A Randomized Controlled Trial to Improve Lymph Node Assessment in Stage II Colon Cancer

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Hypothesis: Physicians seem to learn best from their peers, yet the impact of opinion leaders on physician behavior is unclear. Because colon cancer staging has been identified as being suboptimal in Ontario, Canada, we sought to evaluate the influence of expert and local opinion leaders for colon cancer on optimizing colon cancer lymph node assessment.

Design, Setting, Participants: A cluster-randomized trial including all hospitals in Ontario that identified a local opinion leader with intervention between January 5 and June 17, 2004.

Intervention: All 42 centers received a standardized lecture about colon cancer lymph node assessment delivered by an expert opinion leader in colon cancer. The 21 intervention hospitals also received academic detailing of a local opinion leader by the expert opinion leader and a toolkit.

Main Outcome Measures: Mean number of lymph nodes assessed in patients with stage II colon cancer and the proportion of cases staged with a minimum of 12 lymph nodes before and after a standardized lecture were assessed.

Results: Patient demographic and tumor factors were similar in both groups before and after the standardized lecture. Lymph node assessment significantly improved after the standardized lecture at intervention and control sites (P<.001). No additional benefit of academic detailing and toolkit provision in the intervention was demonstrated.

Conclusions: In-person provision of information by an expert opinion leader in colon cancer may stimulate performance regarding lymph node assessment for colon cancer. Academic detailing of a local opinion leader did not further improve lymph node assessment.

Trial Registration: isrctn.org Identifier: ISRCTN56824239


Colon cancer is the second most common cause of cancer death in North America. At first presentation of disease, 36% of patients with colon cancer have localized or node-negative disease (stages I and II) and 37% have regional or node-positive disease (stage III). It is important to identify which patients have node-positive disease because these patients will often be offered adjuvant chemotherapy that confers a 15% absolute survival benefit. In 1992, the National Cancer Institute suggested that a minimum of 12 lymph nodes be assessed to ensure adequate staging. A recent systematic review found that stage II and III colon cancer survival was improved when more lymph nodes were evaluated. Consequently, although patient and treatment factors can affect the number of lymph nodes retrieved, it is an important quality measure.

See Invited Critique at end of article

Adequate colon cancer staging requires clinician knowledge of the minimum number of lymph nodes to assess, an appropriate mesenteric resection by the surgical team, and thorough identification and assessment of the mesenteric lymph nodes by the pathology unit. In Ontario, Canada, we conducted a population-based study that revealed that 73% of patients with stage II colon cancer had an inadequate lymph node assessment as part of their staging. Multivariate analyses suggested that patient age, tumor size, academic status, use of pathology templates, and specimen length were predic-

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tors of the number of lymph nodes assessed. In another study, we demonstrated that few pathologists were aware of the recommended number of lymph nodes to assess in a colon cancer specimen. Differences between optimal practice and the actual practice of surgery have been repeatedly documented. However, traditional continuing professional development has not reliably bridged the gap between research and evidence-based guidelines and clinical practice. Although it is currently unclear which approaches best improve physician practice, interactive and work-situated methods are believed to be effective. Because we know that physicians frequently turn to colleagues when they have clinical questions, the concept of an opinion leader is promising.

Local opinion leaders are defined by Hiss et al as physicians who (1) encourage learning and enjoy sharing their knowledge, (2) are clinical experts and always seem up-to-date, and (3) treat others as equals (humanists). Local opinion leaders may be able to influence physician behavior in a local health care institution. An expert opinion leader, a physician considered influential across multiple hospitals and who often works out of an academic center, is often viewed by physicians as influential enough to stimulate adoption of a practice. Young et al noted that opinion leaders are considered to be influential by surgeons. Despite this, a recent Cochrane Review found that the influence of an opinion leader on professional practice remains uncertain and suggested that further research is required to determine in what context opinion leaders are most likely to influence the practice of their peers.

We found that lymph node assessment was suboptimal in Ontario. The best way to change physician practice is currently unknown. To address this problem, we completed a population-based, randomized study to examine the effectiveness of local and expert opinion leaders on improving lymph node assessment for patients with stage II colon cancer.

