Pilot study for appropriate anti-infective community therapy

Effect of a guideline-based strategy to optimize use of antibiotics

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abstract

OBJECTIVE To determine whether a community-wide, multi-intervention educational strategy (CoMPLI model) could enhance adoption of clinical guidelines and improve the use of antibiotics.

DESIGN Before-after trial using baseline and study periods with a control group.

SETTING A small community in central Ontario.

PARTICIPANTS Health professionals, the general public, and the pharmaceutical industry.

INTERVENTIONS The educational strategy (CoMPLI), carried out during 6 winter months, consisted of continuing medical education sessions for health professionals and pharmaceutical representatives and a parallel public education campaign that included town hall meetings and pamphlets distributed by local pharmacists. The two main messages were: do not use antibiotics for viral respiratory infections, and use drugs recommended in the publication, Anti-infective Guidelines for Community-Acquired Infections.

MAIN OUTCOME MEASURES Total number of antibiotic claims and adjusted odds ratios (OR) were used to measure the likelihood of physicians prescribing first- or second-line agents compared with the previous year and compared with control physicians.

RESULTS Claims in the study community decreased by nearly 10% during the 6-month study period compared with the baseline period from the previous year. Study physicians were 29% less likely (OR⁻¹ = 0.71, range 0.67 to 0.76) to prescribe second-line antibiotics during the study period than physicians in the rest of the province. CONCLUSIONS Physicians participating in the pilot study were more likely to follow drug

résumé

OBJECTIF Déterminer si une stratégie éducative à interventions multiples et à l'échelle de la collectivité (le modèle CoMPLI) pourrait accroître l'adoption de directives cliniques et améliorer l'utilisation à bon escient des antibiotiques. CONCEPTION Une analyse avant-après se fondant sur une base de référence et des périodes d'étude avec un groupe de contrôle.

CONTEXTE Une petite communauté du centre de l'Ontario.

recommendations outlined in published guidelines.

PARTICIPANTS Des professionnels de la santé, le grand public et l'industrie des produits pharmaceutiques. INTERVENTIONS La stratégie éducative (CoMPLI), qui s'est déroulée durant six mois d'hiver, comportait des séances de formation médicale continue pour les professionnels de la santé et les représentants de l'industrie pharmaceutique ainsi qu'une campagne parallèle d'éducation publique, notamment des assemblées publiques locales et la distribution de brochures par les pharmaciens de la localité. Les deux principaux messages étaient de ne pas utiliser d'antibiotiques pour des infections respiratoires virales et d'avoir recours aux médicaments recommandés dans une publication concernant des directives anti-infectieuses pour des infections acquises dans la communauté.

PRINCIPALES MESURES DES RÉSULTATS Le nombre total de demandes d'antibiotiques et les risques relatifs (RR) ajustés ont servi à mesurer la probabilité chez les médecins de prescrire des médicaments de première et de deuxième intentions par rapport à l'année précédente et au groupe de contrôle de médecins. RÉSULTATS Les demandes dans la communauté à l'étude ont chuté de près de 10% durant l'étude de six mois en comparaison de la période de référence de l'année antérieure. Les médecins assujettis à l'étude étaient moins enclins dans une proportion de 29% (RR¹ = 0,71, variant de 0,67 à 0,76) à prescrire des antibiotiques de deuxième intention durant la période analysée que les médecins dans le reste de la province.

CONCLUSIONS Les médecins qui ont pris part à l'étude expérimentale étaient davantage enclins à respecter les recommandations relatives aux médicaments énoncées dans les directives publiées.

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rescribing medication as effectively and efficiently as possible has been a longstanding goal in international health. The costly consequences of inappropriate use of medication, however, continue to challenge both the medical and pharmaceutical professions.

Use of pharmaceuticals has been scrutinized in a variety of reports, inquiries, and expert committees whose findings consistently highlight the shortcomings of the present system. 1-6 Recently, two major analyses have confirmed a problem with use of antibiotics for both adults and children.7,8 These findings, combined with a steady increase in the prevalence of antibiotic-resistant organisms⁹ and serious streptococcal infections, ¹⁰ have made optimal use of anti-infective drugs an important issue.

