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Mass administration of azithromycin and *Streptococcus pneumoniae* carriage: cross-sectional surveys in the Gambia

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**Objective** To evaluate the effect of repeated mass drug administration (MDA) of azithromycin in the Gambia on the nasopharyngeal carriage of *Streptococcus pneumoniae* and on the emergence of antibiotic-resistant strains.

**Methods** This study involved villages that participated in a cluster randomized trial comparing the effect of one versus three azithromycin MDA rounds on the prevalence of trachoma. Only villages in which most children received 7-valent pneumococcal conjugate vaccine were included. Three cross-sectional surveys were performed in two villages that received three annual MDA rounds: the first immediately before the third MDA round and the second and third, 1 and 6 months, respectively, after the third MDA round. The third survey also covered six villages that had received one MDA round 30 months previously. Pneumococcal carriage was assessed using nasopharyngeal swabs and azithromycin resistance was detected using the Etest.

**Findings** The prevalence of pneumococcal carriage decreased from 43.4% to 19.2% between the first and second surveys ($P < 0.001$) but rebounded by the third survey (45.8%; $P = 0.591$). Being a carrier at the first survey was a risk factor for being a carrier at the second (odds ratio: 3.71; $P < 0.001$). At the third survey, the prevalence of carriage was similar after one and three MDA rounds (50.3% versus 45.8%, respectively; $P = 0.170$), as was the prevalence of azithromycin resistance (0.3% versus 0.9%, respectively; $P = 0.340$).

**Conclusion** Three azithromycin MDA rounds did not increase the prevalence of nasopharyngeal carriage of azithromycin-resistant *S. pneumoniae* strains compared with one round.

Abstract: in العربية, Français, Русский и Español at the end of each article.

### Introduction

Trachoma, which is due to ocular infection with the intracellular bacterium *Chlamydia trachomatis*, is the leading infectious cause of blindness worldwide. The discovery that ocular *C. trachomatis* infection can be successfully treated with a single, oral dose of azithromycin marked a significant advance in trachoma control. Today, mass drug administration (MDA) with azithromycin is a key component of a multifaceted strategy designed to control all phases of trachoma and recommended by the World Health Organization (WHO): the SAFE strategy, where S stands for surgery for trichiasis; A, for antibiotics to reduce the reservoir of *C. trachomatis* infection; F, for facial cleanliness to reduce transmission from ocular and nasal secretions; and E, for environmental improvements to interrupt transmission of the bacterium and prevent re-emergence of the infection.

Current WHO guidelines suggest that three annual rounds of azithromycin MDA should be completed before the prevalence of trachoma is reassessed. However, evidence from the Gambia and the United Republic of Tanzania indicates that three rounds are unnecessary in low prevalence settings. In such situations, repeated azithromycin MDA may be detrimental if it results in the selection of macrolide-resistant pathogens. Although currently there is no evidence that repeated MDA increases the prevalence of azithromycin-resistant *C. trachomatis*, there is epidemiological evidence suggesting that pharyngeal carriage of macrolide-resistant *Streptococcus pneumoniae* increases following repeated MDA for trachoma control. Because *S. pneumoniae* is a leading cause of childhood mortality, especially in Africa, and because asymptomatic nasopharyngeal carriage is the initial step in the pathogenesis of pneumococcal disease, increased carriage of macrolide-resistant strains is a public health concern.

The Gambia, which is situated in western Africa and is in the Sahel belt, has seen a decline in the prevalence of follicular trachoma in children in recent decades: the prevalence (adjusted for the 1- to 9-year-old age group) derived from national surveys fell from 20% in 1986 to 7% in 1996. The country’s National Eye Health Programme, which was established in 1986, has implemented all aspects of the SAFE strategy. An evaluation of the implementation of SAFE interventions indicated that Gambian households have good access to water and latrines but a low awareness of community health education programmes that promote face washing. Recent survey work carried out in four health districts following the national azithromycin MDA campaign that ran from 2007 to 2010 suggests that the prevalence of follicular trachoma in the country is now nearing 5%, which is the threshold for elimination.