METHODS

STUDY SETTING AND DESIGN

This study was conducted in Ontario, a province with a population of 12.4 million and an area greater than a million square kilometers. In total, there were 99 hospitals in Ontario in 2003. Of these 99 hospitals, 42 identified a local opinion leader in colon cancer, and these hospitals were included in the study. We conducted a cluster-randomized trial with hospitals as the unit of random assignment at which a local opinion leader had been identified (Figure). All 42 randomized hospitals received a standardized formal lecture led by the same expert opinion leader in colon cancer. In the intervention arm, the expert opinion leader in colon cancer also met with all but 1 of the locally identified opinion leaders in colon cancer to discuss the importance of adequate lymph node assessment (academic detailing). The pathology template was included to enable synoptic reporting, which has been demonstrated to improve compliance with reporting standards. The poster and pocket cards were intended to remind physicians about the importance of adequate lymph node staging. Instructions to use the materials in a systematic way were not provided with the toolkit because it is hypothesized that formalization decreases an opinion leader’s motivation to behave in an influential manner. Academic detailing of the local opinion leader was conducted to ensure that local opinion leaders would be in a position to express a supportive opinion concerning adequate lymph node counts when a colleague requested their views. A follow-up reminder package was sent 6 months after the presentation to the treat-
ment group only. The package included a cover letter from the expert opinion leader in colon cancer, a peer-reviewed article regarding optimization of lymph node assessment by using lymph node clearing solutions, and more of the same pocket cards.45

Opinion leaders in the control arm were not told that their peers had identified them. Participants (surgeons, pathologists, and local opinion leaders) were not explicitly informed that they were part of a study or that colon cancer lymph node counts would be reassessed. The remaining hospitals for which an opinion leader in colon cancer was not identified did not receive an educational session and did not participate in the trial.

The primary outcome measures were the mean number of lymph nodes assessed in patients with stage II colon cancer and the proportion of cases with at least 12 lymph nodes retrieved for the control and intervention groups. These hospitals consequently were excluded. Furthermore, 1 hospital in the treatment arm had no colon cancer cases after the intervention was completed and was also excluded. This left 16 hospitals in the treatment arm and 18 in the control arm for analysis.

The effect of the intervention on the number of nodes removed was assessed using Poisson regression and using the generalized estimating equation algorithm to adjust for clustering. Logistic regression using the generalized estimating equation algorithm to adjust for clustering was used to evaluate the effect of the intervention on whether 12 lymph nodes were retrieved. Models included lymph node counts in the 360 days before the intervention to adjust for preintervention lymph node removal. P < .05 was considered statistically significant. A statistical software program (SAS version 9.1; SAS Institute Inc, Cary, North Carolina) was used to analyze the data. Ethical approval for this trial was obtained from the Sunnybrook and Women’s College Health Sciences Centre research ethics review board.

### RESULTS

#### PARTICIPATION AND RECRUITMENT

All 42 centers agreed to have a provincially recognized expert opinion leader in colon cancer provide a formal lecture on lymph node staging. These sessions took place between January 5 and June 17, 2004. All but one of the local opinion leaders in the intervention arm received academic detailing for 15 to 30 minutes from the expert opinion leader in colon cancer. The remaining local opinion leader received academic detailing by telephone and e-mail.45

#### PATIENT CHARACTERISTICS

No clinically important differences in either patient or tumor characteristics were identified between the colon cancer cases in the control and intervention arms 360 days before or 360 days after the standardized lecture (Table 1). However, there were differences in the number of lymph nodes retrieved, with more nodes being retrieved from the intervention arm (mean, 14.3 nodes; 61.7% had ≥12 nodes) than in the control arm (mean, 14.9 nodes; 63.7% had ≥12 nodes) before the standardized lecture (Table 2).

#### LYMPH NODE ASSESSMENT: CONTROL VS INTERVENTION

Although a greater number of lymph nodes were removed in the intervention arm (mean, 18.1 nodes; 75.6% had ≥12 nodes) than in the control arm (mean, 14.9 nodes; 63.7% had ≥12 nodes), the effect of the academic detailing of the local opinion leader was not significant (P = .54 for the number of nodes; P = .99 for ≥12 nodes removed) when taking into account the greater number of lymph nodes retrieved in the intervention arm 360 days before the standardized lecture.

#### EFFECT OF STRATIFICATION

Stratification by hospital volume and academic status did not have a consistent effect on the number of lymph nodes assessed.

