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Impact of a 16-Community Trial to Promote Judicious Antibiotic Use in Massachusetts

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ABSTRACT

OBJECTIVES. Reducing unnecessary antibiotic use, particularly among children, continues to be a public health priority. Previous intervention studies have been limited by size or design and have shown mixed results. The objective of this study was to determine the impact of a multifaceted, community-wide intervention on overall antibiotic use for young children and on use of broad-spectrum agents. In addition, we sought to compare the intervention’s impact on commercially and Medicaid-insured children.

METHODS. We conducted a controlled, community-level, cluster-randomized trial in 16 nonoverlapping Massachusetts communities, studied from 1998 to 2003. During 3 years, we implemented a physician behavior-change strategy that included guideline dissemination, small-group education, frequent updates and educational materials, and prescribing feedback. Parents received educational materials by mail and in primary care practices, pharmacies, and child care settings. Using health-plan data, we measured changes in antibiotics dispensed per person-year of observation among children who were aged 3 to <72 months, resided in study communities, and were insured by a participating commercial health plan or Medicaid.

RESULTS. The data include 223 135 person-years of observation. Antibiotic-use rates at baseline were 2.8, 1.7, and 1.4 antibiotics per person-year among those aged 3 to <24, 24 to <48, and 48 to <72 months, respectively. We observed a substantial downward trend in antibiotic prescribing, even in the absence of intervention. The intervention had no additional effect among children aged 3 to <24 months but was responsible for a 4.2% decrease among those aged 24 to <48 months and a 6.7% decrease among those aged 48 to <72 months. The intervention effect was greater among Medicaid-insured children and for broad-spectrum agents.

CONCLUSIONS. A sustained, multifaceted, community-level intervention was only modestly successful at decreasing overall antibiotic use beyond substantial secular trends. The more robust impact among Medicaid-insured children and for specific medication classes provides an argument for specific targeting of resources for patient and physician behavior change.

Reducing antibiotic overuse, particularly among children, has been identified as a public health priority since the mid-1990s. The rapid increase in resistance among common bacterial pathogens, such as Streptococcus pneumoniae, is widely believed to be fueled by high rates of antibiotic use, much of which is unnecessary. Because of the communicability of bacterial pathogens, the consequences of resis-
Isolates of *S. pneumoniae* in the early 1990s, data are mixed on the ability of community-level interventions to change antibiotic-use rates. Although overall national antibiotic-use rates have decreased markedly since the early 1990s, data are mixed on the ability of community-level interventions to change antibiotic-use rates. Most have been limited in the number of communities studied, the ability to control for differences among them, or the duration of intervention.

We sought to determine, as precisely as possible, the impact of a sustained, community-wide program designed to change both physician and patient behavior to decrease unnecessary antibiotic use. Antibiotic resistance is a community-level public health concern, and randomized intervention of individual patients or providers would be susceptible to unacceptable contamination between intervention and control states; therefore, we conducted a 16-community, cluster-randomized trial of the Reducing Antibiotics for Children in Massachusetts (REACH Mass) intervention. We previously reported measures of parental knowledge, physician self-reported behavior, and antibiotic resistance rates among colonizing isolates of *S. pneumoniae*; however, our primary goal was to test whether a 3-year sustained intervention decreased the number of dispensings of antibiotics to children overall. A secondary analysis tested whether the intervention increased the fraction of appropriate, narrow-spectrum agents used, compared with patterns seen in control communities. Finally, after analysis of baseline (October 2000) survey data from these communities showing that parents of Medicaid-insured children had more misconceptions regarding appropriate antibiotic use, we became particularly interested in whether differential effects of the intervention would be seen among children from low-income families.