The Partnership for the Rapid Elimination of Trachoma (PRET) study was a cluster randomized trial embedded within the Gambia’s MDA campaign that compared the prevalence of active trachoma in Gambian communities which had received azithromycin annually for three years with that in communities which received a single treatment round. The aim of the present study was to determine whether the nasopharyngeal...
carriage of azithromycin-resistant *S. pneumoniae* was more prevalent in communities that received three MDA rounds than in those that received one. We considered only data from villages in which children had been vaccinated with a 7-valent pneumococcal conjugate vaccine (PCV-7) because we wanted our results to be relevant to the increasing number of African countries that include these vaccines in their vaccination schedules.

**Methods**

The study included the residents of eight villages in a rural region of western Gambia where the population predominantly comprises subsistence farmers who grow millet and maize for home consumption and groundnuts as a cash crop. The people belong mainly to the Jola and Mandinka ethnic groups. The climate of the Gambia is tropical and there is one rainy season, lasting from June to October.

All study villages had participated in a cluster randomized trial of the impact of PCV-7 on pneumococcal nasopharyngeal carriage that ran from July 2006 to July 2008. All children who were under the age of 30 months when the vaccine trial started, who were born during the trial period or who moved into a study village during the trial period received PCV-7. In August 2009, PCV-7 was introduced into the Gambian Expanded Programme on Immunization.

The PRET study was a cluster randomized, controlled trial whose design has been described elsewhere. Briefly, enumeration areas with a population of 600 to 800 individuals were randomized either to receive MDA with azithromycin annually for three years or to have treatment discontinued if the prevalence of either active trachoma or ocular *C. trachomatis* infection in children aged 5 years or younger fell below 5% (i.e. the stopping rule). Six months after the first MDA round, the prevalence of active trachoma and of *C. trachomatis* infection in communities randomized to the stopping rule were 2.4% and 0%, respectively, and MDA therefore ceased in all those communities.

Our study comprised two treatment arms and involved only villages in which children had received PCV-7 (Fig. 1). The first arm included two villages that had been randomized to three annual MDA rounds. Three cross-sectional surveys were conducted in these villages: the first took place 11 months after the second MDA round, the second took place 1 month after the third MDA round and the third took place 6 months after the third MDA round. The second arm included six villages that had been randomized to the stopping rule and where MDA had been carried out only once. In these villages, one cross-sectional survey was conducted 30 months after the single MDA round – it took place at the same time as the third cross-sectional survey in villages that received three MDA rounds (Fig. 1).

Census data were gathered in the week before the first cross-sectional survey. All children under the age of 15 years who were included in the census and who were present at the time of the survey were invited to participate. In addition, 150 individuals aged 15 years or more were randomly selected to participate in each cross-sectional survey, including the single survey conducted in villages randomized to the stopping rule. Although random selection was carried out independently for each survey, the second and third surveys in villages that received three MDA rounds included only individuals who had received azithromycin during the third MDA round in July 2010.

During each survey, a questionnaire was administered and a nasopharyngeal specimen was taken from each participant by means of a calcium alginate swab, which was then inoculated in a transport medium of skimmed milk, tryptone, glucose and glycerol in a sterile vial. In the field, the samples were kept on wet ice. They were transferred to a refrigerator set to 4 °C within 8 hours of collection and moved to long-term storage at −70 °C within 24 hours of collection.

