

# Artificial intelligence in colorectal cancer screening

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Colorectal cancer (CRC) is one of the most commonly diagnosed cancers in Canada and leads to death in 10% of cases.<sup>1</sup> In Canada, organized CRC screening usually involves a fecal immunochemical test or guaiac fecal occult blood test every 2 years for individuals aged 50–75 years. For those with a first-degree relative with a history of CRC, screening starts at a younger age and consists of colonoscopy every 5–10 years.<sup>1</sup>

Colonoscopy is indicated for patients with positive biochemical results, and has both diagnostic and therapeutic implications that enable stratification for further testing and evaluation.<sup>1</sup> Colonoscopy may lead to identification of adenomatous and sessile serrated polyps, which vary in malignant potential, and hyperplastic lesions (a type of serrated polyp not associated with a substantial risk for malignant potential). Use of endoscopic surveillance has been shown to decrease the incidence of CRC in Canada through the detection and resection of precancerous lesions.<sup>1</sup>

Artificial intelligence (AI) in CRC screening increases the rate of adenoma detection, decreases existing technical variation among colonoscopists (i.e., intercolonoscopist variation) and enables characterization of diminutive polyps with high accuracy for further management.<sup>2</sup>

## How can AI be used in screening for colorectal cancer?

Broadly, AI involves the use of machine learning to infer patterns from large training data sets to make predictions on data from individual patients.<sup>3</sup> Two of the more prominent applications of AI for colorectal cancer screening include computer-aided detection (CADe) and computer-aided diagnosis or differentiation (CADx). Using complex models that involve layered and sequential algorithms, or convolutional neural networks, CADe is used in the detection of lesions, whereas CADx characterizes detected lesions by performing optical biopsies, obviating the need for histopathological evaluation.<sup>2</sup>

Optical biopsy employs properties of light to enable real-time diagnosis of tissue, previously possible only through *ex vivo* histological analysis.<sup>3</sup> This novel technique of evaluating human tissue *in vivo* encompasses several different methods, including types of virtual chromoendoscopy or image-enhanced colonoscopy (e.g., narrow-band imaging), or high-magnification

## Key points

- Artificial intelligence application for colorectal cancer screening include computer-aided detection (CADe) and computer-aided diagnosis or differentiation (CADx).
- Computer-aided detection identifies precancerous lesions during colonoscopy by using machine learning algorithms, thereby reducing poor outcomes secondary to intercolonoscopist variation, whereas CADx characterizes detected lesions by performing optical biopsies, obviating the need for histopathological evaluation.
- Although emergent evidence suggests that the performance of such models is superior to current standards of practice, further research is being done that could help to reduce false characterization of lesions, and to mitigate privacy concerns and inadvertent biases.
- Several CADe systems have been approved for clinical use internationally, including in Canada; however, no CADx systems have yet been approved in North America.

techniques (e.g., confocal laser endomicroscopy, endocytoscopy). The techniques use backscattering of near-infrared light to approximate tissue penetration and depth of mucosal invasion, similar to that of histological evaluation.<sup>3</sup> The use of CADe and CADx systems still necessitates fundamental colonoscopic techniques, including 360° inspection, appropriate suction of fluid and debris, and sufficient insufflation of the colonic lumen.

## What problems could be addressed by CADe and CADx?

Strategies to improve detection of polyps during colonoscopy include optimizing bowel preparation, abiding by suggested minimum times for scope withdrawal from the cecum, using caps on the end of the scope to improve visualization and using high-definition scopes.<sup>4,5</sup> Despite these techniques, the rate of polyp detection and subsequent resection of precancerous lesions is largely dependent on the operator, with studies reporting a wide range in adenoma detection rate, from 7%–53% among different endoscopists.<sup>2</sup> If some endoscopists miss adenomas, patients are at risk of interval development of CRC.<sup>4</sup>

Every 1% increase in adenoma detection rate is associated with a 3% decrease in colon cancer mortality, so anything that can be done to improve polyp detection and reduce the impacts of variable endoscopist performance is to be encouraged.<sup>5</sup> Computer-aided detection could improve reliable detection of precancerous lesions during colonoscopy, and reduce poor outcomes related to intercolonoscopist variation in detecting lesions.

