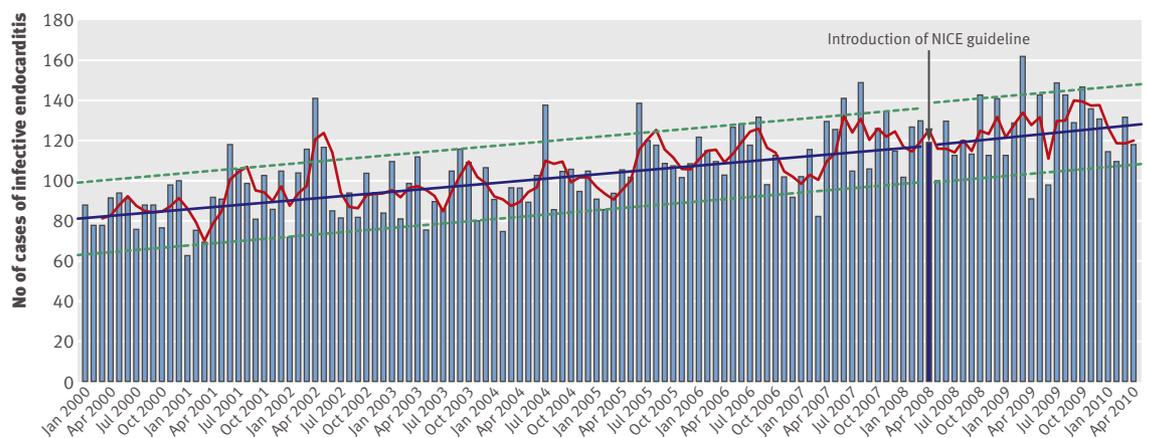
**Limitations of the study**

The study has several limitations. Firstly, it was retrospective and limited to England and therefore may not be generalisable to other populations. Secondly, the

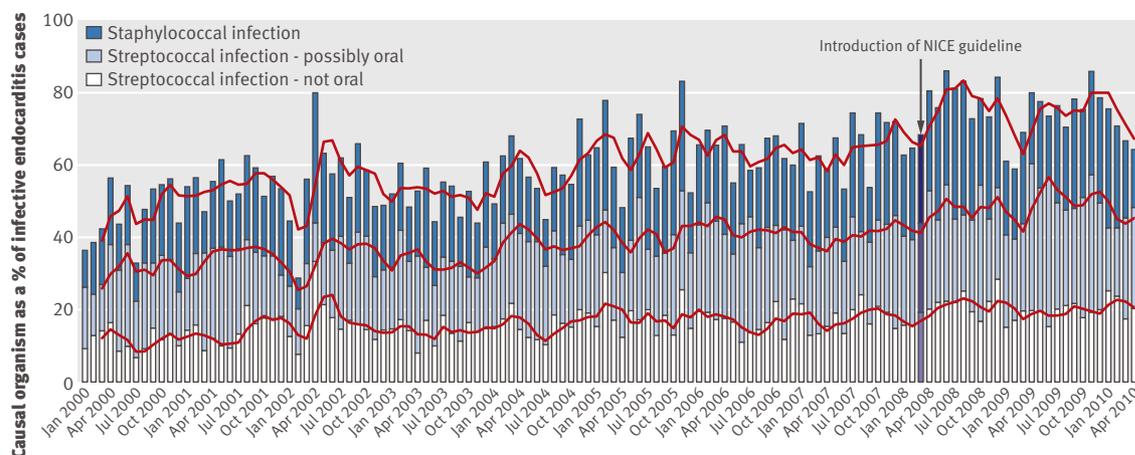
data rely on hospital coding. In the United Kingdom, data are collected on every patient admitted to hospital, and the coding is done by trained and accredited staff. Although these data can be subject to coding errors, the coding has been shown to be more reliable and complete in capturing data on, for example, all cases of vascular surgery than a national research database specifically designed for that purpose.<sup>18</sup> Furthermore, as the coding was done independently of the study it was not subject to study bias or influenced in any way by the introduction of the NICE guideline. As the study sample was based on national data, the size of the dataset and the consistency of the process are likely to average out any error.