For analysis, the nasopharyngeal swab samples were thawed at room temperature and 10 μL of the transport medium was inoculated onto Columbia agar supplemented with 5% sheep’s blood and 5 μg/mL of gentamicin. The agar plates were then incubated for 18 to 24 hours at 35 °C in an atmosphere containing 5% carbon dioxide. Presumptive *S. pneumoniae* colonies were identified on the basis of their morphology and optochin sensitivity and the presence of *S. pneumoniae* was confirmed using a

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**Fig. 1.** Flowchart for the study of the effect of mass azithromycin administration on nasopharyngeal carriage of *Streptococcus pneumoniae*, Gambia, 2008–2010

![Flowchart](https://example.com/flowchart.png)

"MDA: mass drug administration. The first cross-sectional survey was carried out 11 months after the second azithromycin MDA round in villages that took part in three rounds. The second survey was carried out 1 month after the third MDA round. The third survey was carried out 6 months after the third MDA round in villages that took part in three rounds and, at the same time, 30 months after the single MDA round in villages that received only one round."
polymerase chain reaction (PCR) technique that targeted the cpsA gene. The density of nasopharyngeal carriage was scored semiquantitatively as previously described. For each nasopharyngeal swab sample, up to four S. pneumoniae colonies with different morphologies were screened by disc diffusion for their sensitivity to azithromycin. The colonies with different morphologies were screened by disc diffusion for their sensitivity to azithromycin. The colonies were scraped from the first quadrant of the agar plate and total, genomic DNA was extracted using the QIAamp DNA MiniKit (Qiagen, Hilden, Germany) according to the manufacturer’s instructions. The primer concentrations and cycling conditions were as recommended by the United States Centers for Disease Control and Prevention protocol.

Statistical analysis

Data were double-entered into an OpenClinica database (OpenClinica, Waltham, United States of America). Differences between survey samples and between treatment groups in the proportion of patients who carried any pneumococci or azithromycin-resistant pneumococci were evaluated using Fisher’s exact test. In addition, logistic regression analysis was used to identify risk factors for pneumococcal carriage, to control for confounders and to test for interactions. The results were reported in terms of odds ratios (ORs) and 95% confidence intervals (CIs). Both CIs and P-values were estimated using clustered (by village) robust standard errors.

The primary analysis considered the overall prevalence of pneumococcal nasopharyngeal carriage and the secondary analysis considered the prevalence of the carriage of azithromycin-resistant strains (i.e. those with a minimal inhibitory concentration of azithromycin of 16 μg/mL or more) and of individual serotypes and serotype groups. Five serotype groups were investigated: (i) the most frequent serotypes, which were defined as those detected in at least 10 individuals; (ii) PCV-7 serotypes, which included pneumococcal serotypes 4, 6B, 9V, 14, 18C, 19F and 23F, and serotypes 6A and 6C; (iii) serotypes not in PCV-7, which included any other pneumococcal serotypes detectable by the multiplex PCR method; (iv) paediatric serotypes, which were defined as serotypes 4, 6, 7, 9, 14, 18, 19 and 23; and (v) non-serotypeable pneumococci. All P-values were adjusted for multiple testing using the Benjamini and Hochberg false discovery rate procedure. Fisher’s exact test was used to evaluate heterogeneity in the serotype distribution between villages.

This study adhered to the tenets of the Declaration of Helsinki and was approved by the Gambian Government/Medical Research Council Unit and the Gambia Joint Ethics Committee. Written, informed consent was freely obtained from all participants of the PRET trial and additional written consent was obtained from participants in our ancillary study. For minors, informed consent was obtained from a parent or guardian.

Results

The first cross-sectional survey collected data on 415 individuals from villages that took part in three azithromycin MDA rounds and the second survey collected data on 417 similar individuals. The third survey included a total of 743 participants: 343 from villages that took part in three MDA rounds and 400 from villages randomized to the stopping rule.
and that took part in one round (Fig. 1). The demographic characteristics of the participants sampled in each survey are listed in Table 1.