In studies, optical biopsy enables either a “diagnose-and-leave” strategy — whereby diminutive ( $\leq 5$  mm),<sup>1</sup> essentially harmless rectosigmoid hyperplastic polyps are left in situ — or a “resect-and-discard” strategy, which results in resection and immediate discarding of diminutive adenomatous polyps without the need for histopathological evaluation.<sup>6</sup> In practice, many colonoscopists continue to resect diminutive ( $\leq 5$  mm) polyps and send them to the pathology laboratory.<sup>6</sup> In the United Kingdom, a resect-and-discard strategy for diminutive polyps has been approved since 2017; however, it has yet to be widely adopted owing to intercolonoscopist variation.<sup>7</sup>

The lack of colonoscopist competency to characterize diminutive polyps accurately in vivo using current optical biopsy technologies results in unnecessary histopathological evaluation of resected diminutive polyps. This has substantial costs and resource implications. The use of CADx can mitigate unnecessary histological evaluation of diminutive polyps by offering live interpretation.

### How are CADE and CADx systems delivered?

The output of CADE and CADx systems can be overlaid on the primary output of the colonoscopy or can be displayed separately using a dual-monitor system. In either system, polyps identified by CADE are highlighted to the user during colonoscopy with-

drawal by a visible boundary box around the polyp and an audible alert to attract the attention of the colonoscopist (Figure 1).<sup>8</sup>

With CADx, optical biopsies can be delivered in real-time, along with the results of the AI clinical decision support tool; the colonoscopist can accept or reject the findings (Figure 2).

### What is the evidence for the benefits of CADE and CADx?

A growing body of evidence suggests that CADE is superior to the current standard of practice. In 2020, a randomized controlled trial (RCT) that compared a commercially available CADE system to routine white-light colonoscopy through tandem procedures (whereby patients assigned to one procedure type then underwent the second procedure by the same colonoscopist, in tandem fashion) found that the adenoma miss rate for colonoscopies using CADE was lower than for routine white-light colonoscopies (13.89% v. 40.00%,  $p < 0.0001$ ), across both diminutive and nonpedunculated polyps.<sup>9</sup> Another tandem RCT assessed outcomes of 232 patients randomized to CADE colonoscopy or high-definition, white-light colonoscopy first.<sup>10</sup> The adenoma miss rate was lower among those who first received CADE than among those who first received the high-definition, white-light colonoscopy (20.12% v. 31.25%,  $p < 0.05$ ), including a lower miss rate for sessile serrated lesions. In this study, the rate of false-positive results during CADE colonoscopy did not differ significantly by group. In a recent meta-analysis, use of CADE was associated with significantly increased detection of diminutive, small and large adenomas, as well as increased detection of sessile serrated lesions and advanced neoplasia, compared with control groups that did not receive an AI-assisted intervention.<sup>11</sup>