The literature suggests that prescribing is influenced by many factors. Physicians have beliefs and practice habits that are reinforced by numerous influences in their local environments that include educational, administrative, personal, economic, patient, and community-based factors. 11 Several strategies have been developed to improve drug use in the community, and a clearer picture of the most successful strategies is beginning to emerge. 12,13

Newsletters, guidelines, and visually stimulating printed materials might increase physicians' knowledge and provide the foundation for more sophisticated strategies, but have minimal effect on prescribing behaviour. The most successful approaches involve case reviews and adult learning principles.14,15 A review of randomized trials revealed only five strategies that appeared successful in educating prescribers: using local opinion leaders, academic detailing, reminder systems, personalized audit and feedback, and continuous quality improvement.16 Educational interventions that seek to inform patients are useful, 17 but they have not generally been well evaluated.

Approaching complex issues, such as optimizing use of anti-infectives, might require several interventions combined. The objective of this project was to use multiple community-based strategies to improve use of antibiotic medication.

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METHODS

Setting and participants

The study was conducted in Port Perry, Ont, where most people receive health care exclusively from the local group practice, which provides broad-spectrum primary care. Study participants included all 15 physicians from the Medical Associates of Port Perry, a group practice responsible for approximately 30 000 active patient files and sole provider of coverage at the local urgent care (walk-in) clinic and emergency department. Participants also included pharmacists (local and two research consultants), local pharmaceutical industry representatives, the general public, and community-based nurses.

The educational intervention had two main components: one targeted local health professionals and pharmaceutical representatives and another targeted the general public.

Study design

Using baseline (October 1995 to March 1996) and study (October 1996 to March 1997) periods, we conducted a before-after trial. We used prescription claims in the rest of Ontario as the control.

Intervention

An educational model conceptualized under the acronym "CoMPLI" was the basis of the intervention. The acronym is made up of "Co" for *Co*mmunity-wide in scope, "M" for Multistakeholders and Multi-interventions, "P" for the Patient-focused approach, "L" for the Leadership of health professionals, and "I" for the Interactive nature of the guideline-based continuing medical education (GB-CME) sessions.

Before testing the model, discussions were held with key stakeholders, including representatives from the pharmaceutical industry and the Drug Programs Branch of the Ontario Ministry of Health to help refine the scope of the study. The pharmaceutical industry was instrumental in fostering these discussions, and this led to a multistakeholder partnership being developed with the main objective of optimizing therapy and health outcomes.

Program for health professionals

The first step in implementing the intervention was to designate a lead or "local champion" health professional, in this instance a family physician. The next step was to gain and solidify support for the program from local physicians and pharmacists. During two meetings before the intervention commenced, we

Table 1. Sample of a treatment table from the Anti-infective Guidelines for Community-Acquired Infections

Modifying Probable Circumstances Organism(s)	Antibiotic Choice(s)	Usual Dosage	Cost per day
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Acute Bronchitis: Adults 1

MILD TO SEVERE	VIRAL		No antibiotic indicated		
	BACTERIAL Mycoplasma pneumonia	FIRST LENE	Tetracycline	250mg QID	\$0.08
	S. pneumonia C. pneumonia		Erythromycin	1g/day divided BID TID or QID	\$0.21- \$1.50
		SECOND LINE	Doxycycline ²	100mg BID first day then 100mg daily	\$1.70
			Clarithromycin	250-500mg BID	\$2.96- \$5.92
			Azithromycin ³	500mg first day then 250mg daily x 4 days	5 day treatment: \$29.60

- 80% of all cases of acute bronchitis are viral, however, it is difficult to reliably distinguish between these etiologies since both viral and bacterial pathogens may result in purulent sputum (Boldy et al., 1990). Onset of productive cough and wheezing are the most common symptoms. An evaluation of the current literature does not support routine antibiotic treatment for acute bronchitis (Orr, 1993). Primary prevention must be emphasized, such as the reduction of risk factors (e.g., smoking).
- There is limited evidence that doxycycline may have small beneficial effects in patients with acute cough and purulent sputum (Verheij, 1994). These beneficial effects are more prominent in patients age 55 years and over.
- Azithromycin has a long half-life (69 hrs) and requires only a single 5 day course of treatment.

reviewed the objectives of the program and mutual expectations. These meetings set the tone for the entire intervention; throughout the program, participants felt free to offer suggestions. All suggestions were addressed.