**METHODS**

**Design and Setting**

REACH Mass was a community-level, cluster-randomized trial that was conducted in 16 Massachusetts communities in collaboration with the Massachusetts Department of Public Health and 4 large health insurers (including Medicaid). We selected communities for randomization to be nonoverlapping in geography and in patterns of medical care. To achieve this, we analyzed data from a single large health insurer and identified clusters of contiguous zip codes (communities) that (1) maximized the fraction of resident children who also had a primary care physician within their own community and (2) minimized the number of children who lived outside the community and received primary care within the community. We identified 16 nonoverlapping towns, dichotomized them into small and large towns, paired them by a composite of percentage of Medicaid and percentage of racial minority residents on the basis of US Census 1990 data, and randomly assigned pairs to intervention or control status by using a computer routine (SAS; SAS Institute, Inc, Cary, NC). Neither physicians nor others in these 16 communities were approached regarding their willingness to participate in any aspect of this study before randomization. Deidentified data from all patients who were insured by the participating health plans are included, regardless of whether they or their providers participated in intervention activities.

**Intervention**

The intervention was conducted during 3 successive cold and influenza seasons, (October through March) from 2000 to 2003. Activities were directed at providers and their practices and at patients (through direct mail, a Web site, pharmacies, and child care centers). A panel of local content experts and representatives of the Massachusetts Department of Public Health and local health plans adapted CDC guidelines for judicious antibiotic prescribing for use in Massachusetts. All REACH Mass messages and materials were designed to be consistent with these guidelines.

**Materials Development**

Materials were designed by using principles of academic detailing and social marketing to be simple, to be attractive, and to change specific behaviors of physicians or parents. Parent resources included a trifold brochure entitled “Kids and Antibiotics” with general information about antibiotic use and resistance; 4 illness-specific patient information cards on antibiotic use in colds, ear infections, fluid in the middle ear, and sore throat; and office posters with key messages about antibiotic use. Major messages presented in study materials included the following: (1) antibiotics are not helpful for cough, cold, and flu-like illnesses; (2) unnecessary antibiotic use contributes to resistance in individuals and communities; and (3) green nasal discharge does not indicate a need for antibiotics. In the final year of the study, information was presented to encourage parents and providers to discuss the option of “watchful waiting” for mild ear infections. An information sheet was specifically designed to be used as part of a discussion of appropriate antibiotic use at well-child visits. "Prescrip-
Physician Intervention

An introductory letter was mailed to all pediatricians and family physicians in intervention communities in the spring of 2000. All practices were approached, and, whenever possible, a single physician contact was established. Prescribing providers were invited to attend kickoff dinners for all practices in a community during the first intervention winter in which the general problem of antibiotic overuse and resistance was presented and the intervention was described in detail. In particular, we proposed to (1) provide a range of patient education materials to physician offices without charge, (2) provide ongoing information about antibiotic-use rates and resistance in the community, (3) provide feedback about prescribing by practice, and (4) serve as a general resource on issues of antibiotic prescribing and resistance. Physicians were also given copies of educational materials that parents would be receiving through direct mail during the course of the subsequent 3 winters to combat patient “demand” for unnecessary antibiotic use.

During the 3 intervention seasons, the physicians received approximately bimonthly faxed or e-mailed briefs (≤1 page) on a topic related to antibiotic use, respiratory tract infections, or antibiotic resistance. Visits to each practice were made by an educational coordinator to answer questions about the study and to provide additional materials to physicians and practice staff. A second series of community dinner meetings for providers was conducted in the third intervention season to reinforce key messages and focus additionally on the diagnosis and treatment of acute otitis media. Although this study predated the release of professional guidelines in the United States endorsing “watchful waiting,”18 of selected cases of acute otitis media, data about the safety of this approach were reviewed. Investigators also presented at grand rounds in community hospitals wherever possible.

