The excessive use of antibiotics in ambulatory practice has contributed to the emergence and spread of antibiotic-resistant bacteria in our communities. Most alarming is the rapid rise in the prevalence of antibiotic-resistant *Streptococcus pneumoniae* observed over the past 15 years, specifically, *S pneumoniae* exhibiting nonsusceptibility (minimum inhibitory concentration [MIC], ≥0.1 µg/mL) and high-level resistance (MIC, ≥2.0 µg/mL) to penicillin. Often, these strains are also resistant to macrolides, trimethoprim-sulfamethoxazole, and second- and third-generation cephalosporins. Special attention to antibiotic resistance in *S pneumoniae* is warranted since this pathogen is the leading bacterial cause of community-acquired pneumonia, meningitis, and otitis media in the United States.

The environmental and genetic mechanisms that result in the development of penicillin resistance by *S pneumoniae* are complex. However, the major risk factor for carriage and spread of resistant *S pneumoniae* is clear: prior antibiotic use. Retrospective and prospective studies have documented the strong association between prior antibiotic use and the risk of carriage and invasive infection with resistant *S pneumoniae*. In addition, studies from Iceland and Finland have demonstrated that decreasing community-wide antibiotic use can lead to decreases in the prevalence of antibiotic-resistant bac-
teria. In Iceland, penicillin resistance in *S pneumoniae* isolates carried by children in day care centers decreased by 25% over a 3-year period, during which public and physician campaigns to reduce antibiotic use were successfully implemented. In Finland, a 40% reduction in community macrolide use was associated with a 48% decrease in the prevalence of erythromycin resistance among group A streptococcal isolates over a 4-year period.

Intervention strategies for reducing unnecessary antibiotic use in ambulatory practice must address the management of acute respiratory tract infections. In the United States, these illnesses are the indication for up to 75% of all antibiotics prescribed in the ambulatory setting each year, and, as a group, are the most frequent reasons Americans seek medical attention. Particularly relevant to reducing total antibiotic use are colds, upper respiratory tract infections (URIs), and bronchitis, since the vast majority of these illnesses have a viral cause and do not benefit from antibiotic treatment. About half of all office visits for colds and URIs, and up to 80% of all visits for bronchitis, are treated with antibiotics in the United States each year.

The majority of efforts to improve antibiotic prescribing practices in the ambulatory setting have emphasized judicious antibiotic selection, such as eliminating the use of contraindicated antibiotics and decreasing the use of broad-spectrum antibiotics. Although decreasing broad-spectrum antibiotic use in favor of narrow-spectrum antibiotic use is important, a reduction in total antibiotic use is most likely the critical step to decreasing the prevalence of antibiotic-resistant *S pneumoniae* in our communities. Our review of the literature identified a study from the United States that has reported on a successful intervention to decrease total antibiotic use in ambulatory practice and another in which coinurance was associated with lower total antibiotic prescriptions. The first, a noncontrolled study from the New Mexico Experimental Medical Care Re-

**METHODS**

**Setting**

Kaiser Permanente (KP) is a non-profit, group-model health maintenance organization that consists of 17 medical office practices serving approximately 350,000 members in the Denver-Boulder, Colo., metropolitan area. Members receive primary care services solely from KP clinicians, staff, laboratories, and, for 94% of members, KP pharmacies. Members make a variable copayment for office visits and prescriptions that is largely determined by the member’s employer contribution. Most patients with acute or urgent illnesses are given same-day appointments in these practices, rather than being seen in urgent care centers or emergency departments. Other health plan characteristics include a telephone advice-nurse system and a free self-care manual for each family.

**Study Design**

We conducted a nonrandomized, prospective controlled trial of a multidimensional intervention to reduce antibiotic use for uncomplicated acute bronchitis using a multiple time series design. The baseline period was November 1996 through February 1997, and the study period included the same months during the following year.