The core intervention for health professionals and pharmaceutical representatives was small-group GB-CME sessions developed, coordinated, and facilitated by the lead physician and two research pharmacists. The educational package contained information from the Anti-infective Guidelines for Community-Acquired

Infections (Guidelines),18 articles from the scientific literature, and material provided by pharmaceutical companies. First and second editions of the Guidelines (Table 1) were released in December 1994 and April 1997. These guidelines were unique in Canada, having been developed by an independent consensus panel comprising family physicians, specialists, and pharmacists using a transparent process that included a wide external review by a network of family practitioners. Funded through an unrestricted educational grant from the Ontario Ministry of Health, they were designed as a validated educational tool to help promote optimal use of anti-infectives.

Four sessions were held over the course of 6 months (October 1996 to March 1997); two identical parallel sessions were held on each topic to ensure participation of all local physicians, pharmacists, and industry representatives. The first session included a general discussion about development of the Guidelines, how they should be used, and how drugs of choice (eg, first-line agents) and alternative options had been developed. Topics addressed during the sessions were respiratory tract, skin, and urinary tract infections. The two main messages were to avoid using antibiotics for viral respiratory infections and to use the drugs of choice recommended in the guidelines for bacterial infections.

All local physicians, pharmacists, home care nurses, and industry representatives were invited to attend. Total number attending any one session ranged from seven to 15 people. The presentation protocol for each session consisted of a quiz before the session, a presentation by the lead physician, interactive group discussion on a series of case studies, and a quiz after the session. An evaluation survey was also administered to determine the relevance of the exercise and to gauge participants' satisfaction with program content and format. At the end of the first session, physicians received a "non-drug prescription pad" to use during patient visits. The pad was useful for explaining to patients why antibiotics are not necessary for viral infections. Physicians and pharmacists received three newsletters during the program to update them on program activities.

Program for the community

Community education strategies were carried out through the combined resources of the lead physician, research pharmacists, and the pharmaceutical industry. Strategies included a town hall meeting where the public was invited to a presentation by the lead physician about issues surrounding use of antiinfectives followed by a question-and-answer period. This meeting was attended by 75 people, including the local media. Educational handouts were developed by the lead physician and two research pharmacists and reviewed (face validated) by local health professionals. The handouts were distributed in physicians' offices, the walk-in clinic, and pharmacies in conjunction with counseling.

Presentations were made to school and community groups. The lead physician wrote articles for the local

media about responsible use of anti-infectives and the importance of good physician-patient communication.

Outcome measurement

Data collection. Trends in antibiotic use were examined through an analysis of prescription claims and diagnosis data for the 6-month study period (October 1996 to March 1997) and a control period 1 year earlier (October 1995 to March 1996). Written permission was obtained to collect diagnostic and prescription data in aggregate form from all 15 participating physicians.

Prescription claims data were obtained (with permission) from all four local retail pharmacies, the provincial drug benefit ODB (Ontario Drug Benefit) database, and from a private health information company (IMS Health). The ODB database includes all claims data (over 40 million a year) from a publicly administered drug program that reimburses seniors and those receiving social assistance for prescription drugs. The IMS database includes prescription claims collected monthly through a representative sampling of 2100 pharmacies throughout Canada. These data represent prescriptions dispensed to uninsured and publicly or privately insured people and is stratified by province, type of pharmacy (chain, independent), and size of pharmacy (small, medium, large).

Data on diagnostic visits for Port Perry Medical Associates are stored in a centralized computer system. All relevant diagnostic codes for infectious diseases for the study and control periods were extracted and tabulated. This gave an accurate count of the number of visits for overall and specific infectious diseases. The following outcome parameters were examined for the study group (Port Perry) and the control group (the rest of Ontario excluding Port Perry):

- total claims for antibiotics (data source: four local pharmacies, ODB, and IMS Health);
- · total and individual infectious disease diagnoses (source: local medical clinic);
- odds ratios (OR) for first- and second-line antibiotic prescribing during the control period relative to the study period; and
- · odds ratios for first-line antibiotic prescribing relative to second-line prescribing during control and study periods.

Data analysis. Outcomes in this analysis are presented as ORs with appropriate 95% confidence intervals (CI). This allows quantitative inferences to be made about the effect of the program on total prescription claims during the study period.