Table 2 reports the overall prevalence of nasopharyngeal S. pneumoniae carriage in individuals from villages that took part in three MDA rounds. In the first survey, 11 months after the second MDA round, the prevalence was 43.4%. By the second survey, 1 month after the third MDA round, the prevalence had decreased significantly, to 19.2%. However, by the third survey, 6 months after the third MDA round, it was 45.8%, similar to the initial level. In each survey, the prevalence of nasopharyngeal carriage was lower among individuals aged 10 years or older than among younger individuals. Table 3 shows that, in the third survey, there was no significant difference in prevalence between individuals from villages that took part in three MDA rounds and those from villages that took part in one: the prevalence was 45.8% and 50.3% in the two treatment arms, respectively.

No evidence of pneumococcal azithromycin resistance was found in the first cross-sectional survey among individuals from villages that took part in three MDA rounds. The prevalence of the pneumococcal nasopharyngeal carriage of azithromycin-resistant isolates among sampled individuals rose to 1.2% in the second survey but decreased to 0.9% in the third (Table 4). In the third survey, the prevalence of the carriage of azithromycin-resistant strains was similar in individuals from villages that took part in three MDA rounds and in those from villages that took part in one: 0.9% versus 0.3%, respectively (Table 4).

Serotyping of pneumococci isolated in the third survey showed no significant difference in the prevalence of the carriage of PCV-7 serotypes between the treatment arms (Table 5). Nor was there a significant difference in the prevalence of serotypes not in PCV-7, of paediatric serotypes or of non-serotypeable pneumococci. However, the prevalence of serotypes 15B and/or 15C was significantly higher in individuals from villages that took part in three MDA rounds than in those from villages that took part in one (9.0% versus 2.3%, respectively; \( P = 0.001 \)). The prevalence of serotype 10A was also higher (6.1% versus 0.6%, respectively; \( P < 0.001 \)), whereas that of serotype 35B was lower (1.2% versus 4.5%, respectively; \( P = 0.031 \); Table 5). The distribution of serotype 10A in villages that took part in three MDA rounds was significantly heterogeneous (\( P = 0.012 \)), as was the distribution of serotype 35B in villages that took part in one round (\( P = 0.006 \)). By contrast, there was no significant difference in the distribution of serotypes 15B and/or 15C between the two villages that took part in three MDA rounds (\( P = 0.348 \)), which provides further evidence for the existence of a difference between the two treatment arms.

Further analysis indicated that individuals who were S. pneumoniae carriers in the first cross-sectional survey were significantly more likely than those who were not to be carriers in the second survey (adjusted OR, aOR: 3.71; Table 6). However, there was no significant association between the density of carriage at the first survey and carriage at the second survey: the aOR for carriage at the second survey for high-density versus low-density carriage at the first survey was 1.09 (95% CI: 0.66–1.80). In the second survey, pneumococcal carriage was less likely in individuals aged 10 years or older than in younger children (aOR: 0.33) and less likely in students (aOR: 0.24) and agricultural workers (aOR: 0.32) than in individuals with no occupation (Table 6).

### Table 2. Prevalence of nasopharyngeal Streptococcus pneumoniae carriage in individuals from villages exposed to three mass azithromycin administration rounds, by survey, Gambia, 2010

