Computer Assisted Detection of Neoplasia during Colonoscopy Evaluation (CADeNCE)

Study Protocol

October 8, 2025

NCT05888623

Jason A Dominitz, MD, MHS
Executive Director, National Gastroenterology and Hepatology Program (NGHP)
Director, National Colorectal Cancer Screening Program
Veterans Health Administration, Washington, DC
Professor of Medicine, Division of Gastroenterology
University of Washington School of Medicine, Seattle, WA

Andrew J. Gawron, MD, PhD
Associate Director for Quality, NGHP
Professor of Medicine, Division of Gastroenterology
University of Utah School of Medicine, Salt Lake City, UT

Grace McKee, PhD
Measurement Science Quality Enhancement Research Initiative
San Francisco VA Medical Center, San Francisco, CA
Division of General Internal Medicine,
University of California School of Medicine, San Francisco, California, USA

Katherine J. Hoggatt, PhD, MPH
Measurement Science Quality Enhancement Research Initiative
San Francisco VA Medical Center, San Francisco, CA
Professor of Medicine, Department of Medicine
University of California School of Medicine, San Francisco, California

Tonya Kaltenbach, MD, MS, MEd
Measurement Science Quality Enhancement Research Initiative
San Francisco VA Medical Center, San Francisco, CA
Professor of Medicine, Division of Gastroenterology
University of California School of Medicine, San Francisco, California

Computer Assisted Detection of Neoplasia during Colonoscopy Evaluation (CADeNCE)

Contents

Computer Assisted Detection of Neoplasia during Colonoscopy Evaluation (CADeNCE)

Study Protocol Version 1.0

March 6, 2023

Evaluation Team:
Jason A. Dominitz, MD, MHS
Tonya Kaltenbach, MD, MS, MEd
Andrew Gawron, MD, PhD
Grace McKee, PhD

Background: Colonoscopy is a key diagnostic and therapeutic procedure for the prevention of colorectal cancer (CRC) incidence and mortality. Central to colonoscopy's effectiveness is the identification and removal of colorectal neoplasia, including adenomatous polyps and sessile serrated lesions. The endoscopist's adenoma detection rate (ADR), classically defined as the proportion of screening colonoscopies in which one or more adenomas are detected, has been demonstrated to be strongly inversely associated with their patients' risk of post-colonoscopy colorectal cancer. Therefore, improving adenoma detection is a major target of quality assurance efforts.

The Veterans Health Administration's (VA) National Gastroenterology and Hepatology Program (NGHP) has embarked on a number of efforts to measure, monitor, and improve colonoscopy quality across the VA enterprise. One of these efforts is the VA Endoscopy Quality Improvement Program (VA-EQuIP) which is a collaboration between the VA Quality Enhancement Research Initiative (QUERI), the Office of Research and Development (ORD) and the NGHP. Investigators in the Measurement Science QUERI have developed processes for assessing the ADR of individual physicians and facilities through extraction of data from the Corporate Data Warehouse (CDW). Through collaboration with the VA Clinical Assessment Reporting and Tracking Program (CART), more detailed colonoscopy report information is available for 29 VA medical centers, with additional VA facilities expected to be added to the list soon. Overall, the VA ADR for colonoscopies of all indications is 47%[1], well above the benchmark of 30% for men undergoing screening colonoscopy.

In 2021, the FDA approved the first artificial intelligence (AI) system for computer assisted detection (CADe) of colorectal neoplasia. These CADe devices project an image on the endoscopy monitor (i.e., a bounding box) to alert the endoscopist to the presence of a suspected polyp within the colon. Initial studies, including randomized controlled trials, have demonstrated that use of CADe systems result in a significant improvement in adenoma detection, with a reduction in the miss rate of adenomas (i.e., fewer adenomas are found on a

second colonoscopy when the first colonoscopy was performed with a CADe system compared to when the first colonoscopy did not use CADe).[2-4] However, more recent studies have not demonstrated a clear benefit of these devices.[5,6] Moreover, most of the additional adenomas that are detected are diminutive polyps, the vast majority of which are thought to be of minimal, if any, clinical significance. When multiple adenomas are detected during colonoscopy, current guidelines recommend repeating colonoscopy sooner than would otherwise be recommended. Also, the CADe systems may have unintended consequences, such as creating alert fatigue through false alarms or negatively impacting training of gastroenterology fellows.

Objective: The NGHP planned to formally evaluate the quantitative and qualitative impact and outcomes of use of CADe within VA medical centers following the purchase and distribution to randomly selected gastrointestinal endoscopy units.

Setting: Veteran Health Administration (VA) Medical Centers

Intervention: As part of ongoing quality assurance efforts, the NGHP purchased 115 Medtronic GI Genius® CADe devices in late 2022. All facilities were sorted according to their facility-level ADR (for all indications) and categorized as below 30%, 30% to <40% or ≥40%. A random number generator was then used to sort the VA medical centers within each of these 3 ADR strata. Alternating facilities (i.e., approximately 50%) of facilities within the 2 lower ADR stratum were allocated the CADe devices. To assure equitable distribution of the remaining CADe devices across the 18 VA Integrated Service Networks (VISNs), the remaining devices were offered to randomly selected facilities (all within the ≥40% ADR stratum) such that each VISN had 2-3 facilities with CADe devices.

Upon identification of a potential site, the Gastroenterology Section Chief (or equivalent) at that randomly selected site was asked if they were interested in receiving the devices and if all endoscopists at their facility would agree to use the device during colonoscopy. The physicians were not mandated to use the devices but were asked to notify the NGHP if endoscopists were not routinely using the devices so that the devices could be reallocated to other VA facilities that would make use of the CADe devices. Upon receiving concurrence from the Gastroenterology Section Chief, the devices were installed in all procedure rooms that are routinely used for colonoscopy at that facility. The devices were not installed on travel carts for emergency procedures. One facility did decline to receive the devices due to concerns that the devices would negatively impact efficiency in the endoscopy unit. That facility was replaced with another randomly selected VA medical center. Ultimately, 43 VA facilities received and installed the 115 CADe devices.