The primary outcome of the current analysis was the likelihood (presented as an OR) of Port Perry physicians prescribing first-line and second-line antibiotics during the control period relative to the study period. The second outcome was the likelihood of Port Perry physicians prescribing first-line antibiotics rather than second-line antibiotics during control and study periods. Separate analyses were done for ODB claims and other data from Port Perry pharmacies. The control group for the ODB claims was all ODB claims in Ontario (excluding Port Perry) reported during the study and control periods. The control group for other analysis was Ontario prescription projections (excluding Port Perry) obtained from IMS Health. Eleven first-line and 10 second-line antibiotics were compared in the analyses.

The Mantel-Haenszel χ^2 procedure (log-rank test) for combining categorical data was used to estimate the adjusted OR for each antibiotic stratum. 19 Individual ORs were adjusted by type of first- and second-line antibiotic claims. Miettinen's Test-Based Limits test was then used to calculate the 95% CI for the adjusted OR in each stratum. 19 Interstrata homogeneity was then evaluated by the method of Fleiss.²⁰ Odds ratios and 95% CIs were calculated for first-line antibiotic prescribing relative to second-line antibiotic prescribing.

RESULTS

Overall antibiotic claims

There was a substantial reduction (9.4%) in the overall number of claims for antibiotics during the study period compared with the control period (Table 2). This occurred while overall patient visits for infections increased by 4.4%. Hence, the overall ratio of claims to diagnostic visits (a measure of antibiotic prescribing tendency) dropped during the study period. Table 3 shows changes for selected diagnoses. The most significant increase occurred with upper respiratory tract infection (viral) diagnoses; the most dramatic decrease was with bronchitis.

First-line antibiotics

The first test of homogeneity between strata suggested an interaction between first- and second-line antibiotics. Consequently, individual ORs for each antibiotic stratum had to be calculated. For first-line agents for ODB patients (Table 4), results of analysis generated an adjusted OR of 1.01 (95% CI 0.93 to 1.09). The broad CI suggests that Port Perry

Table 2. Anti-infective prescription claims and office visits for infections: Comparison between control and study periods.

CLAIMS AND VISITS	CONTROL PERIOD	STUDY PERIOD	CHANGE (%)
Total anti-infective claims*	10 071	9125	946 (-9.4)
Total visits for infections [†]	10 727	11 197	470 (+ 4.4)
Ratio of claims to visits	0.94	0.81	0.13 (-13.8)

^{*}Data from local pharmacies.

practitioners were equally likely to prescribe first-line antibiotics during control and study periods.

Similar outcomes were observed using Port Perry local pharmacy data. The adjusted OR was 1.02 (95% CI 0.99 to 1.06), which indicates slightly higher firstline antibiotic prescribing before the educational intervention. The difference, however, was not statistically significant. It appears that the total volume of first-line antibiotics prescribed by Port Perry physicians was similar during control and study periods.

Table 3. Number of office visits for selected diagnoses*: Comparison between control and study periods.

	CONTROL	STUDY	
DIAGNOSIS	PERIOD	PERIOD	CHANGE (%)
Upper respiratory tract infections (viral)	2892	3555	663 (+22.9)
Bronchitis	1902	1564	338 (-17.8)
Chronic bronchitis	119	93	26 (-21.9)
Influenza	681	729	48 (+7.1)
Pneumonia	366	292	74 (-20.2)

^{*} Data from local medical centre

Second-line antibiotics

Contrary to results with first-line antibiotics, a statistically significant reduction in prescription claims for second-line antibiotics was observed in Port Perry during the study period compared with the control period. The adjusted OR for ODB patients was 1.41 (95% CI 1.23 to 1.62). These results can be interpreted to mean that, during the control period, clinicians in Port Perry were 41% more likely to prescribe second-line antibiotics to patients eligible for ODB (Table 4).

[†]Data from local medical centre.

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Table 4. Odds ratios for control period* compared with study period, adjusted for type of antibiotic: Results of the Mantel-Haenszel statistical procedure.

statistical proced	urc.			
	ADJUSTED			OVERALL
STRATUM	ODDS RATIO	95% CI	P VALUE	EFFECT† (%)
FIRST-LINE AGENTS				
• ODB data	1.01	0.93-1.09	.8	No change
All pharmacies data	1.02	0.99-1.06	.65	No change
SECOND-LINE AGENTS				
• ODB data	1.41	1.23-1.62	<.001	-29
All pharmacies data	1.40	1.32-1.49	<.001	-29

ODB-Ontario Drug Benefit.