<table>
<thead>
<tr>
<th>Age of survey participants</th>
<th>Cross-sectional survey</th>
<th>No. of survey participants</th>
<th>No. (%) of S. pneumoniae carriers</th>
<th>Crude OR (95% CI)</th>
<th>Adjusted OR (^a) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 10 years</td>
<td>First (^b)</td>
<td>205</td>
<td>124 (60.5)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>Second (^b)</td>
<td>173</td>
<td>61 (35.3)</td>
<td>0.35 (0.23–0.53)</td>
<td>0.35 (0.23–0.53)</td>
</tr>
<tr>
<td></td>
<td>Third (^b)</td>
<td>182</td>
<td>116 (63.7)</td>
<td>1.14 (0.75–1.73)</td>
<td>1.14 (0.75–1.73)</td>
</tr>
<tr>
<td>≥ 10 years</td>
<td>First (^b)</td>
<td>210</td>
<td>56 (26.7)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>Second (^c)</td>
<td>244</td>
<td>19 (7.8)</td>
<td>0.22 (0.13–0.39)</td>
<td>0.23 (0.13–0.40)</td>
</tr>
<tr>
<td></td>
<td>Third (^c)</td>
<td>161</td>
<td>41 (25.5)</td>
<td>0.91 (0.57–1.47)</td>
<td>0.96 (0.59–1.55)</td>
</tr>
<tr>
<td>All</td>
<td>First (^b)</td>
<td>415</td>
<td>180 (43.4)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>Second (^c)</td>
<td>417</td>
<td>80 (19.2)</td>
<td>0.30 (0.22–0.41)</td>
<td>0.30 (0.22–0.42)</td>
</tr>
<tr>
<td></td>
<td>Third (^c)</td>
<td>343</td>
<td>157 (45.8)</td>
<td>1.09 (0.82–1.46)</td>
<td>1.09 (0.80–1.48)</td>
</tr>
</tbody>
</table>

CI: confidence interval; MDA: mass drug administration; OR: odds ratios. 
\(^a\) The OR was adjusted for age and sex and the within-village correlation of participants was taken into account using clustered robust standard errors. 
\(^b\) The first survey was carried out 11 months after the second MDA round. 
\(^c\) The second survey was carried out 1 month after the third MDA round. 
\(^d\) The third survey was carried out 6 months after the third MDA round.

### Table 3. Prevalence of nasopharyngeal Streptococcus pneumoniae carriage at the third survey, by azithromycin treatment, Gambia, 2010

<table>
<thead>
<tr>
<th>Age of survey participants</th>
<th>No. of MDA rounds</th>
<th>No. of survey participants</th>
<th>No. (%) of S. pneumoniae carriers</th>
<th>Crude OR (95% CI)</th>
<th>Adjusted OR (^a) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 10 years</td>
<td>1</td>
<td>182</td>
<td>136 (74.7)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>182</td>
<td>116 (63.7)</td>
<td>0.59 (0.29–1.17)</td>
<td>0.59 (0.30–1.17)</td>
</tr>
<tr>
<td>≥ 10 years</td>
<td>1</td>
<td>218</td>
<td>65 (29.8)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>161</td>
<td>41 (25.5)</td>
<td>0.72 (0.36–1.5)</td>
<td>0.69 (0.34–1.39)</td>
</tr>
<tr>
<td>All</td>
<td>1</td>
<td>400</td>
<td>201 (50.3)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>343</td>
<td>157 (45.8)</td>
<td>0.77 (0.41–1.44)</td>
<td>0.65 (0.35–1.20)</td>
</tr>
</tbody>
</table>

CI: confidence interval; OR: odds ratios; MDA: mass drug administration. 
\(^a\) The third survey was carried out 6 months after the third mass drug administration round. 
\(^c\) The OR was adjusted for age and sex and the within-village correlation of risk factors was taken into account using clustered robust standard errors.

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Azithromycin treatment and S. pneumoniae carriage in the Gambia

In that study, azithromycin-resistant pneumococcal strains was low, we observed that receiving three annual azithromycin MDA rounds was associated with a short-term decrease in pneumococcal carriage that was not accompanied by a significant increase in azithromycin resistance. There was no evidence of azithromycin resistance at the first cross-sectional survey in communities that received two MDA rounds. Moreover, since a previous study carried out in the same geographical area showed no evidence of erythromycin resistance in individuals carrying pneumococcus,22 we did not expect macrolide-resistant strains to be circulating before treatment. The absence of azithromycin resistance at the first cross-sectional survey is consistent with previous studies carried out in Australia, Nepal and the United Republic of Tanzania, all of which showed that substantial azithromycin resistance did not develop following a single treatment dose in areas where the baseline prevalence of the carriage of resistant strains was low.20,21 The prevalence of the carriage of azithromycin-resistant pneumococci rose to just over 1% at the second cross-sectional survey. However, at the third survey, there was no significant difference in prevalence between villages that received three annual MDA rounds and those that received one.