A full intervention site, a limited intervention site, and 2 usual care control sites were selected from the largest of 17 medical office practices at KP. The full intervention site received household and office-based patient educational materials, as well as a clinician educational intervention (described in more detail below). The limited intervention site received office-based educational materials only. The full intervention was assigned to the site that had a medical director who was prepared to accept the role of opinion leader, and the limited intervention was assigned to the site that had a nurse supervisor who was agreeable to placing the office-based educational materials in each examination room. Two usual care control sites were identified that matched (as a group) the full and limited intervention sites. Matching variables included total adult membership size, age, sex, and relative prevalence (observed-to-expected ratios) of certain chronic medical conditions (diabetes mellitus, chronic obstructive pulmonary disease, and circulatory disorders) that were based on rates of prescriptions for pertinent drugs (D. Roblin, PhD, written communication, July 1997). The identification of the 2 usual care control sites was performed prior to data collection and analysis. All statistical tests were performed, and results expressed, with the combination of these 2 sites representing the control population.
Intervention
We conducted several preliminary studies to gain a greater understanding of why physicians prescribe, and patients expect, antibiotics for acute bronchitis. The major findings from these studies used in our intervention strategy included the following: (1) clinicians, in general, appear to use the diagnosis of acute bronchitis as an indication for antibiotic treatment, rather than rely on specific clinical features of the illness; (2) patient expectations for antibiotic treatment of acute bronchitis are strongly associated with previous antibiotic treatment of bronchitis; and (3) the diagnosis of "chest cold" rather than "bronchitis" for a productive cough illness is associated with lower patient expectations for antibiotic treatment. As a result of these findings, the major themes of the educational message to patients and physicians were as follows: (1) antibiotics do not benefit and are usually not indicated for uncomplicated acute bronchitis; (2) because excessive antibiotic use for acute respiratory tract infections is fueling the current epidemic of community antibiotic-resistant bacteria, we must now be more selective in prescribing antibiotics for only those conditions likely to benefit from treatment; (3) recent antibiotic exposure places individual patients and families at increased risk for carriage of and infection with antibiotic-resistant bacteria; and (4) clinicians should refer to a cough illness as a "chest cold" when antibiotics appear not to be indicated.

Household educational materials were mailed to all full intervention households (n = 25 000) receiving primary care services at the full intervention site at the beginning of the study period (November 1997). These materials included the following: (1) large refrigerator magnets outlining issues related to prevention, self-care, when to seek care, and what to expect from the office visit for colds, flu, and bronchitis; (2) a pamphlet entitled "Your Child and Antibiotics—Sometimes Antibiotics Can Be Harmful" produced by the Centers for Disease Control and Prevention, Atlanta, Ga; (3) a pamphlet entitled "Operation Clean Hands" that addressed proper handwashing techniques, produced by Bayer Pharmaceutical Division, West Haven, Conn; and (4) a letter from the medical director of the full intervention site announcing the campaign to combat antibiotic resistance by reducing unnecessary antibiotic use.

The office-based educational materials were directed at patients as well as clinicians and were specific for acute bronchitis. Materials were delivered at the beginning of the study period to the nursing supervisors of the full and limited intervention sites, who were instructed to place the materials in every primary care examination room (family medicine and internal medicine). Materials consisted of colorful posters that were attached to the wall of each room and were accompanied by information sheets on the limited role of antibiotic treatment of "acute bronchitis or chest colds" for patients to take home. The posters included 3 graphics: (1) the lack of effect of antibiotic treatment on duration of illness for "bronchitis or chest colds"; (2) the epidemic curve for the prevalence of invasive antibiotic-resistant S pneumoniae in Colorado; and (3) a graph depicting the risk of carriage of antibiotic-resistant S pneumoniae stratified by prior antibiotic use. (Examples of these educational materials are available for viewing on the Internet at http://www.uuchsc.edu/u1gim/educate/bronchitis .html.)

The clinician intervention was administered to the full intervention site at the beginning of the study period and consisted of a description of the patient educational intervention, site-specific (but not provider-specific) antibiotic prescription rates for acute bronchitis calculated from the previous winter (practice profiling), education on the evidence-based management of acute bronchitis, and advice on how to say "no" to patient demands for antibiotics. The clinician intervention was presented over a single 30-minute time period during regularly scheduled family medicine and internal medicine staff educational meetings. These meetings were led by the medical director of the facility and were attended by clinic physicians, nurse practitioners (NPs), physician assistants (PAs), and registered nurses (RNs). Although a formal count of the proportion of clinicians present at each meeting was not performed, most clinicians were present. The meeting was concluded with setting future goals for antibiotic prescription rates for acute bronchitis.