Although patients with infective endocarditis may present to different hospital specialties and the disease may be difficult to diagnose initially, data from hospital episode statistics records only the discharge diagnosis and should therefore reflect as accurately as possible the actual number of cases treated. None the less, because the diagnosis of endocarditis is sometimes uncertain, some cases will undoubtedly have been missed and others will have been erroneously labelled as endocarditis. The number of deaths from infective endocarditis in hospital were obtained from hospital episode statistics data, defining the status at discharge from hospital (dead or alive). Thus the data reflect deaths that are the immediate result of a hospital admission for infective endocarditis and will not have captured deaths before admission or deaths at home as a result of the late complications of the disease. The mortality data are therefore not directly comparable to long term follow-up studies of patients with infective endocarditis.

Thirdly, there is no requirement to record anything other than a primary diagnosis for each patient; a causal organism was recorded in only around 70% of cases towards the end of the study. In addition there is no specific ICD-10 code for viridians group streptococci. We therefore had to use codes for “unspecified” or “other” streptococci to identify cases of infective



**Fig 2 |** Monthly number of cases of infective endocarditis. Also plotted are separate lines for linear trend within 2 standard deviations (broken lines) for periods before and after introduction of NICE guideline. Red lines represent moving average figure for number of cases every three months



**Fig 3** | Proportion of infective endocarditis cases recorded each month with a code for streptococci or staphylococci as cause. Red lines represent moving average figure for cases every three months

endocarditis with a possible viridians group streptococcal cause. Nevertheless, these codes exclude group A, B, and D streptococci and *S pneumoniae* and, given the microbiology of the oral cavity and infective endocarditis, it is possible that oral viridians group streptococci account for a high proportion of the organisms in this group.<sup>19,20</sup>

Fourthly, although 35-45% of cases of infective endocarditis are caused by oral viridians group streptococci,<sup>5-9</sup> good data are lacking on the proportion resulting from an invasive dental procedure. However, the strategy of giving antibiotic prophylaxis to prevent infective endocarditis is based on the premise that a high proportion of these cases result from oral bacteria entering the circulation during dental procedures. An alternative view, however, is growing that oral bacteria continuously enter the circulation<sup>21,22</sup> as a result of daily activities such as chewing food and tooth brushing, and these may be far more important causes of oral viridians group streptococci associated cases of infective endocarditis. If true, the proportion of cases caused by invasive dental procedures could be low. The reality could, however, lie anywhere between these two extremes.

Without accurate data on the proportion of cases caused by dental procedures it is difficult for statistical analysis purposes to predefine a clinically relevant level of change after the cessation of antibiotic prophylaxis, or to determine the sample size needed to detect the change. Using the premise that a high proportion of cases are caused by dental procedures, a large increase in the number of cases would be expected if antibiotic prophylaxis was stopped and was effective, and a comparatively small population would be needed to detect a statistically significant change. On the other hand, if the number of cases caused by dental procedures was small, it would require an infinitely large population to detect any increase in the number. Indeed, to exclude a 1% increase in the incidence of infective endocarditis above the baseline trend, assuming a similar incidence of infective endocarditis and variability in the numbers

of cases on a month by month basis, would require a study population of 478.5 million people. For this reason, even with a study covering the entire population of England, the possibility of a small increase in cases after cessation of antibiotic prophylaxis cannot be excluded. However, that we identified no significant increase in cases in a population of this size, despite a large decrease in prescribing of antibiotic prophylaxis, suggests that invasive dental procedures are unlikely to account for a high proportion of the cases.