Parent Intervention

Addresses of families with at least 1 child who was younger than 6 years and residing in intervention communities were supplied by the 4 participating health plans. Intervention activities directed at parents included the following:

- an initial letter mailed to families in the 8 intervention communities in January of the first intervention winter with a copy of the core brochure;
- REACH Mass newsletters mailed twice each winter to address key topics related to antibiotic use and to combat misconceptions that were found to be prevalent in these communities27;
- the REACH Mass Web site (www.reach-mass.org) with all content used in patient education materials, as well as interactive activities for parents and children;
- posters, illness-specific handouts, and stickers distributed in the offices of participating physicians;
- counter-top displays with handouts and stickers distributed to chain and independent pharmacies in intervention communities;
- training (in year 3) of local child care center directors and teachers by a REACH Mass health educator and a local physician covering topics of antibiotic resistance and appropriate exclusion policies for upper respiratory illnesses.

Data Collection and Analysis

We analyzed health insurance claims data from all children who were ≤6 years of age and resided in study communities (as defined by zip code clusters) and were insured by 1 of the participating health plans, with coverage for medications, for 90 days or more between September 1, 1998, and March 31, 2004. Total days of health-plan membership were divided by 365 to obtain person-years of observation in 3 age groups in each of the study years: 3 to <24, 24 to <48, and 48 to <72 months. Outcomes were analyzed as antibiotic dispensings per person-year of observation.

Claims (with International Classification of Diseases, Ninth Revision, diagnosis codes) for all ambulatory, emergency department, and inpatient hospital encounters were analyzed. A separate file contained pharmacy claims of all oral antimicrobial agents, identified by a list of national drug codes of interest. These pharmacy claims included only medicines that were actually dispensed to patients, including both primary prescriptions and refills.

The primary outcome of interest was the overall number of oral antibiotic dispensings per person-year of observation in the 3 age groups of interest in each study year. Antibiotic-dispensing rates were calculated on an annual basis from September 1, 1998, to August 31, 2003, to reflect the beginning of a new school year and respiratory illness season. Data were collected for 2 preintervention years (September 1, 1998, to August 31, 2000) and for 3 years during which intervention activities occurred (September 1, 2000, to August 31, 2003). Annual dispensing rates per person-year were plotted for patients who lived in intervention and control communities, stratified by age and commercial insurance or Medicaid. To account for clustering of individuals within communities, we used generalized linear mixed models, assuming a Poisson distribution for counts per person-year of antibiotic prescriptions dispensed. For analysis of secular trend, we modeled the annual rates by age in control communities only, accounting for clustering of observations within communities but no other covari-
ates. Age-stratified models were used to assess intervention impact and included terms to allow for differences in baseline prescribing levels between intervention and control communities, secular trend during the study period, gender, and insurance type (for models not stratified by insurance). These models produced adjusted estimates of the percentage change in antibiotics dispensed per person-year during the 3-year intervention period. Intervention impact (the primary outcome) was calculated as the difference between this change in intervention and control communities. Similar age-stratified models were created to assess intervention impact among commercially insured and Medicaid-insured patients. Finally, we examined intervention impact on prescriptions by antibiotic class using the same analytic and statistical methods, with special attention to changing rates of amoxicillin-clavulanate and second-generation macrolide (azithromycin and clarithromycin) prescriptions. All analyses were performed by using SAS 9.1 (SAS Institute, Cary, NC).

RESULTS

Population Characteristics

The 16 communities ranged in population size from 30,000 to 139,000 and were sociodemographically diverse, as reflected by available US Census 2000 data on median family income and percentage of minority residents (Table 1). The analysis includes all of the 16 communities (clusters) initially randomized. During the 5 years of the study (including 2 years before the intervention and 3 years of intervention), there were 223,135 person-years of observation of children who were 3 months to < 72 months of age from the 4 participating insurers. In the 5 study years, the average contribution of individual children in each year varied by year from 0.67 to 0.71 person-years of observation. Intervention and control communities were well matched on population size, median income, and percentage of nonwhite individuals.