Outcomes:

1) VA Facility Level
    a) Adenoma detection rate for all indications
        i) The proportion of colonoscopies in which one or more adenomas are found.
        ii) Limit to ages 45-75 years
        iii) Also evaluate for all ages

b) Number of polyps per colonoscopy
    i) Limited to Provation sites
c) Size of polyps detected
    i) Limited to Provation sites
    ii) Average size
    iii) Categorized as
        (1) 1-5mm
        (2) 6-9mm
        (3) ≥10mm
d) Surveillance recommendations after colonoscopy
    i) Use health factors for follow-up recommendation after colonoscopy
    ii) Limit to ages 45-65 years
    iii) Repeat colonoscopy interval
        (1) <3 years
        (2) 3 years
        (3) 4 years
        (4) 5 years
        (5) 6 years
        (6) 7 years
        (7) 8 years
        (8) 9 years
        (9) 10 years
    iv) Resume average risk screening
        (1) <3 years
        (2) 3 years
        (3) 4 years
        (4) 5 years
        (5) 6 years
        (6) 7 years
        (7) 8 years
        (8) 9 years
        (9) 10 years
    v) No further screening
    vi) No health factor found
e) Withdrawal time when no maneuvers are performed
    i) Limited to Provation Sites (unless EndoPro comes online)
f) Withdrawal time, including the performance of maneuvers
    i) Limited to Provation Sites (unless EndoPro comes online)
g) Total procedure time
    i) When no maneuvers are performed
    ii) When all procedures are included
h) Bowel preparation quality
    i) Adequate vs. inadequate
    ii) Excellent vs. good vs. fair vs. poor

iii) Boston Bowel Preparation Score

i) Adenocarcinoma detection rate
   i) The proportion of colonoscopies found to have adenocarcinoma

2) VA Provider Level
   a) Adenoma detection rate for all indications
      i) The proportion of colonoscopies in which one or more adenomas are found.
      ii) Limit to ages 45-75 years
      iii) Also evaluate for all ages
   b) Number of polyps per colonoscopy
   c) Size of polyps detected
      i) Average size
      ii) Categorized as
         (1) 1-5mm
         (2) 6-9mm
         (3) ≥10mm
   d) Surveillance recommendations after colonoscopy
      i) Use health factors for follow-up recommendation after colonoscopy
      ii) Limit to ages 45-65 years
      iii) Repeat colonoscopy interval
         (1) <3 years
         (2) 3 years
         (3) 4 years
         (4) 5 years
         (5) 6 years
         (6) 7 years
         (7) 8 years
         (8) 9 years
         (9) 10 years
      iv) Resume average risk screening
         (1) <3 years
         (2) 3 years
         (3) 4 years
         (4) 5 years
         (5) 6 years
         (6) 7 years
         (7) 8 years
         (8) 9 years
         (9) 10 years
      v) No further screening/surveillance
      vi) No recommendation found
   e) Withdrawal time when no maneuvers are performed
      i) Limited to Provation Sites (unless EndoPro comes online)
   f) Withdrawal time, including the performance of maneuvers

i) Limited to Provation Sites (unless EndoPro comes online)

g) Total procedure time
   i) When no maneuvers are performed
   ii) When all procedures are included

h) Bowel preparation quality
   i) Adequate vs. inadequate
   ii) Excellent vs. good vs. fair vs. poor
   iii) Boston Bowel Preparation Score

i) Adenocarcinoma detection rate
   i) The proportion of colonoscopies found to have adenocarcinoma

j) Qualitative assessment (from survey)
   i) Benefits of CADe
   ii) Negative aspects of CADe
   iii) False positive alerts
   iv) Impact on fellow training
   v) Overall satisfaction with CADe

Database:

Colonoscopy details are extracted from the Corporate Data Warehouse and, when possible, the endoscopy reporting system via the CART database, including:

1. VA facility
2. Patient characteristics
   a. Age
   b. Gender
   c. Race
   d. Ethnicity
3. Colonoscopy indication
   a. Screening
   b. Surveillance
   c. FOBT+
   d. Other
   e. Unknown
4. Bowel preparation quality
   a. Adequate vs. inadequate
   b. Aronchick
   c. Boston Bowel Preparation Score
5. Colonoscopy findings
   a. Adenoma detection
   b. Adenocarcinoma detection
   c. Number of polyps detected
   d. Number of polyps detected according to size
      i. 1-5mm
      ii. 6-9mm
      iii. ≥10mm

    e. Withdrawal time
    f. Total procedure time
6. Follow-up Plans after colonoscopy (using Gap Reminder health factors)
7. A new variable coding the presence or absence of CADe will be added to each colonoscopy based upon the date of installation of the GI Genius CADe device at each facility.
    a. In order to allow for endoscopists to adapt to performing colonoscopy with the CADe device, all colonoscopies performed within 21 days of the date of installation will be classified as "CADe Training" and will be excluded from the analysis.