Subjects
Eligible patients included all adults 18 years of age and older with an office visit for acute bronchitis, sinusitis, or URI during the baseline and study periods. All clinicians caring for patients diagnosed as having these conditions were included in the analysis, including board-certified internal medicine and family practice physicians, NPs, PAs, and RNs. Visits to RNs were discussed with a supervising physician, and prescriptions by RNs always required the supervising physician's signature. The clinicians at the limited intervention and usual care control sites were not informed of the study's objectives. However, because of the nature of the intervention, it was not possible to blind clinicians at the full intervention site to the intent of the intervention.

Measurements
Incident adult office visits during which patients were diagnosed as having acute bronchitis (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] code 466.0) during the specified periods were identified from the KP office visit administrative database. Incident visits were defined as representing the first office visit for any acute respiratory illness during the baseline or study period. We defined a return visit as a subsequent visit occurring within 30 days of an incident visit. To calculate antibiotic prescription rates for uncomplicated acute bronchitis, we excluded visits with sec-
ondary diagnoses of chronic heart and lung disease, as well as visits that also listed ICD-9-CM codes for other concomitant acute respiratory tract illnesses for which antibiotic therapy might be indicated (sinusitis, pharyngitis, otitis media, pneumonia). To evaluate whether the intervention might lead some clinicians to select related diagnoses that were not being studied, we also measured incident office visits for uncomplicated sinusitis (ICD-9-CM code 461.9) and uncomplicated URIs (ICD-9-CM code 465.9) and calculated antibiotic prescription rates using similar exclusion criteria.

Prescribing data were extracted from a separate pharmacy administrative database and reflect the number of antibiotic prescriptions dispensed. The reliability and validity of this database is maintained through routine internal auditing. We used American Hospital Formulary Service Drug Information 36 (AHFS) codes 080000 to 084999 to identify antibiotic prescriptions that coincided by exact date with the office visits of interest. The AHFS codes were also used for calculating prescription rates for inhaled bronchodilators (AHFS codes 121200 and 120808), cough suppressants (AHFS codes 480800 and 481600), and analgesics (AHFS codes 280804, 280808, and 280892).

All office visit and prescription data were extracted by individuals who were unaware of the study’s objectives. Other data collected for each visit from the office visit administrative database included patient age and sex, department specialty (family medicine, internal medicine, or other), and clinician type (physician, NP, PA, and RN). Individual provider identification numbers were available for staff physicians, NPs, and PAs, but not for RNs or part-time temporary physicians.

**Statistical Analysis**

Univariate measures were used to compare usual care control, limited intervention, and full intervention sites with respect to member age, sex, and chronic medical conditions, as well as clinician type and specialty. Incident office visit rates for uncomplicated acute bronchitis and other acute respiratory tract infections during the baseline and study periods were calculated by dividing the total number of incident visits for each condition by the average adult membership during each period. To evaluate the impact of the intervention on prescribing practices within and between sites, we used a mixed-effects model, using the PROC MIXED macro in the SAS statistical application program, to control for potential clustering (random effects) of clinicians by site. Mixed-effects models are the appropriate statistical test for population-based intervention studies when it is not feasible to randomize individuals (or physicians) to intervention and control groups, yet patient-level observations remain the unit of analysis. 37 For within-site analyses, month, patient age and sex, and clinician type and specialty were included as fixed effects. For between-sites analyses, we also added site as a fixed effect, and statistical significance was defined as P < .05 for the interaction term site times the month, indicating that the slope of the antibiotic prescription rate over time differed between sites. 38 All statistical analyses were performed using the SAS Statistical Application Program (release 6.12, SAS Institute, Inc, Cary, NC).