Participation in Intervention Activities

Judicious antibiotic-use guidelines were mailed to all prescribing clinicians in intervention communities, and 54 of the 207 clinicians in these communities attended the local kickoff dinners (others attended grand rounds at local hospitals). During the second year, small-group discussions with clinicians were held at 11 of the largest pediatric practices. Follow-up community-wide dinner presentations were attended by 74 clinicians in the third season. The REACH Mass educator made visits to 56 of the 70 practices in the first year to distribute patient education materials described. In year 1, ~22,000 copies of the introductory brochure and first newsletter were mailed, with 2 similar-sized mailings in each of the subsequent years. Toward the end of the first intervention season, materials were also mailed to 156 child care centers, with workshops for child care professionals conducted in each of the 8 intervention communities in year 3. Prescribing reports were mailed to 77 clinicians with sufficient prescribing data available. A total of 19 issues of REACH Notes were faxed or e-mailed to 250 clinicians during the second and third intervention seasons. The REACH Mass educator maintained contact with both office staff and the primary clinician contact at each of the practices through telephone and in-person visits.
Secular Trends and Intervention Impact

Overall, antibiotic-use rates in year 1 of the study (baseline) were 2.8, 1.7, and 1.4 dispensings per person-year in the 3 age groups, 3 to <24, 24 to <48, and 48 to <72 months, respectively, and were similar among intervention and control communities (Table 2). Baseline use rates were slightly higher among children with Medicaid insurance compared with those with commercial insurance ($P < .001$). Because of these baseline differences in antibiotic use and knowledge between parents of Medicaid- and commercially insured children, we present both overall analyses and subanalyses stratified according to insurance type.

Figure 1 displays yearly crude antibiotic-prescribing rates, stratified by insurance type and age group, to show year-to-year variability, secular trends, and the magnitude of the unadjusted intervention effect. Among all insurance groups, we observed a significant downward trend in antibiotic use, even in control communities, among those aged 3 to <24 months ($P < .001$) and those aged 24 to <48 months ($P < .001$). More year-to-year variability is seen among children aged 48 to <72 months, with a small decrease observed for non–Medicaid-insured children ($P = .02$) but none for Medicaid-insured children ($P = .73$).

Table 2 provides both the crude rates in the first baseline study year and the adjusted percentage change in antibiotic prescribing during intervention years 3 to 5, accounting for clustering of data within communities and for potential confounders. For the population overall (including both Medicaid- and commercially insured children), in the youngest age group (3 to <24 months) we observed dramatic (>20%) adjusted decreases in antibiotic use in both control and intervention communities during the 5-year study period. We observed no effect of our intervention in this age group. In contrast, among children aged 24 to <48 months, we observed a 4.2% intervention effect ($P < .01$), and among children aged 48 to <72 months, we observed a 6.7% intervention effect ($P < .001$) in the population overall.

The intervention effect was greater among Medicaid-insured children compared with commercially insured children. For example, among those insured by Medicaid, the decrease in antibiotic prescribing attributable to the 3-year intervention was 4.5% among children aged 3 to <24 months ($P = .01$), 5.5% among those aged 24 to <48 months ($P = .01$), and 9% among those aged 48 to <72 months ($P < .01$). In contrast, among commercially insured children, a significant intervention effect of 5.1% was observed among children aged 48 to <72 months ($P = .01$) but not for the other age groups.

In year 1, first-line penicillins (penicillin and amoxicillin) accounted for slightly more than half (51%) of all antibiotic use. The fraction of antibiotic dispensings accounted for by each class was similar across age groups, with broad-spectrum macrolides (primarily azithromycin) accounting for 12%, 14%, and 13% in the 3 age groups, respectively. Because the educational intervention for physicians encouraged use of narrow-spectrum agents when appropriate, we examined the intervention impact on the prescribing of second-line penicillins (primarily amoxicillin-clavulanate) and second-line macrolides (primarily azithromycin; Table 3). The intervention was responsible for a decrease in second-line penicillin use of 9.2% ($P = .03$) and 21.3% ($P < .0001$) among all children aged 24 to <48 months and 48 to <72 months, respectively. The intervention impact for this class was most consistent among Medicaid-insured children, with intervention effects of 9.0% ($P = .04$), 14.3% ($P = .02$), and 22.7% ($P < .01$) in the 3 age groups, respectively. The intervention decreased second-line macrolide use in all 3 age groups. The 3-year intervention was responsible for a 6.7% decrease among children aged 3 to <24 months ($P = .02$), 12.7% among those aged 24 to <48 months ($P < .01$), and 22.5% among those aged 48 to <72 months ($P < .0001$). For