Statistical Methods:

1. Within facility comparison (pre- vs. post): All outcome variables will be compared between the pre-CADe and post-CADe time periods (starting 21 days after CADe installation). We will aim for a minimum of 3 months on post-CADe assessment, compared to 6 months of pre-CADe colonoscopies.
2. Between facility comparison: The 43 VA facilities that received CADe devices will be compared to over 100 VA facilities that did not receive CADe devices.
3. Categorical variables will be compared using the Chi-square test.
4. Continuous variables will be compared with the t-test or Wilcoxon rank sums test, as appropriate.
5. To adjust for potential confounders, multivariable models will be constructed.
    a. Logistic regression will be used for dichotomous outcomes (e.g., adenoma detection)
    b. Polytomous logistic regression will be used for ordinal outcomes (e.g., colonoscopy surveillance recommendations)
    c. Linear regression will be used for continuous outcomes (e.g., withdrawal time)
    d. Shell tables are provided below, detailing the variables to be included in the models

Computer Assisted Detection of Neoplasia during Colonoscopy Evaluation (CADeNCE)

Study Protocol Version 1.1

June 3, 2023

Evaluation Team:
Jason A. Dominitz, MD, MHS
Tonya Kaltenbach, MD, MS, MEd
Andrew J. Gawron, MD, PhD
Grace McKee, PhD

Summary of major revisions and rationale:

(a) Addition of survey methodology
    (i) To assess the end-user experience (i.e., endoscopists), a Microsoft Office Forms survey was developed by NGHP leadership for distribution via email to VA endoscopists
(b) Addition of study oversight information

Background: Colonoscopy is a key diagnostic and therapeutic procedure for the prevention of colorectal cancer (CRC) incidence and mortality. Central to colonoscopy's effectiveness is the identification and removal of colorectal neoplasia, including adenomatous polyps and sessile serrated lesions. The endoscopist's adenoma detection rate (ADR), classically defined as the proportion of screening colonoscopies in which one or more adenomas are detected, has been demonstrated to be strongly inversely associated with their patients' risk of post-colonoscopy colorectal cancer. Therefore, improving adenoma detection is a major target of quality assurance efforts.

The Veterans Health Administration's (VA) National Gastroenterology and Hepatology Program (NGHP) has embarked on a number of efforts to measure, monitor, and improve colonoscopy quality across the VA enterprise. One of these efforts is the VA Endoscopy Quality Improvement Program (VA-EQuIP) which is a collaboration between the VA Quality Enhancement Research Initiative (QUERI), the Office of Research and Development (ORD) and the NGHP. Investigators in the Measurement Science QUERI have developed processes for assessing the ADR of individual physicians and facilities through extraction of data from the Corporate Data Warehouse (CDW). Through collaboration with the VA Clinical Assessment Reporting and Tracking Program (CART), more detailed colonoscopy report information is available for 29 VA medical centers, with additional VA facilities expected to be added to the list soon. Overall, the VA ADR for colonoscopies of all indications is 47%[1], well above the benchmark of 30% for men undergoing screening colonoscopy.

In 2021, the FDA approved the first artificial intelligence (AI) system for computer assisted detection (CADe) of colorectal neoplasia. These CADe devices project an image on the endoscopy monitor (i.e., a bounding box) to alert the endoscopist to the presence of a suspected polyp within the colon. Initial studies, including randomized controlled trials, have demonstrated that use of CADe systems result in a significant improvement in adenoma detection, with a reduction in the miss rate of adenomas (i.e., fewer adenomas are found on a second colonoscopy when the first colonoscopy was performed with a CADe system compared to when the first colonoscopy did not use CADe).[2-4] However, more recent studies have not demonstrated a clear benefit of these devices.[5,6] Moreover, most of the additional adenomas that are detected are diminutive polyps, the vast majority of which are thought to be of minimal, if any, clinical significance. When multiple adenomas are detected during colonoscopy, current guidelines recommend repeating colonoscopy sooner than would otherwise be recommended. Also, the CADe systems may have unintended consequences, such as creating alert fatigue through false alarms or negatively impacting training of gastroenterology fellows.

Objective: The NGHP planned to formally evaluate the quantitative and qualitative impact and outcomes of use of CADe within VA medical centers following the purchase and distribution to randomly selected gastrointestinal endoscopy units.

Setting: Veteran Health Administration (VA) Medical Centers

Intervention: As part of ongoing quality assurance efforts, the NGHP purchased 115 Medtronic GI Genius® CADe devices in late 2022. All facilities were sorted according to their facility-level ADR (for all indications) and categorized as below 30%, 30% to <40% or ≥40%. A random number generator was then used to sort the VA medical centers within each of these 3 ADR strata. Alternating facilities (i.e., approximately 50%) of facilities within the 2 lower ADR stratum were allocated the CADe devices. To assure equitable distribution of the remaining CADe devices across the 18 VA Integrated Service Networks (VISNs), the remaining devices were offered to randomly selected facilities (all within the ≥40% ADR stratum) such that each VISN had 2-3 facilities with CADe devices.

Upon identification of a potential site, the Gastroenterology Section Chief (or equivalent) at that randomly selected site was asked if they were interested in receiving the devices and if all endoscopists at their facility would agree to use the device during colonoscopy. The physicians were not mandated to use the devices but were asked to notify the NGHP if endoscopists were not routinely using the devices so that the devices could be reallocated to other VA facilities that would make use of the CADe devices. Upon receiving concurrence from the Gastroenterology Section Chief, the devices were installed in all procedure rooms that are routinely used for colonoscopy at that facility. The devices were not installed on travel carts for emergency procedures. One facility did decline to receive the devices due to concerns that the devices would negatively impact efficiency in the endoscopy unit. That facility was replaced with another randomly selected VA medical center. Ultimately, 43 VA facilities received and installed the 115 CADe devices.

Survey: To assess the end-user experience, a Microsoft Forms electronic survey will be distributed to VA endoscopists who performed at least 25 colonoscopies between December 1, 2022 and May 31, 2023. Endoscopists will be invited via email with up to two follow-up reminders. Survey questions will address self-reported use of CADe for different colonoscopy indications, assessment of the benefits and negative impacts of CADe (e.g., impact on neoplasia detection or withdrawal time), and overall impression of CADe. Survey completion will be optional. Only staff gastroenterologists and surgeons will be eligible to complete the survey.

Oversight: This quality assurance evaluation was conducted under the auspices of the VA NGHP. Evaluation of the quality of colonoscopy, including the effectiveness of CADe, was previously deemed to be quality assurance by the University of Utah and Salt Lake City VA Medical Center (IRB_00119922); a continuing review of this IRB with amendment was approved for evaluation of AI implementation in 2022.