#### LYMPH NODE ASSESSMENT BEFORE AND AFTER THE STANDARDIZED LECTURE

There was a significant increase in the mean number of lymph nodes assessed and the proportion of cases with 12 or more lymph nodes retrieved for the control and

### Table 1. Patient and Tumor Characteristics for Surgical Procedures 360 Days Before the Standardized Lecture

<table>
<thead>
<tr>
<th>Study centers, No.</th>
<th>Control Arm</th>
<th>Intervention Arm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, No.</td>
<td>338</td>
<td>278</td>
</tr>
<tr>
<td>Age at surgery, mean (SD), y</td>
<td>62.9 (9.0)</td>
<td>63.3 (8.4)</td>
</tr>
<tr>
<td>Tumor size, mean (SD), cm</td>
<td>53.5 (22.0)</td>
<td>53.4 (22.4)</td>
</tr>
<tr>
<td>Specimen length, mean (SD), mm</td>
<td>271.4 (193.1)</td>
<td>281.2 (164.4)</td>
</tr>
<tr>
<td>Male sex, No. (%)</td>
<td>211 (62.4)</td>
<td>166 (59.7)</td>
</tr>
<tr>
<td>Resection type, No./total No. (%)</td>
<td>136/334 (40.7)</td>
<td>98/273 (35.9)</td>
</tr>
</tbody>
</table>

#### STATISTICAL ANALYSIS

Using a computer-generated scheme, we randomized 21 hospitals to the treatment arm and 21 to the control arm. Assuming an average of 3 patients per hospital at the final assessment, and an intracluster correlation coefficient of 0.1, this would provide 80% power to detect an increase from 26% to 52% in the proportion of patients with stage II colon cancer having at least 12 nodes examined at a 2-tailed type I error rate of 5%. Hospitals were stratified according to academic status and hospital size. Six hospitals were classified as small academic, 6 as large academic, 16 as small nonacademic, and 14 as large nonacademic.

### EXCLUSIONS

During the study, 7 hospitals, 4 in the treatment arm and 3 in the control arm, were involved in mergers, which resulted in treatment contamination and the inability to identify the original institutions; these hospitals consequently were excluded. Furthermore, 1 hospital in the treatment arm had no colon cancer cases after the intervention was completed and was also excluded. This left 16 hospitals in the treatment arm and 18 in the control arm available for analysis.

The effect of the intervention on the number of nodes removed was assessed using Poisson regression and using the generalized estimating equation algorithm to adjust for clustering. Logistic regression using the generalized estimating equation algorithm to adjust for clustering was used to evaluate the
the intervention after the standardized lecture ($P < .001$) (Table 2). However, no additional increase was noted when the opinion leader received academic detailing and a toolkit (intervention arm).

**COMMENT**

This study evaluated the influence of local and expert opinion leaders on lymph node assessment in colon cancer and represents one of the few large-scale quality improvement efforts targeting surgeons and pathologists who provide cancer care. We demonstrated that a formal lecture by an expert opinion leader in colon cancer who visited the local hospital was associated with an increase in the number of lymph nodes assessed in colon cancer possibly by creating awareness among pathologists about the clinical importance of lymph node assessment. Academic detailing of the systematically identified local opinion leader by the expert opinion leader in colon cancer did not result in a further increase in the number of lymph nodes assessed. The proportion of cases with more than 12 lymph nodes assessed in Ontario has continued to increase after the completion of this study and likely reflects the influence of the provincial cancer agency’s quality index, which was initiated after this study and provides cancer care. We previously described a successful intervention using an expert opinion leader in colon cancer to improve lymph node counts at a single center. In this multicenter study, it also seems that the expert opinion leader in colon cancer was influential. These findings support the work of Locock et al, who suggested that expert opinion leaders are important in the initial stages of an educational intervention, when evidence needs to be endorsed and translated into a form that is acceptable to local practitioners.

Local or peer opinion leaders are believed to be important in the later phases of implementation, when they model new behavior and give colleagues confidence to initiate change. However, we did not find that academic detailing of the local opinion leader or provision of a toolkit further increased lymph node counts. It is possible that the local opinion leader was not correctly identified, although the Hiss opinion leader identification technique has been successfully used by other investigators in primary care and specialist settings. Other investigators have commented that local opinion leaders often request instructions and suggestions on how to implement change, and, hence, it is possible that the local opinion leaders did not enact change because they were not sure how to improve lymph node staging at their site, or it may be that they have mixed feelings about the formalization of their role and, consequently, did not take on additional activities to try to influence physician behavior. Curran et al have also suggested that a lack of informal or formal social networks may not allow opinion leaders to easily contact other physicians and influence their behavior. Certainly, there were instances in this intervention when the expert opinion leader in colon cancer noted that surgeon and pathologist participants were meeting for the first time. It is also possible that academic detailing, which has been demonstrated to be most effective in changing prescribing habits, may not inspire opinion leaders to actively attempt to change their colleagues’ behavior.