### Table 2: Impact of Community-Level Intervention According to Age Group and Insurance Type

| Parameter | Unadjusted Rate, Baseline Year 1a | Adjusted % Changeb | Unadjusted Rate, Baseline Year 1a | Adjusted % Changeb | Intervention Impactc | P |
|-----------|----------------------------------|-------------------|----------------------------------|-------------------|----------------------|---|
| Overall   | 3 to <24 mo | 2.8 | -20.7 | 2.9 | -21.2 | -0.5 | .69 |
|           | 24 to <48 mo | 1.7 | -10.3 | 1.7 | -14.5 | -4.2 | <.01 |
|           | 48 to <72 mo | 1.4 | -2.5 | 1.4 | -9.3 | -6.7 | <.0001 |
| Medicaid  | 3 to <24 mo | 3.0 | -16.1 | 3.0 | -20.6 | -4.5 | .01 |
|           | 24 to <48 mo | 1.8 | -12.9 | 1.8 | -18.4 | -5.5 | .01 |
|           | 48 to <72 mo | 1.4 | -1.7 | 1.4 | -10.7 | -9.0 | <.01 |
| Commercial | 3 to <24 mo | 2.7 | -23.5 | 2.8 | -21.0 | 2.6 | .11 |
|           | 24 to <48 mo | 1.6 | -8.8 | 1.6 | -11.5 | -2.7 | .17 |
|           | 48 to <72 mo | 1.3 | -2.8 | 1.4 | -7.9 | -5.1 | .01 |

* Unadjusted rates were calculated as the sum of all antibiotic dispensings divided by the sum of person-years observed.

* Adjusted percentage change over all 3 intervention years (study years 3–5, September 1, 2000, to August 31, 2003) from generalized linear mixed models, accounting for clustering by community, baseline prescribing rate, differences in baseline trend (year 1 to 2), secular trend during the intervention period, and gender. Insurance type (Medicaid versus commercial) was included as a covariate in the model for overall effect.

* Difference in adjusted percentage change between intervention and control communities.

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this medication class, the magnitude of effect was generally larger among commercially insured children than for those with Medicaid.

DISCUSSION

We intervened in 16 independent, demographically diverse communities, using a combination of evidence-based strategies for physician behavior change, as well as social marketing approaches to align the expectations of parents and the prescribing practices of their physicians. This cluster-randomized design allowed us both to quantify the magnitude of recent secular trends in prescribing rates and to measure the impact of the intervention beyond such trends. Although we did not detect an intervention effect in all groups, we were successful in achieving modest decreases of between 4.5% and 9.0% among Medicaid-insured children, depending on age group. These children represent an important subgroup because they had higher baseline rates of use and their parents may have less knowledge about appropriate antibiotic indications. Among commercially insured children, the intervention had no significant impact on those who were younger than 4 years but was responsible for an additional 5.1% decrease in the oldest age group (48 to 72 months). We speculate that clinicians’ antibiotic use for older children may be more responsive to intervention, because they may be more willing to withhold antibiotics for marginal indications.

We, like others, are particularly concerned by the increasing use of broad-spectrum macrolides (particularly azithromycin) in children, even in age groups in which few indications exist. The intervention significantly attenuated the rate of increase of use of these drugs.