Outcomes:

3) VA Facility Level
    a) Adenoma detection rate for all indications
        i) The proportion of colonoscopies in which one or more adenomas are found.
        ii) Limit to ages 45-75 years
        iii) Also evaluate for all ages
    b) Number of polyps per colonoscopy

i) Limited to Provation sites

c) Size of polyps detected
    i) Limited to Provation sites
    ii) Average size
    iii) Categorized as
        (1) 1-5mm
        (2) 6-9mm
        (3) ≥10mm

d) Surveillance recommendations after colonoscopy
    i) Use health factors for follow-up recommendation after colonoscopy
    ii) Limit to ages 45-65 years
    iii) Repeat colonoscopy interval
        (1) <3 years
        (2) 3 years
        (3) 4 years
        (4) 5 years
        (5) 6 years
        (6) 7 years
        (7) 8 years
        (8) 9 years
        (9) 10 years
    iv) Resume average risk screening
        (1) <3 years
        (2) 3 years
        (3) 4 years
        (4) 5 years
        (5) 6 years
        (6) 7 years
        (7) 8 years
        (8) 9 years
        (9) 10 years
    v) No further screening
    vi) No health factor found

e) Withdrawal time when no maneuvers are performed
    i) Limited to Provation Sites (unless EndoPro comes online)

f) Withdrawal time, including the performance of maneuvers
    i) Limited to Provation Sites (unless EndoPro comes online)

g) Total procedure time
    i) When no maneuvers are performed
    ii) When all procedures are included

h) Bowel preparation quality
    i) Adequate vs. inadequate
    ii) Excellent vs. good vs. fair vs. poor
    iii) Boston Bowel Preparation Score

i) Adenocarcinoma detection rate
    i) The proportion of colonoscopies found to have adenocarcinoma

4) VA Provider Level
    a) Adenoma detection rate for all indications
        i) The proportion of colonoscopies in which one or more adenomas are found.
        ii) Limit to ages 45-75 years
        iii) Also evaluate for all ages
    b) Number of polyps per colonoscopy
    c) Size of polyps detected
        i) Average size
        ii) Categorized as
            (1) 1-5mm
            (2) 6-9mm
            (3) ≥10mm
    d) Surveillance recommendations after colonoscopy
        i) Use health factors for follow-up recommendation after colonoscopy
        ii) Limit to ages 45-65 years
        iii) Repeat colonoscopy interval
            (1) <3 years
            (2) 3 years
            (3) 4 years
            (4) 5 years
            (5) 6 years
            (6) 7 years
            (7) 8 years
            (8) 9 years
            (9) 10 years
        iv) Resume average risk screening
            (1) <3 years
            (2) 3 years
            (3) 4 years
            (4) 5 years
            (5) 6 years
            (6) 7 years
            (7) 8 years
            (8) 9 years
            (9) 10 years
        v) No further screening/surveillance
        vi) No recommendation found
    e) Withdrawal time when no maneuvers are performed
        i) Limited to Provation Sites (unless EndoPro comes online)
    f) Withdrawal time, including the performance of maneuvers
        i) Limited to Provation Sites (unless EndoPro comes online)

g) Total procedure time
    i) When no maneuvers are performed
    ii) When all procedures are included
h) Bowel preparation quality
    i) Adequate vs. inadequate
    ii) Excellent vs. good vs. fair vs. poor
    iii) Boston Bowel Preparation Score
i) Adenocarcinoma detection rate
    i) The proportion of colonoscopies found to have adenocarcinoma
j) Qualitative assessment (from survey)
    i) Benefits of CADe
    ii) Negative aspects of CADe
    iii) False positive alerts
    iv) Impact on fellow training
    v) Overall satisfaction with CADe

Database:
Colonoscopy details are extracted from the Corporate Data Warehouse and, when possible, the endoscopy reporting system via the CART database, including:

1) VA facility
2) Patient characteristics
    a) Age
    b) Gender
    c) Race
    d) Ethnicity
3) Colonoscopy indication
    a) Screening
    b) Surveillance
    c) FOBT+
    d) Other
    e) Unknown
4) Bowel preparation quality
    a) Adequate vs. inadequate
    b) Aronchick
    c) Boston Bowel Preparation Score
5) Colonoscopy findings
    a) Adenoma detection
    b) Adenocarcinoma detection
    c) Number of polyps detected
    d) Number of polyps detected according to size
        i) 1-5mm
        ii) 6-9mm
        iii) ≥10mm
    e) Withdrawal time

f) Total procedure time

6) Follow-up Plans after colonoscopy (using Gap Reminder health factors)
7) A new variable coding the presence or absence of CADe will be added to each colonoscopy based upon the date of installation of the GI Genius CADe device at each facility.
   a) In order to allow for endoscopists to adapt to performing colonoscopy with the CADe device, all colonoscopies performed within 21 days of the date of installation will be classified as "CADe Training" and will be excluded from the analysis.