**RESULTS**

A demographic comparison of the control, limited intervention, and full intervention sites is presented in Table 1. Total adult membership for each study population ranged from 34 978 to 46 767 at the beginning of the intervention period (November 1997). Total staffing during the intervention period included 56 physicians, 28 nurse practitioners or physician assistants, and 9 registered nurses.

Antibiotic prescription rates for adults diagnosed as having uncomplicated acute bronchitis, uncomplicated URIs, and uncomplicated sinusitis during the baseline and intervention periods are displayed in Figure 1. A total of 2462 adults were included at baseline and 2027 adults were included in the study. During the baseline period, within-site analyses of antibiotic prescription rates for bronchitis were constant at the control, limited intervention, and full intervention sites (P = .58, 40, and .13, respectively). During the study period, the full intervention site demonstrated a substantial decline in antibiotic prescribing for bronchitis (from 74% to 48%; P = .003), whereas the control and limited intervention sites showed no significant changes (from 78% to 76% [P = .81] and 82% to 77% [P = .68], respectively). Between-sites analysis also confirms that the

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### Table 1. Study Site Characteristics, November 1997

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Control* (n = 46 767)</th>
<th>Limited Intervention (n = 36 404)</th>
<th>Full Intervention (n = 34 978)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age in yrs, %</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-44</td>
<td>49</td>
<td>47</td>
<td>51</td>
</tr>
<tr>
<td>45-64</td>
<td>35</td>
<td>35</td>
<td>34</td>
</tr>
<tr>
<td>≥65</td>
<td>16</td>
<td>18</td>
<td>15</td>
</tr>
<tr>
<td><strong>Female, %</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>54</td>
<td>55</td>
<td>54</td>
</tr>
<tr>
<td><strong>Chronic medical conditions, observed-to-expected ratios†</strong></td>
<td>1.15</td>
<td>1.03</td>
<td>1.15</td>
</tr>
<tr>
<td><strong>Staffing, No.</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family medicine department</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physician</td>
<td>4 (4/0)</td>
<td>5 (4/1)</td>
<td>5 (4/1)</td>
</tr>
<tr>
<td>Nonphysician provider‡</td>
<td>12 (8/4)</td>
<td>6 (5/1)</td>
<td>5 (3/2)</td>
</tr>
<tr>
<td>Internal medicine department</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physician</td>
<td>18</td>
<td>14</td>
<td>12</td>
</tr>
<tr>
<td>Nonphysician provider‡</td>
<td>0</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>34</td>
<td>31</td>
<td>28</td>
</tr>
</tbody>
</table>

*Control group represents the combination of 2 practice sites (see “Methods” section). †Observed-to-expected ratios (relative prevalence) based on rates of prescriptions for drugs related to diabetes mellitus, chronic obstructive pulmonary disease, and circulatory disorders. ‡Numbers in parentheses are numbers of nurse practitioners or physician assistants/registered nurses.
rate of change in monthly antibiotic prescription rates for uncomplicated acute bronchitis was greater at the intervention site than at the control and limited intervention sites ($P = .02$).

The decrease in antibiotic prescribing for uncomplicated acute bronchitis was not associated with increases in antibiotic prescribing for other similar conditions (Figure 1). Antibiotic prescribing for uncomplicated URIs declined at all sites between the baseline and study periods, but to a similar extent at all sites ($P > .05$ for all comparisons). Antibiotic prescribing for uncomplicated sinusitis was relatively unchanged between the baseline and control periods (control, 88% to 88%; limited intervention, 85% to 91%; and full intervention site, 87% to 89%).

Figure 1. Antibiotic Prescription Rates for Uncomplicated Acute Bronchitis, Uncomplicated Upper Respiratory Tract Infections (URIs), and Uncomplicated Sinusitis During the Baseline and Study Periods at the Control, Limited Intervention, and Full Intervention Sites

The antibiotic prescription rate, which was defined as the proportion of incident office visits where the patient received an antibiotic prescription, for each month is shown. Antibiotic prescriptions for January 1997 (1/97) at the control sites are imputed because of missing pharmacy data. Imputation was performed using the average monthly antibiotic prescription rate at the control site during the other baseline months. The control group represents the combination of 2 practice sites (see “Methods” section). The asterisk indicates $P = .003$ for within-site decrease in the monthly antibiotic prescription rate. The dagger indicates $P = .02$ for between-sites differences in the monthly antibiotic prescription rates. No other comparisons achieved statistical significance ($P < .05$). All comparisons were performed using a mixed-effects model and adjusted for patient age and sex, and clinician type and specialty.