Because of this, and because of the nature of the statistical test we applied, we used the quality of the available data to determine the limits of detection rather than estimate a clinically relevant level of change. The 15% margin of error set for the statistical analysis was determined a priori based on the variability in monthly incidence figures for cases of and deaths from infective endocarditis in the period before March 2008. After the analysis was done, however, we were able to exclude a 9.3% increase in the number of cases and a 12.3% increase in deaths in the setting of a 78.6% decrease in prescribing of antibiotic prophylaxis. Although oral viridians group streptococci are likely to account for only 35-45% of cases, if antibiotic prophylaxis was effective we would expect the number of cases and deaths to increase significantly more than 9.3% and 12.3%, respectively, and the number of cases with a probable oral streptococcal origin to rise much higher.

There is the concern that the period of follow-up was not long enough. However, in over 90% of cases the incubation period for infective endocarditis is less than six weeks, and other studies have used three months as the cut off for capturing all cases of infective endocarditis that will develop after exposure to the risk of infection.<sup>8,9</sup> We therefore believe that if antibiotic prophylaxis was effective in preventing infective endocarditis the large decrease in prescribing of antibiotic prophylaxis that occurred after the introduction of the NICE guideline would have resulted in a detectable increase in cases during the 25 months of the study.

Any such change should have been particularly noticeable among those cases where the causal organism was of possible oral streptococcal origin. Regardless, we intend to periodically monitor the rate of endocarditis in the English population over time.

The 78.6% decrease in prescribing of antibiotic prophylaxis in the months after the introduction of the guideline was large and suggests much better compliance than is often seen after policy changes in medicine. Compliance was particularly good among dentists who, as well as being strongly urged to adopt the new guidelines by the chief dental officer, NICE, and the dental press, were advised by the malpractice insurance organisations that it would be difficult to defend cases where the new guidelines had not been followed. A residual level of prescribing does, however, seem to persist at around 20% of the level before the guideline. There are several possible explanations for this. Firstly, the guideline allows antibiotic prophylaxis to be prescribed to patients who have previously received it and insist on continuing to have it, even after the rationale for the change in policy has been fully explained. Secondly, anecdotal evidence suggests that some cardiologists are pressuring dentists or, where dentists refuse to prescribe, the patient's general medical practitioner to provide antibiotic prophylaxis for patients they regard as particularly high risk of infective endocarditis, such as patients with significant congenital heart lesions, prosthetic heart valves, or a history of infective endocarditis. In other words, some clinicians in the United Kingdom may be implementing the European Society for Cardiology or American Heart Association guidelines rather than the NICE guideline.<sup>23</sup> Finally, anecdotal evidence also suggests that a small proportion of dentists in the United Kingdom prescribe a 3 g dose of amoxicillin (or 600 mg dose of clindamycin) to treat acute dental infections. The precise contribution of each of these explanations to the residual 20% prescribing figure is hard to quantify.

Over the past 10 years a general move has been to reduce antibiotic prescribing to save cost and to prevent the development of antibiotic resistant bacteria. Although this could have played a part in the reduction in prescribing of antibiotic prophylaxis, it seems unlikely given the size and suddenness of the reduction, its coincidence with the introduction of the NICE guideline, the low cost of a single dose of amoxicillin or clindamycin, and national prescribing data that show a slight increase in the general prescribing of penicillins and macrolide antibiotics over the same period.

The results of this analysis cover a large group of patients for whom antibiotic prophylaxis was prescribed before the introduction of the NICE guideline. Our results suggest that for most of these patients, including those with a history of rheumatic fever or a heart murmur, there may be little or no benefit in giving antibiotic prophylaxis to prevent infective endocarditis. However, because we cannot exclude the possibility that residual antibiotic prophylaxis prescribing targets those perceived to be at highest risk

of infective endocarditis, it does not completely tackle the problem of whether a subset of patients, particularly those with prosthetic heart valves or a history of infective endocarditis, might still benefit from antibiotic prophylaxis. To more directly answer this question a carefully designed, randomised, placebo controlled trial of antibiotic prophylaxis in these patients would be required.