An alternative interpretation can be offered by taking the inverse of the adjusted OR (OR-1 = 0.71 [0.62 to 0.81]). Simply stated, the results imply that Port Perry physicians were 29% (1-0.71) less likely to prescribe second-line antibiotics to ODB patients after the educational sessions. These observations indicate that the intervention program was successful because a major objective was to educate physicians about the appropriateness of prescribing (or not prescribing) second-line antibiotics.

An analysis of second-line drug prescribing with data retrieved from all Port Perry pharmacies generated outcomes consistent with results from ODB patients. The adjusted OR (before versus after the intervention) was 1.40 (95% CI 1.32 to 1.49), which suggests that Port Perry physicians were 40% more likely to prescribe second-line antibiotics to patients before the educational program (OR-1 = 0.71 [0.67 to 0.76]). The similarity in adjusted ORs between ODB claims data and information from Port Perry pharmacies supports the internal validity of the analysis.

Odds ratios of first- to second-line antibiotics

The ratio of first- to second-line antibiotic prescribing was determined during control and study periods. During the control period, ODB data revealed an OR of 1.13 (95% CI 1.02 to 1.25), but the OR increased during the study period (OR = 1.75, 95% CI 1.55 to 1.97), suggesting that first-line antibiotic prescribing increased substantially relative to second-line prescribing (**Table 5**). Furthermore, because the 95% CI of the respective ORs do not overlap, it appears that this increase was statistically significant. Similar results were observed when the analysis was performed with data obtained from all Port Perry pharmacies and IMS, suggesting a uniform educational effect on all groups.

DISCUSSION

After the intervention, the overall number of antiinfective prescription claims decreased in the study community and the proportion of diagnoses of viral illness increased. Also, when compared with other Ontario physicians, Port Perry physicians were 29% less likely to prescribe second-line antibiotics and more than twice as likely to prescribe first-line relative to second-line antibotics after the educational

Table 5. Odds ratio for first-line relative to second-line antibiotic prescribing in Port Perry

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STRATUM	ODDS RATIO*	95% CI	P VALUE	LIKELIHOOD OF PRESCRIBING FIRST- OVER SECOND-LINE ANTIBIOTICS (%)
ODB DATA				
• Control period †	1.13	1.02-1.25	.025	13
Study period	1.75	1.55-1.97	<.001	75
ALL PHARMACIES DATA				
• Control period †	1.44	1.37-1.51	<.001	44
Study period	2.10	1.99-2.20	<.001	110

ODB-Ontario Drug Benefit.

^{*}Projections from IMS data for all of Ontario were used as controls for the comparison.

[†]Likelihood of physicians' prescribing second-line antibiotics after the educational intervention. Overall effect calculated by taking the reciprocal of the adjusted OR.

^{*}Likelihood of prescribing a first-line agent relative to a second-line agent. A higher OR in the study period suggests that the volume of first-line antibiotic prescribing relative to second-line prescribing increased after the educational intervention.

[†]Projections from IMS data for all of Ontario were used as controls for the comparison.

sessions. These observations indicate that the intervention was successful in educating health professionals, pharmaceutical representatives, and the public about appropriate use of antibiotics as outlined in the Guidelines.

The substantial decrease in the overall number of anti-infectives prescribed during the study period was consistent with the dramatic shift in the number of bacterial (bronchitis) to viral (upper respiratory infections) diagnoses. In discussions during the educational sessions, physicians remarked that they were more conscientious about distinguishing viral from bacterial infections and at the same time patients were more willing to accept viral diagnoses. The authors believe that synchronizing professional and public educational efforts was instrumental in facilitating the dramatic improvement in use of anti-infectives.

Innovative elements contributed to success

Several innovative elements of the program contributed to its success. Leadership by local health professionals is critical for coordinating local CME and public education. Supplying motivated health professional leaders with good-quality materials, operational support, and compensation for their time ensures that leadership roles do not become overwhelming. Employing user-friendly, credible educational materials was essential to ensuring that the main messages of the Guidelines were accepted as valid and relevant.

Heightening the public's awareness of antibiotic issues was also essential to the success of this program. A coordinated strategy, led by local health professionals, was effective for disseminating important messages to patients in ways they could understand.