Figure 2. Incident Office Visit Rates for Uncomplicated Acute Bronchitis, Uncomplicated Upper Respiratory Tract Infections (URIs), and Uncomplicated Sinusitis During the Baseline and Study Periods at the Control, Limited Intervention, and Full Intervention Sites

The incident office visit rate was per 1000 members per period and was defined as the first visit per patient per period for a given condition divided by the average total adult health plan membership during each period. The control group represents the combination of 2 practice sites (see “Methods” section).
We were concerned that scrutinizing the management of acute bronchitis could have induced a decrease in the use of that diagnosis, coupled with an increase in the use of a diagnosis for which antibiotics are appropriate (such as acute sinusitis). Therefore, we measured incident office visit rates for adults with uncomplicated acute bronchitis at the control and intervention sites during the baseline and study periods (Figure 2). These visits represent the care of 42, 41, and 37 different clinicians (excluding RN and weekend physician visits) at the control, limited intervention, and full intervention sites, respectively, during the study period. The median number of visits per clinician was also similar between sites (control site, median = 7; limited intervention site, median = 5; and full intervention site, median = 8).

Incident visits declined during the study period at each site (Figure 2). There was a greater decline in incident visits for uncomplicated acute bronchitis at the limited intervention site (−28%; P = .05), but not the full intervention site (−22%; P = .41), compared with the control site (−17%). The decline in office visits (or diagnoses) for uncomplicated acute bronchitis was not associated with increases in visits for uncomplicated URIs or sinusitis. In fact, visits for these conditions also declined at all sites between the baseline and study periods (Figure 2).

We also evaluated whether reducing antibiotic treatment for uncomplicated acute bronchitis was associated with increases in prescriptions for other medications or increases in return office visits. The impact of the intervention on the most common nonantibiotic prescriptions is shown in Table 2. We found that the treatment of acute bronchitis with inhaled bronchodilators increased significantly at all 3 sites between the baseline and study periods; however, the percentage change did not differ between sites after adjusting for patient age and sex, clinician type and specialty, and clinician clustering. The rates of change in cough suppressant and analgesic prescriptions between the baseline and study periods were also not significantly different between sites.

There was no difference in return visit rates (an office visit ≤30 days from an incident visit for uncomplicated acute bronchitis) for the same diagnosis (acute bronchitis) between the baseline and study periods at each site (Table 2). The proportion of patients diagnosed as having uncomplicated acute bronchitis at the incident visit who were subsequently diagnosed as having pneumonia at a return visit was very low and ranged from 0.5% to 1.5%. Compared with the baseline period, the proportion of patients with a return visit for pneumonia during the study period increased at the control and limited intervention sites and decreased slightly at the full intervention site. The percentage change at the full intervention site compared with the control site did not reach statistical significance (P = .08).

Table 2. Proportion of Patients Diagnosed as Having Uncomplicated Acute Bronchitis Receiving Prescriptions for Nonantibiotic Medications and Returning for Care (Within 30 Days) During the Baseline and Study Periods

<table>
<thead>
<tr>
<th>Medications</th>
<th>Control†</th>
<th>Limited Intervention</th>
<th>Full Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Study, % (n = 850)</td>
<td>Study, % (n = 751)</td>
</tr>
<tr>
<td>Bronchodilators</td>
<td>16.8%</td>
<td>27.8%</td>
<td>11.0%</td>
</tr>
<tr>
<td>Cough suppressants</td>
<td>28.2%</td>
<td>37.0%</td>
<td>8.8%</td>
</tr>
<tr>
<td>Analgesics</td>
<td>3.7%</td>
<td>3.5%</td>
<td>−0.2%</td>
</tr>
<tr>
<td>Return office visits</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute bronchitis</td>
<td>5.9%</td>
<td>5.7%</td>
<td>−0.2%</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>0.5%</td>
<td>1.5%</td>
<td>1.0%</td>
</tr>
</tbody>
</table>

* indicates total number of incident office visits for uncomplicated acute bronchitis during each period at each site.
†Control group represents the combination of 2 practice sites (see “Methods” section).
‡Compared with control, P = .08.