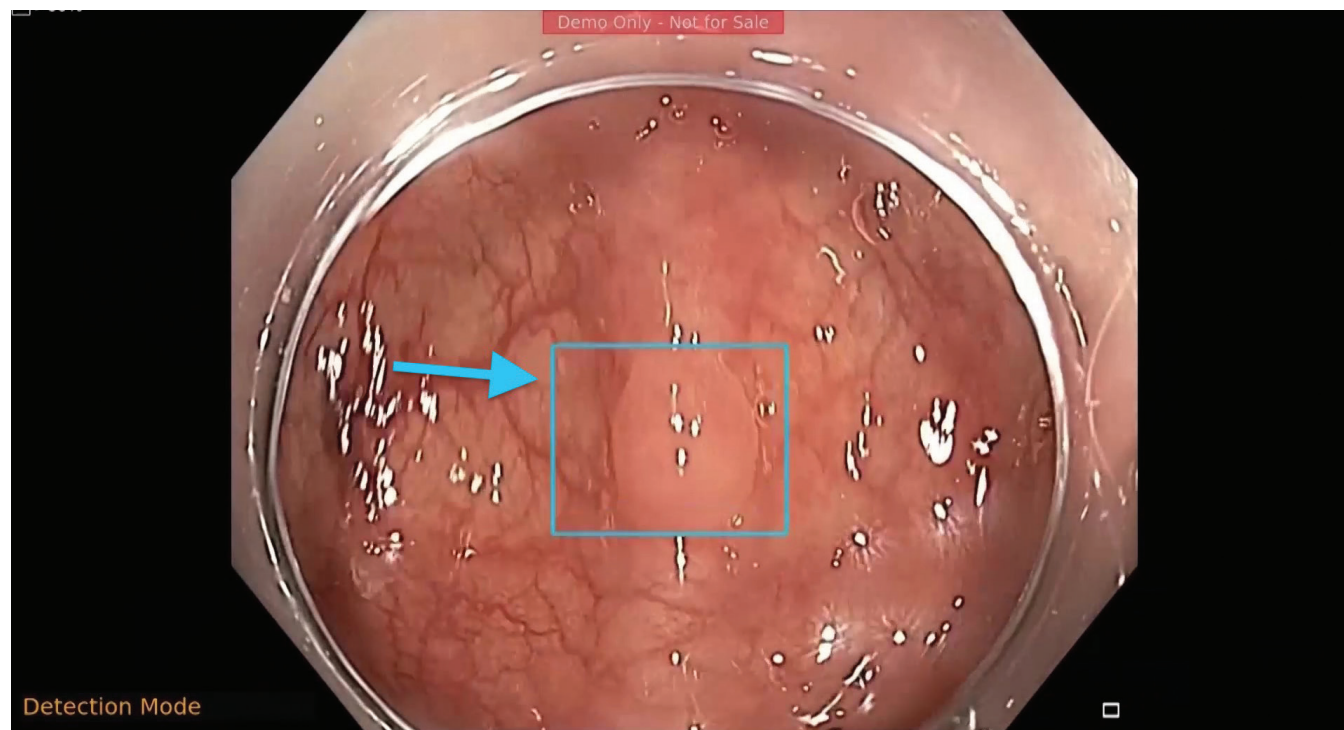


Figure 1: Computer-aided detection of a polyp. Reproduced with permission from Satisfai Health.

In 2019, our group developed a CADx system from more than 60 089 image frames of polyps, captured by narrow-band imaging, to predict the histology of diminutive lesions as either hyperplastic or adenomatous.<sup>12</sup> The overall accuracy of the model in identifying adenomas was 94%, with a sensitivity of 98%, specificity of 83%, negative predictive value of 97% and positive predictive value of 90%, which successfully met national diagnostic thresholds.<sup>12</sup> These results have been replicated by developers of other CADx solutions.<sup>13</sup>

### What are the known harms of AI applications for colorectal cancer screening?

The requirement for large data in the training, testing and quality improvement steps of AI application development has implications for patient privacy and data security. To mitigate privacy concerns, secure cloud computing platforms for electronic health records have been proposed; however, the feasibility and logistics of data harmonization among institutions remain ongoing concerns.<sup>5</sup>

Moreover, the inaccurate classification of a polyp by an application (i.e., a false negative) may lead to patient harm in the form of interval development of cancer. Since CADE and CADx will identify and characterize only the pathology upon which they have been trained, biases prevalent in training sets, such as the lack of representation of demographics or disease processes, may preclude accurate identification and characterization of lesions, and potentially amplify rather than reduce bias.<sup>5</sup> To mitigate this bias, developed algorithms should be exposed to a wide variety of pathology inherent to a diverse patient population —

that is, prospectively collected data from multiple institutions, inputted in large volumes to produce a more heterogeneous, varied and, inherently, less biased data set — to optimize their performance and reduce potential for bias.