Statistical Methods:

1) Within facility comparison (pre- vs. post): All outcome variables will be compared between the pre-CADe and post-CADe time periods (starting 21 days after CADe installation). We will aim for a minimum of 3 months on post-CADe assessment, compared to 6 months of pre-CADe colonoscopies.
2) Between facility comparison: The 43 VA facilities that received CADe devices will be compared to over 100 VA facilities that did not receive CADe devices.
3) Categorical variables will be compared using the Chi-square test.
4) Continuous variables will be compared with the t-test or Wilcoxon rank sums test, as appropriate.
5) To adjust for potential confounders, multivariable models will be constructed.
   a) Logistic regression will be used for dichotomous outcomes (e.g., adenoma detection)
   b) Polytomous logistic regression will be used for ordinal outcomes (e.g., colonoscopy surveillance recommendations)
   c) Linear regression will be used for continuous outcomes (e.g., withdrawal time)
   d) Shell tables are provided below, detailing the variables to be included in the models

Computer Assisted Detection of Neoplasia during Colonoscopy Evaluation (CADeNCE)

Study Protocol Version 2.0

August 8, 2023

Evaluation Team:
Jason A. Dominitz, MD, MHS
Tonya Kaltenbach, MD, MS, MEd
Andrew J. Gawron, MD, PhD
Grace McKee, PhD
Katherine J. Hoggatt, PhD, MPH

Summary of major revisions:

1) Refinement of the statistical analysis plan
   a) Dr. Hoggatt was added to the evaluation team to refine the statistical analysis plan.
2) Refinement of the study outcomes
   a) The VA-EQuIP team developed methods to assess other relevant secondary outcomes (e.g., sessile serrated lesion detection) that were added to the evaluation
   b) As Provation MD data was not readily available to assess many of the proposed secondary outcomes (e.g., indication, polyp size), evaluation of these outcomes is deferred

Background:
Colonoscopy is a key diagnostic and therapeutic procedure for the prevention of colorectal cancer (CRC) incidence and mortality. Central to colonoscopy's effectiveness is the identification and removal of colorectal neoplasia, including adenomatous polyps and sessile serrated lesions. The endoscopist's adenoma detection rate (ADR), classically defined as the proportion of screening colonoscopies in which one or more adenomas are detected, has been demonstrated to be strongly inversely associated with their patients' risk of post-colonoscopy colorectal cancer. Therefore, improving adenoma detection is a major target of quality assurance efforts.

The Veterans Health Administration's (VA) National Gastroenterology and Hepatology Program (NGHP) has embarked on a number of efforts to measure, monitor, and improve colonoscopy quality across the VA enterprise. One of these efforts is the VA Endoscopy Quality Improvement Program (VA-EQuIP) which is a collaboration between the VA Quality Enhancement Research Initiative (QUERI), the Office of Research and Development (ORD) and the NGHP. Investigators in the Measurement Science QUERI have developed processes for assessing the ADR of individual physicians and facilities through extraction of data from the Corporate Data Warehouse (CDW). Through collaboration with the VA Clinical Assessment Reporting and Tracking Program (CART), more detailed colonoscopy report information is available for 29 VA medical centers, with additional VA facilities expected to be added to the list soon. Overall, the VA ADR for colonoscopies of all indications is 47%[1], well above the benchmark of 30% for men undergoing screening colonoscopy.

In 2021, the FDA approved the first artificial intelligence (AI) system for computer assisted detection (CADe) of colorectal neoplasia. These CADe devices project an image on the endoscopy monitor (i.e., a bounding box) to alert the endoscopist to the presence of a suspected polyp within the colon. Initial studies, including randomized controlled trials, have demonstrated that use of CADe systems result in a significant improvement in adenoma detection, with a reduction in the miss rate of adenomas (i.e., fewer adenomas are found on a second colonoscopy when the first colonoscopy was performed with a CADe system compared to when the first colonoscopy did not use CADe).[2-4] However, more recent studies have not demonstrated a clear benefit of these devices.[5,6] Moreover, most of the additional adenomas that are detected are diminutive polyps, the vast majority of which are thought to be of minimal, if any, clinical significance. When multiple adenomas are detected during colonoscopy, current guidelines recommend repeating colonoscopy sooner than would otherwise be recommended. Also, the CADe systems may have unintended consequences, such as creating alert fatigue through false alarms or negatively impacting training of gastroenterology fellows.

Objective:
The NGHP planned to formally evaluate the quantitative and qualitative impact and outcomes of use of CADe within VA medical centers following the purchase and distribution to randomly selected gastrointestinal endoscopy units.

Setting:
Veteran Health Administration (VA) Medical Centers

Intervention:
As part of ongoing quality assurance efforts, the NGHP purchased 115 Medtronic GI Genius® CADe devices in late 2022. All facilities were sorted according to their facility-level ADR (for all indications) and categorized as below 30%, 30% to <40% or ≥40%. A random number generator was then used to sort the VA medical centers within each of these 3 ADR strata. Alternating facilities (i.e., approximately 50%) of facilities within the 2 lower ADR stratum were allocated the CADe devices. To assure equitable distribution of the remaining CADe devices across the 18 VA Integrated Service Networks (VISNs), the remaining devices were offered to randomly selected facilities (all within the ≥40% ADR stratum) such that each VISN had 2-3 facilities with CADe devices.

Upon identification of a potential site, the Gastroenterology Section Chief (or equivalent) at that randomly selected site was asked if they were interested in receiving the devices and if all endoscopists at their facility would agree to use the device during colonoscopy. The physicians were not mandated to use the devices but were asked to notify the NGHP if endoscopists were not routinely using the devices so that the devices could be reallocated to other VA facilities that would make use of the CADe devices. Upon receiving concurrence from facility endoscopy leadership, the devices were installed in all procedure rooms that are routinely used for colonoscopy at that facility. The devices were not installed on travel carts for emergency procedures. One facility did decline to receive the devices due to concerns that the devices would negatively impact efficiency in the endoscopy unit. That facility was replaced with another randomly selected VA medical center. Ultimately, 43 VA facilities received and installed the 115 CADe devices.

Survey: To assess the end-user experience, a Microsoft Forms electronic survey will be distributed to VA endoscopists who performed at least 25 colonoscopies between December 1, 2022 and May 31, 2023. Endoscopists will be invited via email with up to two follow-up reminders. Survey questions will address self-reported use of CADe for different colonoscopy indications, assessment of the benefits and negative impacts of CADe (e.g., impact on neoplasia detection or withdrawal time), and overall impression of CADe. Survey completion will be optional. Only staff gastroenterologists and surgeons will be eligible to complete the survey.