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DECREASING ANTIBIOTIC USE IN AMBULATORY PRACTICE

bronchitis received widespread local and national attention in the medical literature and lay press.17 Despite this publicity, we found little change in the high antibiotic prescription rates for uncomplicated acute bronchitis at the control and limited intervention sites. The persistence of antibiotic prescribing for uncomplicated acute bronchitis underscores the limited effect of these traditional mechanisms of information dissemination on physician practice patterns.18-22 Others have reported that dissemination of a clinical practice guideline for reducing antibiotic use for URIs had only a modest and short-lived impact on antibiotic prescribing.23

Factors that influence the overuse of antibiotics for viral respiratory tract illnesses such as acute bronchitis include patient expectations for antibiotics, purulence of secretions, and physician workload.24,25,28,29 Because multiple reasons lead to prescribing antibiotics for acute bronchitis, it follows that the most effective intervention strategy to reduce antibiotic use must also be multifactorial. The failure to affect antibiotic prescribing at the limited intervention site using office-based materials alone suggests that delivering the message about reducing antibiotic use to the public, patient, and clinician simultaneously created the synergy necessary to decrease antibiotic use for acute bronchitis in our population. It is also possible, however, that the clinician intervention unique to the full intervention site (practice profiling, academic detailing, goal-setting, and feedback by an opinion leader) might have been effective without the member and patient educational components. Academic detailing usually refers to one-on-one educational outreach that is based on pharmaceutical representative strategies to alter physicians’ prescribing practices.30 Specific principles of academic detailing that we applied in our group meetings included emphasizing effective techniques of patient-clinician communication, understanding and targeting motivations (patient and clinician) underlying the practice of interest, involving opinion leaders, encouraging 2-sided communication, using brief graphic materials, and offering practical alternatives.

Several limitations of this study should be considered in interpreting the results. Because we did not randomize the study sites, it is possible that the full intervention site differed from the other sites in its receptivity (by patients and/or clinicians) to decreasing antibiotic use. The equal baseline antibiotic prescription rates between sites and the lack of changes in antibiotic prescriptions for sinusitis and URIs argue against this possibility, but do not rule it out. Similarly, it is also possible that patients who enroll, and clinicians who practice, in group-model health maintenance organizations may be more responsive to the approach we used. For example, clinicians who have their prescribing practices profiled routinely, such as those at KP, are more likely to respond favorably to profiling.31 We did not conduct any formal process evaluations of our intervention on patient and clinician knowledge and attitudes relating to antibiotic use and acute bronchitis, partly due to a desire to minimize potential bias and partly due to resource availability. This information would strengthen cause and effect conclusions and perhaps identify components of the intervention that were not effective. Lack of this information, however, should not threaten the validity of our findings. Finally, because we measured antibiotic prescriptions filled by the KP pharmacy, we did not account for prescriptions written but not filled, as well as patients taking prescriptions to outside pharmacies. There are no indications that these omissions were present to a great degree or that they occurred differentially between sites.

These results demonstrate that a meaningful reduction in antibiotic use for acute respiratory tract illnesses such as acute bronchitis is attainable at a large group-model health maintenance organization. Although it is not known whether the total intervention or its specific components would be effective in other practice settings, we believe the approach we used shows promise as a model for designing future interventions aimed at decreasing ambulatory antibiotic use. This approach emphasizes (1) the identification, within a specific population, of relevant patient, physician, and health care delivery system factors that influence the treatment of interest, and (2) coordinated patient and clinician interventions that target these factors. Future studies are necessary to determine the sustainability of the impact of our intervention on prescribing practices and to characterize the impact of further decreases in antibiotic use on patient-centered outcomes.

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