This study has a variety of limitations. First, the design does not allow us to test for a causal connection between the lecture given by the expert opinion leader in colon cancer and the overall increased rate of lymph node retrieval because both arms of the study received this intervention. Consequently, the increase in the number of lymph nodes assessed could have been due to other factors, such as a general increase in awareness of the need to retrieve 12 lymph nodes, although conferences and lectures have not been shown to be effective in changing physician behavior. However, we are aware from an exploratory study (reported elsewhere) that pathologists acted on the information by searching more diligently for lymph nodes and by using lymph node clearing solutions. Another limitation of the study was the context in which it was conducted. The study period was one of change in the Ontario health care system as hospitals merged to share resources and reduce costs. As a result, the intervention in 7 hospitals was contaminated in that hospitals previously assigned to different arms of the study became merged. A final limitation that we cannot explain is the baseline difference in the mean number of lymph nodes removed between the 2 arms of the study that occurred despite randomization. This factor was adjusted for in the statistical analysis. All other patient and hospital factors were equally distributed between the 2 study arms. Further research is required to understand how opinion leaders can best facilitate the uptake of evidence-based recommendations.
based knowledge. In particular, the role of how an expert opinion leader instigates practice change independent of a local opinion leader bears further investigation. We described a knowledge translation strategy that suggests that a lecture by an expert opinion leader in colon cancer may have prompted greater compliance with recommendations for colon cancer lymph node staging practice possibly by creating awareness among specialists of the importance of lymph node assessment, by opening lines of communication between specialists who previously did not communicate on a regular basis, and by providing individual hospital data. In contrast, academic detailing of the local opinion leader did not further improve lymph node assessment. We suggest that further research is required to understand whether and how expert opinion leaders influence practice and what tools or resources they may require to enact change.

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Author Contributions: Dr Wright had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Wright, Law, Last, Klar, Ryan, and Smith. Acquisition of data: Last, Klevan, Hongjinda, Klar, and Ryan. Analysis and interpretation of data: Wright, Gagliardi, Law, Stitt, Klar, and Ryan. Drafting of the manuscript: Wright, Gagliardi, Last, Stitt, Klar, and Ryan. Critical revision of the manuscript for important intellectual content: Gagliardi, Law, Last, Klevan, Hongjinda, Stitt, Klar, Ryan, and Smith. Statistical analysis: Wright, Gagliardi, Law, Stitt, and Klar. Obtained funding: Wright, Last, and Smith. Administrative, technical, and material support: Wright, Gagliardi, Law, Last, Klevan, and Hongjinda. Study supervision: Wright and Smith.

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REFERENCES

In this article, Wright et al report their findings addressing a quality of care improvement initiative in Ontario and share important discoveries that are appropriate for the current environment of surgery care quality evaluation. The authors are to be congratulated for their efforts in bringing this work forward. There are several things to appreciate in this study.

First, it is a collaborative effort of clinical health services researchers and the community (Ontario). This community-based participatory research effort, where researchers partner with a community to provide improved quality of care,1 is one that we hope will be performed with increasing frequency. The simple concept is to demonstrably improve care in an identified community, but importantly, working with the community such that the improvement has traction and is sustained. For many of the partnerships that have been established in this regard, a simple but powerful vision is for researchers to improve the level of quality of care beginning in their own backyard, not just in their own institution (although that may be included) but in the communities in proximity to their institution. It is a relatively new and important wave of research in surgery. It is an achievable and meaningful way to perform research, and one that Wright et al have nicely undertaken.

Second, on the topic of clinical research, this study was performed using the highest-level design, that is, as a randomized controlled study. At a time when we are lacking level 1 evidence in surgery, this study provides evidence-based results. Knowing the difficulties of performing such a study, the effort should be appreciated and applauded. Related to this issue is the topic of research. Whether it is called quality improvement or performance improvement, studying this issue is vital to surgery. Knowing how best to improve care with what works (and what does not) will be helpful and generalizable to almost everyone. However, good literature and high-level evidence with appropriate study designs on this topic are scarce.

A final item (and probably most apropos to the readership) to be taken from this study is that it addresses the important notion of a leader in an improvement initiative. There are likely several necessary ingredients to improving the quality of care, but having a leader to move the process forward is essential.2 In the quality improvement programs associated with the American College of Surgeons, Division of Research and Optimal Patient Care, each program enlists the help of a local leader. Whether it is the trauma director in the Committee on Trauma, the physician liaison in the Commission on Cancer, or the surgeon champion in the American College of Surgeons National Surgical Quality Improvement Program, these leaders are necessary because they are the point persons for driving the effort to improve quality. They need to have the vision to improve, they need to be able to get others on board, and they need to follow through.

We have learned a variety of things in each of these programs, but one continuing issue is that merely naming a leader is usually insufficient. Instead, the leader must be enthusiastically driven to make improvements, must be given the appropriate authority and support to do so, and must be provided the content to effectively lead. The content has included such items as reliable and valid internal performance data, but also important is the best-