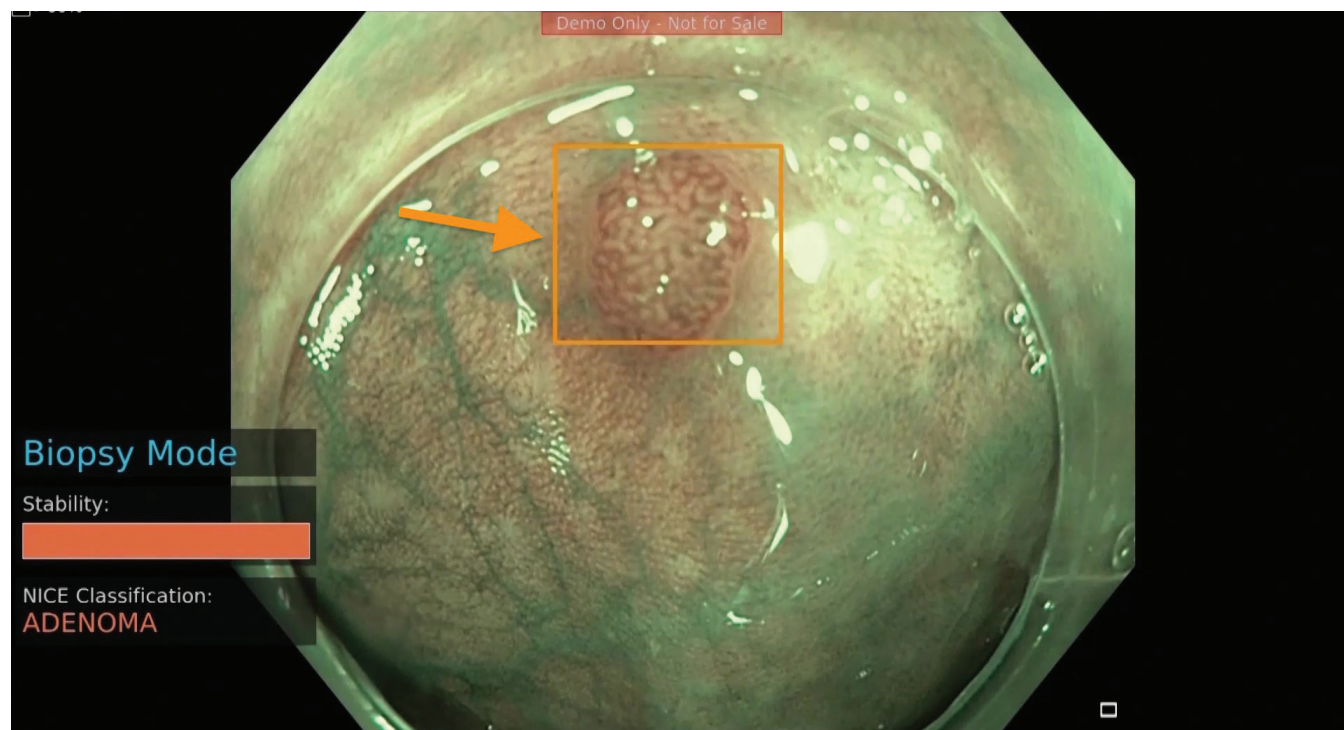
False positive detection and characterization with CADE and CADx may also contribute to harm. False positives often result from inaccurate identification of a polyp from rumpled colon folds, feces, debris and bubbles. This issue can be mitigated through improved bowel exposure using, for instance, water exchange; when used in conjunction with CADx, water exchange increases the adenoma detection rate.<sup>14</sup>

### Who is eligible now?

Several CADE and CADx systems have been approved for use in Europe and Japan. As of November 2021, Health Canada and the United States Food and Drug Administration approved the same CADE system for clinical use. At time of writing, no CADx system has received regulatory approval for use in Canada or the US.

### What are the resource implications?

The cost of the technologies will vary depending on the health care system in which they are deployed. For CADE, the current commercial offerings to customers have a lease rate in the range of US\$2000–\$4000 per unit (per room) per month, often for a 3-year minimum lease. A CADx system would presumably be similar in cost, but could cost more, given its additional features of polyp diagnosis and differentiation, requiring further resources for its development and delivery.



**Figure 2:** The computer-aided diagnosis or differentiation of an adenoma, delivered as a picture-in-picture display. Reproduced with permission from Satisfai Health.

In a study in Japan, Norway, England and the US, Mori and colleagues<sup>15</sup> determined that using CADx and a diagnose-and-leave approach could result in a cost savings of US\$34–125 per colonoscopy, depending on the country. Although the implementation of CAde will result in increased costs through the detection and consequent removal of more polyps, the reduction in CRC incidence, in conjunction with reduced burden for pathology laboratories and clinic time, is likely to lead to a lower overall financial burden on health care systems.<sup>16</sup> Nevertheless, the lack of Canadian financial modelling data remains a barrier to its implementation in Canada.

## What can be expected in the future?

The benefits of AI in the context of CRC will be best appreciated through its improvement of CRC screening once its approval and acceptance into clinical practice is established in Canada. Although current CAde and CADx systems support the detection and characterization of polyps, AI has the potential to improve other quality metrics (e.g., bowel preparation, surface area evaluation) and quantity metrics (e.g., polyp sizing, landmarking [i.e., cecal intubation], automatic timing of withdrawal), contributing to the overall improvement of CRC screening productivity and workflow.

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**Competing interests:** Michael Byrne is the chief executive officer, founder and shareholder of Satisfai Health and founder of the AI4GI joint venture (which has a co-development agreement with Olympus America in artificial intelligence and colorectal polyps). Michael Byrne also reports participation in committees with the World Endoscopy Organization and the American Gastroenterological Association Tech Summit. No other competing interests were declared.

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