An important finding to emerge from this study is that, when health care stakeholders agree on a common goal, such as appropriate use of antibiotics, they can form a working alliance to achieve this goal. The pharmaceutical industry and the Ontario Ministry of Health both contributed resources and expertise that were crucial to implementation and evaluation of the program. A valuable component of the small-group GB-CME sessions was having physicians, pharmacists, and pharmaceutical industry representatives all in attendance so that they received uniform educational messages and had an opportunity for face-toface interaction.

Community-based programs in both Iceland and Finland^{21,22} have also led to decreased consumption of certain antibiotics and declines in rates of antibioticresistant bacteria (ie, penicillin-resistant pneumococci

and erythromycin-resistant group A streptococci). Both programs included education for the public and health professionals, were nation-wide, and included other incentives (Iceland removed a subsidy that meant patients had to pay the full cost of antibiotics, and children carrying penicillin-resistant pneumococci were asked not to attend day-care centres if they had symptoms of upper respiratory tract infections). Results of the Finnish program indicated that, although use of erythromycin decreased, there was no change in the overall volume of antibiotic use. Our study revealed an almost 10% drop in overall use from baseline.

Limitations

Some limitations in this study could be addressed with further research. We did not set out to quantify the effect of specific components of the program because our model was originally designed to be implemented as a total package. Discussions at the educational sessions confirmed, however, that educational strategies aimed concurrently at the public and health professionals are needed to support appropriate changes in attitudes and behaviour.

At the time of the study, only aggregate data were available from the study area. Ideally, patient-specific data that are linked to diagnoses, laboratory tests (including resistance patterns), and drug use would be preferred. The aggregate diagnostic data did not permit us to track individual patients and determine, for example, whether patients not treated required more follow-up visits than treated patients. This question was raised, however, during the sessions, and the consensus was that it was generally not the case. The aggregate data sets used for analysis were considered to be comprehensive because most patients in the study population had their prescriptions filled locally and every prescribing physician in the community participated in the intervention.

Further study of the CoMPLI model and its various adaptations has recently been completed in other jurisdictions, and data analysis will begin shortly. We hope this will provide information on the feasibility of disseminating the CoMPLI model and whether its effect is sustainable.

Conclusion

Results of this study suggest that use of the CoMPLI model enhanced adoption of the recommendations in the Guidelines (ie. no antibiotics for viral infections: use first-line antibiotics first) and improved use of anti-infectives. The Port Perry group demonstrated this by decreasing prescriptions Pilot study for appropriate anti-infective community therapy

Key points

- · A community-wide program was designed to reduce inappropriate use of antibiotics. It included educational sessions for physicians, pharmacists, nurses, and pharmaceutical representatives through the media, town hall meetings, schools, and pamphlets for the public.
- · Following the intervention, antibiotic prescription claims decreased by nearly 10%, and diagnoses of viral infection increased.
- Study physicians were almost 30% less likely to prescribe second-line antibiotics than controls.
- · Inappropriate use of antibiotics can be reduced by an intervention that involves all stakeholders and guidelines.

Points de repère

- Un programme à l'échelle de la communauté a été conçu pour réduire le recours aux antibiotiques lorsque ce dernier n'est pas indiqué. Il comportait des séances éducatives à l'intention des médecins, des pharmaciens, des infirmières et infirmiers et des représentants de l'industrie des produits pharmaceutiques. Il rejoignait le public par l'entremise des médias, d'assemblées publiques, des écoles et de brochures.
- À la suite de l'intervention, les demandes d'ordonnances d'antibiotiques ont baissé de près de 10% et les diagnostics d'infections virales ont augmenté.
- Les médecins à l'étude étaient moins enclins dans une proportion de près de 30% à prescrire des antibiotiques de deuxième intention que le groupe de contrôle.
- · Le recours non indiqué aux antibiotiques peut être réduit par une intervention qui touche tous les intervenants et qui comporte des directives.

for antibiotics overall and increasing use of firstline drugs. Although all other physicians in Ontario had received the Guidelines in 1994, they did not seem to be adopting the main prescribing messages to the same degree as the Port Perry physicians. This would strongly suggest that guidelines require multi-intervention implementation strategies to ensure their adoption into day-to-day practice. Furthermore, educational interventions that do not limit themselves to a single strategy or target but that focus on local support and a total

quality management approach can provide a feasible alternative to restrictive administrative mechanisms for ensuring optimal drug therapy.

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Research

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