Oversight:
This quality assurance evaluation was conducted under the auspices of the VA NGHP. Evaluation of the quality of colonoscopy, including the effectiveness of CADe, was previously deemed to be quality assurance by the University of Utah and Salt Lake City VA Medical Center (IRB_00119922); a continuing review of this IRB with amendment was approved for evaluation of AI implementation in 2022. This quality assurance evaluation is registered with ClinicalTrials.gov (NCT05888623).

Database:
The VA Corporate Data Warehouse administrative and patient care data will be used to temporally link CPT codes for colonoscopy to pathology results to assess detection of neoplasia and other study outcomes. Natural language processing (NLP) with full-text indexing searches is used to classify pathology (i.e., adenoma, sessile serrated lesion, adenocarcinoma). Validation of this method to classify adenomas from the pathology results showed 99.5% accuracy.(Gawron et al. unpublished) Separately, colonoscopy data from sites using Provation MD software (Provation, Minneapolis, MN) is exported to a national VA database for quality assurance purposes. This software includes information on colonoscopy quality, such as withdrawal time, indication, bowel preparation quality. Outcomes will be ascertained for colonoscopies performed between October 1, 2021 through June 30, 2023.

Outcomes:
Primary outcome: The primary outcome is the change in ADR from the pre- to post-deployment periods from colonoscopies performed with CADe available compared to colonoscopies performed where CADe was not available.

Secondary Outcomes:
1) Adenocarcinoma detection rate
2) Sessile serrated lesion detection rate
3) Proportion of colonoscopies where pathology specimens are obtained
4) Proportion of pathology without adenoma or adenocarcinoma
    a) This serves as a surrogate for false positive lesion detection during use of CADe
5) Withdrawal time when no maneuvers are performed
    a) Limited to Provation Sites
    b) To assess the negative impact of CADe on procedure time or a possible Hawthorne effect.
6) Provider satisfaction with CADe for colonoscopy
7) Adenoma detection rate stratified by the endoscopist's pre-CADe ADR quintile

Additional analyses to be considered (due to data availability):
1) Bowel preparation quality
    a) Limited to Provation sites
2) Number of polyps per colonoscopy
    a) Limited to Provation sites
3) Size of polyps detected
    a) Limited to Provation sites
4) Advanced neoplasia detection rates
    a) Limited to Provation sites
5) Surveillance recommendations after colonoscopy

Independent Variables:
1) VA Facility characteristics
    a) Pre-randomization adenoma detection rate

2) Patient characteristics
    a) Age
    b) Gender
    c) Race
    d) Ethnicity
    e) Rurality
3) Provider characteristics
    a) Specialty
    b) Sex
    c) Years since completion of medical training
4) Colonoscopy indication (Provation sites only, if available)
    a) Screening
    b) Surveillance
    c) FOBT+
    d) Other
    e) Unknown
5) Bowel preparation quality (Provation sites only, if available)
    a) Adequate vs. inadequate
    b) Aronchick
    c) Boston Bowel Preparation Score

Statistical Methods:
Colonoscopies performed on the day of CADe installation and the next 5 colonoscopies performed by each endoscopist after the date of installation (or matched date for control sites) will be excluded as a washout period to minimize training adaptation. For the 26 endoscopists who performed colonoscopies at multiple facilities, we will retain only procedures at the facility where they performed the largest number of colonoscopies.

Baseline data will be summarized as number (%), mean (± standard deviation) or median (interquartile range), as appropriate. For binary outcomes, we will estimate the association of CADe on study outcomes using mixed effects logistic regression (PROC GLIMMIX, SAS software, Cary, NC) with a random intercept for endoscopist and a random slope (at the endoscopist level) for study phase. We will also include fixed effects for group, phase, and a group by phase interaction (product term), with colonoscopy serving as the unit of analysis. The group by phase interaction is quantified as a ratio of odds ratios, where a coefficient greater than 1 for the interaction term (or 0 on the log-odds scale) reflects increased neoplasia detection in the post-deployment phase versus the pre-deployment phase in the CADe group compared to the non-CADe group. We will control for pre-randomization ADR stratum, patient demographics (e.g., sex, age, race, ethnicity, and rurality), and endoscopist information (e.g., specialty, sex, years since medical degree) in all analyses.

After estimating the association of CADe on adenoma detection, we will assess whether the effect was moderated by patient and endoscopist characteristics. We will fit additional models

for each potential moderator, adding a main effect for the moderator and interactions (product terms) with group, phase, and group by phase terms as fixed effects.

Withdrawal time information will only be available from the subset of VA facilities that use Provation MD software. As withdrawal time in a continuous variable, we will use a linear mixed effects regression model with the same predictors as described above. We will include only those colonoscopies without an associated pathology report and where cecal intubation was complete.

To assess whether the effect of CADe on ADR is moderated by endoscopist ADR quintile, endoscopists with at least 100 colonoscopies in the pre- and post-deployment phases each will be divided into quintiles based on pre-intervention ADR. The quintile variable will be entered into the model described above as a main effect and an interaction (product term) with the group, phase, and group by phase terms.

Computer Assisted Detection of Neoplasia during Colonoscopy Evaluation (CADeNCE)

Study Protocol Version 2.1

September 10, 2025

Evaluation Team:
Jason A. Dominitz, MD, MHS
Tonya Kaltenbach, MD, MS, MEd
Andrew J. Gawron, MD, PhD
Grace McKee, PhD
Katherine J. Hoggatt, PhD, MPH

Summary of major revisions:

1) In addition to random intercepts for endoscopist and study phase in the regression models, a random intercept for facility was added as this was the unit of randomization

Background:
Colonoscopy is a key diagnostic and therapeutic procedure for the prevention of colorectal cancer (CRC) incidence and mortality. Central to colonoscopy's effectiveness is the identification and removal of colorectal neoplasia, including adenomatous polyps and sessile serrated lesions. The endoscopist's adenoma detection rate (ADR), classically defined as the proportion of screening colonoscopies in which one or more adenomas are detected, has been demonstrated to be strongly inversely associated with their patients' risk of post-colonoscopy colorectal cancer. Therefore, improving adenoma detection is a major target of quality assurance efforts.