In contrast to our findings, a study carried out in central areas of the United Republic of Tanzania reported that a single MDA round significantly increased the prevalence of azithromycin resistance, which was detectable 6 months later.23 In that study, azithromycin-resistant pneumococcal strains...
were present in the community before treatment; 2.1% of pneumococcal strains isolated at baseline were resistant. Six months after the single MDA round, the proportion of resistant isolates was 35%. Since, in our study, we did not collect samples 6 months after MDA in areas that received a single MDA round, we cannot directly compare our results with those of the Tanzanian study and we cannot say what the immediate effect of a single MDA round was in the Gambian population. However, as we did not observe azithromycin resistance 6 months after the third MDA round in communities that received three rounds, it is unlikely that we would have observed resistance 6 months after the first MDA round. In addition, the Tanzanian study also reported a large variation in the proportion of individuals with azithromycin-resistant pneumococci in the untreated study arm: it ranged from 4.4% to 13.1%. Another difference between the two studies was that 65% of the participants in the Tanzanian study reported taking unspecified drugs to treat suspected infections in the 30 days before baseline azithromycin treatment, whereas only 2% of the participants in our study reported recent antibiotic use at the first survey. Moreover, a significant proportion of children in the Tanzanian study received amoxicillin for acute respiratory infections during the study period.

In the villages in our study that received three MDA rounds and where the prevalence of pneumococcal carriage and rates of transmission were high,16,22 the third MDA round decreased the prevalence of pneumococcal carriage from 43.4% at the first survey 11 months after the second MDA round to 19.2% at the second survey 1 month after the third round. However, this effect had already waned 6 months after treatment, by the time of the third survey. This short-lived reduction in pneumococcal nasopharyngeal carriage may, at least in part, explain the decrease in child mortality that has been reported following MDA in communities in Ethiopia16,22 since bacterial carriage is a proxy measure of invasive disease. Despite the significant reduction in the prevalence of pneumococcal carriage associated with the third MDA round, one month later, at the second survey, we were able to identify individuals who were pneumococcal carriers and who could still, therefore, transmit pneumococcus to the community. Being a carrier in the first cross-sectional survey was a risk factor for being a carrier one month after the third MDA round. The other risk factors for carriage after treatment were similar to known risk factors for pneumococcal carriage and included young age—which is consistent with previous findings indicating that children drive pneumococcal transmission.16,22

Serotype replacement is a concern in communities in which vaccines

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**Table 6. Risk factors for nasopharyngeal carriage of Streptococcus pneumoniae at the second survey** among individuals from villages exposed to three rounds of mass azithromycin administration, Gambia, 2010