The relatively small magnitude of impact of this intervention, even among Medicaid members, must be interpreted in light of the community-level approach, in which
resources and exposures are diffused over a great number of individuals. In this case, we chose communities before assessing whether physicians who practiced within them would be receptive to participation in intervention activities. A substantial fraction (but a minority) of clinicians in each community attended educational sessions, and all practices received patient materials and prescribing feedback; however, there was clearly variability regarding engagement in intervention activities. Furthermore, because we measured the impact of the intervention in repeated cross-sections of a dynamic cohort, many of those included in the analysis did not receive the intervention’s components. For example, the youngest children in the follow-up years were not even alive in the first intervention year. Similarly, those who had recently moved to a study community or transferred into 1 of the health plans from which data were obtained would not have had full exposure. Overall, we believe that this type of assessment at the community level, although most conservative in terms of detecting intervention effects, is the appropriate assessment of both secular changes in health care practices and the impact of community-level interventions.

Several studies have reported greater magnitudes of effect of interventions on physician practices. These studies may have engaged practices that were most receptive to change in this area and may be less generalizable to community-level approaches for this and other public health problems. True community-level interventions to promote judicious antibiotic use have shown mixed results. A nonrandomized trial showed a substantial initial impact of a multifaceted intervention among Medicaid members in a single county in Tennessee. In Wisconsin, a community intervention seemed to have resulted in 1 region compared with another, but results of statewide expansion were not as encouraging. In Finland, a recent intervention was unsuccessful at addressing antibiotic prescriptions per 100 person-years using a clinical decision support system in combination with a community intervention in 12 rural communities. The current trial is unique for its exclusive focus on prescribing for children, the number of nonoverlapping communities (both urban and suburban) randomized, and the ability to compare effects among Medicaid and commercially insured children.

The results of this trial should be interpreted in the context of several caveats. Our intervention addressed...
prescribing practices that were already undergoing substantial change, even in the absence of concerted intervention. The decreases that were seen in our control communities clearly support these trends. The overall rates of physician visits per child per year in these communities did not change during the study period. There were small decreases in respiratory illness diagnoses as a group, but these do not account for the antibiotic-use decreases that were observed in control communities. We know of no other concurrent specific programs that were promoting judicious antibiotic use in these communities; however, this intervention was undertaken on a background of initiatives of national groups (including the American Academy of Pediatrics), health plans, and attention in both professional journals and the lay press. All of these likely contributed to the decreases in prescribing that were seen in control communities. Although we believe that the approaches used here may be useful for initiatives in other content areas, additional evaluation of community-wide collaborations is needed to determine factors that are predictive of success. Our data were collected during the period of introduction of universal heptavalent pneumococcal conjugate vaccine immunization to the cohort studied. Although we do not have individual-level information on immunization status, coverage rates are high in Massachusetts and would not be expected to differ between intervention and control communities. We also recognize that Massachusetts communities, physicians, or parents may differ from those in other states; however, we point to the diversity (in size and demographic characteristics) of these communities and note that all were outside the major metropolitan areas in which tertiary hospitals, training programs, and other idiosyncrasies are likely to exert effects.

The issues of antibiotic overuse and resistance are paradigmatic of a variety of community-level health problems in which treatment decisions for individuals have aggregate impact on the community as a whole. In the era of increasing availability of automated health care data (from clinical and billing systems), the type of collaboration achieved here, of public health authorities, health plans, employers, and concerned citizens, is a potentially powerful approach for simultaneously reaching physicians and patients to improve medical care and health outcomes for populations. Future work should assess the cost-effectiveness of such community-wide approaches.

CONCLUSIONS
Antibiotic resistance continues to be a threat to public health, with high rates of human antibiotic use likely to be a substantial contributor. Attention to antibiotic overuse and resistance has increased from physicians, public health authorities, and the lay press. The greatest cause for optimism is the marked decrease in antibiotic-use rates for children and adults in the United States, even in the absence of concerted community-level intervention of the type that we report here; however, we conclude that community-level approaches can be successful in further reducing antibiotic use for children, especially when targeted toward specific populations (eg, Medicaid-insured children) and specific medication classes. Determining the groups that are most likely to benefit will help to use resources most effectively for health-related education at the community level for both parents and providers.

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