The Veterans Health Administration's (VA) National Gastroenterology and Hepatology Program (NGHP) has embarked on a number of efforts to measure, monitor, and improve colonoscopy quality across the VA enterprise. One of these efforts is the VA Endoscopy Quality Improvement Program (VA-EQuIP) which is a collaboration between the VA Quality Enhancement Research Initiative (QUERI), the Office of Research and Development (ORD) and the NGHP. Investigators in the Measurement Science QUERI have developed processes for assessing the ADR of individual physicians and facilities through extraction of data from the Corporate Data Warehouse (CDW). Through collaboration with the VA Clinical Assessment Reporting and Tracking Program (CART), more detailed colonoscopy report information is available for 29 VA medical centers, with additional VA facilities expected to be added to the list soon. Overall, the VA ADR for colonoscopies of all indications is 47%[1], well above the benchmark of 30% for men undergoing screening colonoscopy.

In 2021, the FDA approved the first artificial intelligence (AI) system for computer assisted detection (CADe) of colorectal neoplasia. These CADe devices project an image on the endoscopy monitor (i.e., a bounding box) to alert the endoscopist to the presence of a suspected polyp within the colon. Initial studies, including randomized controlled trials, have demonstrated that use of CADe systems result in a significant improvement in adenoma detection, with a reduction in the miss rate of adenomas (i.e., fewer adenomas are found on a second colonoscopy when the first colonoscopy was performed with a CADe system compared to when the first colonoscopy did not use CADe).[2-4] However, more recent studies have not demonstrated a clear benefit of these devices.[5,6] Moreover, most of the additional adenomas that are detected are diminutive polyps, the vast majority of which are thought to be of minimal, if any, clinical significance. When multiple adenomas are detected during colonoscopy, current guidelines recommend repeating colonoscopy sooner than would otherwise be recommended. Also, the CADe systems may have unintended consequences, such as creating alert fatigue through false alarms or negatively impacting training of gastroenterology fellows.

Objective:
The NGHP planned to formally evaluate the quantitative and qualitative impact and outcomes of use of CADe within VA medical centers following the purchase and distribution to randomly selected gastrointestinal endoscopy units.

Setting:
Veteran Health Administration (VA) Medical Centers

Intervention:
As part of ongoing quality assurance efforts, the NGHP purchased 115 Medtronic GI Genius® CADe devices in late 2022. All facilities were sorted according to their facility-level ADR (for all indications) and categorized as below 30%, 30% to <40% or ≥40%. A random number generator was then used to sort the VA medical centers within each of these 3 ADR strata. Alternating facilities (i.e., approximately 50%) of facilities within the 2 lower ADR stratum were allocated the CADe devices. To assure equitable distribution of the remaining CADe devices across the 18 VA Integrated Service Networks (VISNs), the remaining devices were offered to randomly selected facilities (all within the ≥40% ADR stratum) such that each VISN had 2-3 facilities with CADe devices.

Upon identification of a potential site, the Gastroenterology Section Chief (or equivalent) at that randomly selected site was asked if they were interested in receiving the devices and if all endoscopists at their facility would agree to use the device during colonoscopy. The physicians were not mandated to use the devices but were asked to notify the NGHP if endoscopists were not routinely using the devices so that the devices could be reallocated to other VA facilities that would make use of the CADe devices. Upon receiving concurrence from facility endoscopy leadership, the devices were installed in all procedure rooms that are routinely used for colonoscopy at that facility. The devices were not installed on travel carts for emergency procedures. One facility did decline to receive the devices due to concerns that the devices would negatively impact efficiency in the endoscopy unit. That facility was replaced with another randomly selected VA medical center. Ultimately, 43 VA facilities received and installed the 115 CADe devices.

Survey: To assess the end-user experience, a Microsoft Forms electronic survey will be distributed to VA endoscopists who performed at least 25 colonoscopies between December 1, 2022 and May 31, 2023. Endoscopists will be invited via email with up to two follow-up reminders. Survey questions will address self-reported use of CADe for different colonoscopy indications, assessment of the benefits and negative impacts of CADe (e.g., impact on neoplasia detection or withdrawal time), and overall impression of CADe. Survey completion will be optional. Only staff gastroenterologists and surgeons will be eligible to complete the survey.

Oversight:
This quality assurance evaluation was conducted under the auspices of the VA NGHP. Evaluation of the quality of colonoscopy, including the effectiveness of CADe, was previously deemed to be quality assurance by the University of Utah and Salt Lake City VA Medical Center (IRB_00119922); a continuing review of this IRB with amendment was approved for evaluation of AI implementation in 2022. This quality assurance evaluation is registered with ClinicalTrials.gov (NCT05888623).

Database:
The VA Corporate Data Warehouse administrative and patient care data will be used to temporally link CPT codes for colonoscopy to pathology results to assess detection of neoplasia and other study outcomes. Natural language processing (NLP) with full-text indexing searches is used to classify pathology (i.e., adenoma, sessile serrated lesion, adenocarcinoma). Validation of this method to classify adenomas from the pathology results showed 99.5% accuracy.[7] Separately, colonoscopy data from sites using Provation MD software (Provation, Minneapolis, MN) is exported to a national VA database for quality assurance purposes. This software includes information on colonoscopy quality, such as withdrawal time, indication, bowel preparation quality. Outcomes will be ascertained for colonoscopies performed between October 1, 2021 through June 30, 2023.

Outcomes:
Primary outcome: The primary outcome is the change in ADR from the pre- to post-deployment periods from colonoscopies performed with CADe available compared to colonoscopies performed where CADe was not available.