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. of participants*</th>
<th>No. (%) of carriers of S. pneumoniae</th>
<th>Unadjusted OR (95% CI)</th>
<th>Adjusted ORb (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carrier at first survey*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>154</td>
<td>15 (9.7)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Yes</td>
<td>124</td>
<td>45 (36.3)</td>
<td>5.28 (2.77–10.07)</td>
<td>3.71 (2.44–5.64)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10 years</td>
<td>173</td>
<td>61 (35.3)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>≥10 years</td>
<td>244</td>
<td>19 (7.8)</td>
<td>0.16 (0.12–0.20)</td>
<td>0.33 (0.28–0.38)</td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>162</td>
<td>63 (38.9)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Student</td>
<td>149</td>
<td>13 (8.7)</td>
<td>0.15 (0.06–0.37)</td>
<td>0.24 (0.07–0.86)</td>
</tr>
<tr>
<td>Agricultural worker</td>
<td>104</td>
<td>4 (3.9)</td>
<td>0.06 (0.04–0.10)</td>
<td>0.32 (0.30–0.34)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>209</td>
<td>39 (18.7)</td>
<td>1.0</td>
<td>NA</td>
</tr>
<tr>
<td>Female</td>
<td>208</td>
<td>41 (19.7)</td>
<td>1.07 (0.81–1.41)</td>
<td>NA</td>
</tr>
<tr>
<td>Village*</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>217</td>
<td>32 (14.8)</td>
<td>1.0</td>
<td>NA</td>
</tr>
<tr>
<td>2</td>
<td>200</td>
<td>48 (24.0)</td>
<td>1.83 (1.83–1.83)</td>
<td>NA</td>
</tr>
<tr>
<td>Schooling, years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>258</td>
<td>67 (26.0)</td>
<td>1.0</td>
<td>NA</td>
</tr>
<tr>
<td>1</td>
<td>67</td>
<td>8 (11.9)</td>
<td>0.39 (0.18–0.84)</td>
<td>NA</td>
</tr>
<tr>
<td>2</td>
<td>48</td>
<td>2 (4.2)</td>
<td>0.12 (0.04–0.40)</td>
<td>NA</td>
</tr>
<tr>
<td>≥3</td>
<td>44</td>
<td>3 (6.8)</td>
<td>0.21 (0.18–0.24)</td>
<td>NA</td>
</tr>
<tr>
<td>Able to read</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>259</td>
<td>67 (25.9)</td>
<td>1.0</td>
<td>NA</td>
</tr>
<tr>
<td>Yes</td>
<td>158</td>
<td>13 (8.2)</td>
<td>0.26 (0.14–0.48)</td>
<td>NA</td>
</tr>
<tr>
<td>Able to write</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>259</td>
<td>67 (25.9)</td>
<td>1.0</td>
<td>NA</td>
</tr>
<tr>
<td>Yes</td>
<td>158</td>
<td>13 (8.2)</td>
<td>0.26 (0.14–0.48)</td>
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<tr>
<td>Recent health visit</td>
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<tr>
<td>No</td>
<td>405</td>
<td>75 (18.5)</td>
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</tr>
<tr>
<td>Yes</td>
<td>12</td>
<td>5 (41.7)</td>
<td>3.14 (2.87–3.44)</td>
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<td>Recent antibiotic use</td>
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<td></td>
<td></td>
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<tr>
<td>No</td>
<td>415</td>
<td>79 (19.0)</td>
<td>1.0</td>
<td>NA</td>
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<tr>
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<td>2</td>
<td>1 (50.0)</td>
<td>4.25 (0.15–122.58)</td>
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<td>Smoker in household</td>
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<td></td>
<td></td>
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<tr>
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<td>144</td>
<td>28 (19.4)</td>
<td>1.0</td>
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<tr>
<td>Yes</td>
<td>273</td>
<td>52 (19.1)</td>
<td>0.97 (0.57–1.66)</td>
<td>NA</td>
</tr>
</tbody>
</table>

CI: confidence interval; MDA: mass drug administration; NA: not applicable; OR: odds ratio.

* The second cross-sectional survey was carried out 1 month after the third MDA round.

b The OR was adjusted for carriage of S. pneumoniae at the first cross-sectional survey, age and occupation.

* The first survey was carried out 11 months after the second MDA round.

b Individuals from two villages participated in the survey.

* Within the last 30 days.
with limited valency have been used to protect against pneumococcal disease. However, our data suggest that azithromycin MDA did not modify the carriage of the most prevalent S. pneumoniae serotypes, except for serotypes 15B and/or 15C, which had a higher prevalence at the third site in the two surveys that received three MDA rounds than in villages that received one round. Moreover, the prevalence of the carriage of PCV-7 serotypes was not affected by MDA.