#### Interpretation of the findings

Given that oral viridians group streptococci are clearly implicated in some cases of infective endocarditis, our findings provide support for the growing view that the frequent episodes of bacteraemia that follow daily routines such as eating and tooth brushing may be a greater risk factor for the development of infective endocarditis than the transient bacteraemia that follows an invasive dental procedure.<sup>21</sup> Furthermore, the evidence that the bacteraemia after tooth brushing is significantly greater and more common in patients with poor oral hygiene and gingival disease<sup>22</sup> suggests that improving oral hygiene might be more effective at reducing the number of cases caused by oral bacteria than providing antibiotic prophylaxis for invasive dental procedures.<sup>9</sup>

#### Conclusion

Our data suggest that despite a substantial decrease in prescribing of antibiotic prophylaxis in England since the introduction of NICE guideline No 64 in March 2008 there has been no significant increase in the number of cases of infective endocarditis, as measured using data from hospital episode statistics.

Some clinicians remain concerned that the NICE recommendation to stop antibiotic prophylaxis in the United Kingdom, and the reduced number of patients receiving antibiotic prophylaxis in the United States and Europe as a result of the restriction of antibiotic prophylaxis to patients thought to be at high risk in the latest American Heart Association<sup>2</sup> and European Society of Cardiology<sup>3</sup> guidelines, will result in an increased incidence of infective endocarditis. Although one small study found no cause for concern after the change in the American Heart Association guidelines<sup>24</sup> the present trial is the first large scale study to evaluate the effect of the NICE guideline recommendation to stop antibiotic prophylaxis to prevent infective endocarditis.

Although these findings lend support to the NICE guideline recommendations and suggest that antibiotic prophylaxis before invasive dental procedures is unlikely to be of value in preventing infective endocarditis in patients with a history of rheumatic fever or a heart murmur, our findings do not exclude the possibility that a small number of patients at highest risk, such as those with prosthetic valves, might benefit. Ongoing monitoring of the data is required for confirmation, and further studies are needed to determine if antibiotic prophylaxis has a role in protecting a small group of patients at highest risk from infective endocarditis.

## WHAT IS ALREADY KNOWN ON THIS TOPIC

Previous policy in the United Kingdom was to provide antibiotic prophylaxis to patients at risk of infective endocarditis before invasive dental procedures

Antibiotic prophylaxis for patients thought to be at high risk of infective endocarditis is still the policy in most other parts of the world

In March 2008 NICE recommended the complete cessation of antibiotic prophylaxis before dental and other invasive procedures

## WHAT THIS STUDY ADDS

After the introduction of NICE clinical guideline No 64 a large (78.6%) and rapid decrease occurred in prescribing of antibiotic prophylaxis

Despite this reduction, no large increase occurred in the incidence of infective endocarditis cases or deaths in the two years after the guideline was introduced

The findings support the cessation of prescribing of antibiotic prophylaxis recommended by the guideline

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**Contributors:** MHT and MJD contributed to all aspects of the study. PBL, GRC, and VHC contributed to the literature search, data interpretation, and writing of the manuscript. JMF was involved in data collection and interpretation. DJC was involved in the statistical analysis, data interpretation, and writing of the manuscript.

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**Competing interests:** All authors have completed the Unified Competing Interest form at [http://www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) (available on request from the corresponding author) and declare: (1) MJD received some financial support from the Somerset Health Research Fund; (2) in the last 3 years GRC has acted as a consultant and expert witness for Cubist Pharmaceuticals that might have an interest in the submitted work; (3) no other relationships or activities that could appear to have influenced the submitted work. None of the authors of this paper were members of the NICE guideline committee that introduced NICE guideline No 64. PBL, however, was a member of the 2007 guideline committee of the American Heart Association.

**Ethical approval:** Not required.

**Data sharing:** No additional data available.

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