Secondary Outcomes:
1) Adenocarcinoma detection rate
2) Sessile serrated lesion detection rate
3) Proportion of colonoscopies where pathology specimens are obtained
4) Proportion of pathology without adenoma or adenocarcinoma
    a) This serves as a surrogate for false positive lesion detection during use of CADe
5) Withdrawal time when no maneuvers are performed
    a) Limited to Provation Sites
    b) To assess the negative impact of CADe on procedure time or a possible Hawthorne effect.
6) Provider satisfaction with CADe for colonoscopy
7) Adenoma detection rate stratified by the endoscopist's pre-CADe ADR quintile

Additional analyses to be considered (due to data availability):
1) Bowel preparation quality
    a) Limited to Provation sites
2) Number of polyps per colonoscopy
    a) Limited to Provation sites
3) Size of polyps detected
    a) Limited to Provation sites
4) Advanced neoplasia detection rates
    a) Limited to Provation sites
5) Surveillance recommendations after colonoscopy

Independent Variables:
1) VA Facility characteristics
    a) Pre-randomization adenoma detection rate

2) Patient characteristics
    a) Age
    b) Gender
    c) Race
    d) Ethnicity
    e) Rurality
3) Provider characteristics
    a) Specialty
    b) Sex
    c) Years since completion of medical training
4) Colonoscopy indication (Provation sites only, if available)
    a) Screening
    b) Surveillance
    c) FOBT+
    d) Other
    e) Unknown
5) Bowel preparation quality (Provation sites only, if available)
    a) Adequate vs. inadequate
    b) Aronchick
    c) Boston Bowel Preparation Score

Statistical Methods:
Colonoscopies performed on the day of CADe installation and the next 5 colonoscopies performed by each endoscopist after the date of installation (or matched date for control sites) will be excluded as a washout period to minimize training adaptation. For the 26 endoscopists who performed colonoscopies at multiple facilities, we will retain only procedures at the facility where they performed the largest number of colonoscopies.

Baseline data will be summarized as number (%), mean (± standard deviation) or median (interquartile range), as appropriate. For binary outcomes, we will estimate the association of CADe on study outcomes using mixed effects logistic regression (PROC GLIMMIX, SAS software, Cary, NC) with random intercepts for facility and endoscopist and random slopes (at the facility and endoscopist level) for study phase. We will also include fixed effects for group, phase, and a group by phase interaction (product term), with colonoscopy serving as the unit of analysis. The group by phase interaction is quantified as a ratio of odds ratios, where a coefficient greater than 1 for the interaction term (or 0 on the log-odds scale) reflects increased neoplasia detection in the post-deployment phase versus the pre-deployment phase in the CADe group compared to the non-CADe group. We will control for pre-randomization ADR stratum, patient demographics (e.g., sex, age, race, ethnicity and rurality), and endoscopist information (e.g., specialty, sex, years since medical degree) in all analyses.

After estimating the association of CADe on adenoma detection, we will assess whether the effect was moderated by patient and endoscopist characteristics. We will fit additional models

for each potential moderator, adding a main effect for the moderator and interactions (product terms) with group, phase, and group by phase terms as fixed effects.

Withdrawal time information will only be available from the subset of VA facilities that use Provation MD software. As withdrawal time in a continuous variable, we will use a linear mixed effects regression model with the same predictors as described above. We will include only those colonoscopies without an associated pathology report and where cecal intubation was complete.

To assess whether the effect of CADe on ADR is moderated by endoscopist ADR quintile, endoscopists with at least 100 colonoscopies in the pre- and post-deployment phases each will be divided into quintiles based on pre-intervention ADR. The quintile variable will be entered into the model described above as a main effect and an interaction (product term) with the group, phase, and group by phase terms.

References:

1. Gawron AJ, Yao Y, Gupta S, et al. Simplifying Measurement of Adenoma Detection Rates for Colonoscopy. *Dig Dis Sci*. Sep 2021;66(9):3149-3155. doi:10.1007/s10620-020-06627-2
2. Hassan C, Spadaccini M, Iannone A, et al. Performance of artificial intelligence in colonoscopy for adenoma and polyp detection: a systematic review and meta-analysis. *Gastrointest Endosc*. Jan 2021;93(1):77-85 e6. doi:10.1016/j.gie.2020.06.059
3. Repici A, Badalamenti M, Maselli R, et al. Efficacy of Real-Time Computer-Aided Detection of Colorectal Neoplasia in a Randomized Trial. *Gastroenterology*. Aug 2020;159(2):512-520 e7. doi:10.1053/j.gastro.2020.04.062
4. Wallace MB, Sharma P, Bhandari P, et al. Impact of Artificial Intelligence on Miss Rate of Colorectal Neoplasia. *Gastroenterology*. Jul 2022;163(1):295-304 e5. doi:10.1053/j.gastro.2022.03.007
5. Ladabaum U, Shepard J, Weng Y, Desai M, Singer SJ, Mannalithara A. Computer-aided Detection of Polyps Does Not Improve Colonoscopist Performance in a Pragmatic Implementation Trial. *Gastroenterology*. Mar 2023;164(3):481-483 e6. doi:10.1053/j.gastro.2022.12.004
6. Levy I, Bruckmayer L, Klang E, Ben-Horin S, Kopylov U. Artificial Intelligence-Aided Colonoscopy Does Not Increase Adenoma Detection Rate in Routine Clinical Practice. *Am J Gastroenterol*. Nov 1 2022;117(11):1871-1873. doi:10.14309/ajg.0000000000001970
7. Gawron AJ, McKee G, Dominitz JA, Yao Y, Whooley M, Kaltenbach T. Validation of a National Pathology Database for Colonoscopy Quality Reporting and Assurance. *Clin Gastroenterol Hepatol*. Apr 2025;23(5):866-868 e1. doi:10.1016/j.cgh.2024.08.017