One limitation of this study is the small number of villages included. This was a consequence of our decision to include only villages in which children had received PCV-7, as recommended by WHO, because we wanted our findings to be relevant to countries that include PCV-7 in their national immunization programmes. As a result, we selected villages that had participated in the PRET trial and in a trial of the impact of pneumococcal nasopharyngeal carriage. We found that three MDA rounds, administered according to WHO guidelines, did not increase the prevalence of the carriage of azithromycin-resistant pneumococcal strains over the long term and that children played an important role in pneumococcal transmission in the community following azithromycin MDA.

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Funding: This study was funded by the Bill & Melinda Gates Foundation and the Medical Research Council, United Kingdom of Great Britain and Northern Ireland.

Competing interests: None declared.

MLA CYRUS
MS 7

Total Azithromycin MDA on the Population and Nasopharyngeal Pneumococcal carriage: Multi-Seasonal Surveys in Gambia

Sarah E Burr et al.

Research

Azithromycin treatment and S. pneumoniae carriage in the Gambia

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Tertiary azithromycin MDA in the setting of pneumococcal transmission: Multi-seasonal surveys in Gambia

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The main finding of this study was that azithromycin MDA did not affect the prevalence of nasopharyngeal carriage of pneumococci. However, the data suggest that azithromycin MDA may affect the transmission of pneumococci by children.

Achyle-Romsole and pneumococcal carriage: A young village in Gambia

The study evaluated the prevalence of nasopharyngeal pneumococcal carriage by children in a young village in Gambia. The purpose was to evaluate the effect of azithromycin MDA on nasopharyngeal carriage of pneumococci and to determine the role of the community in the transmission of pneumococci.

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Administration massive d’azithromycine et portage du Streptococcus pneumoniae: études transversales en Gambie

Objectif Evaluer l’effet de l’administration de médicament massif (AMM) répétée en Gambie sur le portage du Streptococcus pneumoniae dans le nasopharynx et sur l’émergence de souches résistantes aux antibiotiques.

Méthodes Cette étude a impliqué des villages qui ont participé à un essai randomisé par groupes, comparant l’effet d’un cycle d’AMM d’azithromycine par rapport à 3 cycles d’AMM d’azithromycine sur la prévalence du trachome. Seuls les villages dans lesquels la plupart des enfants ont reçu le vaccin antipneumococcique conjugué ont été inclus dans l’étude. Trois études transversales ont été menées dans 2 villages ayant reçu 3 cycles d’AMM; la première étude juste avant la troisième AMM, et les deuxième et troisième études 1 et 6 mois, respectivement, après la troisième AMM. La troisième étude a également couvert 6 villages qui avaient reçu une seule AMM 30 mois auparavant. Le portage pneumococcique a été évalué par le biais de prélèvements nasopharyngés, et la résistance à l’azithromycine a été détectée à l’aide de l’Etest.

Résultats La prévalence du portage pneumococcique a diminué de 43,4% à 19,2% entre la première et la deuxième étude (P < 0,001), mais elle a rebondi à la troisième étude (45,8%; P = 0,591). Le fait d’être porteur lors de la première étude était un facteur de risque pour être porteur lors de la deuxième étude (rapport des cotes: 3,71; P < 0,001). Dans la troisième étude, la prévalence du portage semblait similaire après un et 3 cycles d’AMM (50,3% contre 45,8%, respectivement; P = 0,170).

Conclusion Trois cycles d’AMM n’augmentent pas la prévalence du portage de souches Streptococcus pneumoniae résistantes à l’azithromycine dans le nasopharynx, par rapport à un seul cycle.
Porcentaje de posibilidades: 3,71%; P < 0,001. En la tercera encuesta, la prevalencia del transporte fue similar tras una y tres rondas de MDA (50,3% frente a 45,8%, respectivamente; P = 0,170), al igual que la prevalencia de la resistencia a la azitromicina (0,3% frente a 0,9%, respectivamente; P = 0,340).

**Conclusión** Las tres rondas de MDA de azitromicina no aumentaron la prevalencia del transporte nasofaringeo de cepas de S. pneumoniae resistentes a la azitromicina en comparación con una única ronda.

**Referencias**