Nye metoder: Innspill til metoder (forslag/metodevarsler/oppdrag)

Alle har anledning til å komme med tilleggsopplysninger til en metode som er foreslått for nasjonal metodevurdering. Det er ønskelig at innspill kommer inn så tidlig som mulig i prosessen, fortrinnsvis før behandling i Bestillerforum RHF.

Bruk dette skjemaet for å gi innspill til forslag, metodevarsler og oppdrag. På nyemetoder.no vil nye forslag/metodevarsler ha statusen «Forslag mottatt/åpent for innspill» før behandling i Bestillerforum RHF. Utfylt skjema sendes nyemetoder@helse-sorost.no.

NB: **Punkt 1-3 og 11 fylles ut av alle.** Punkt 4-9 fylles ut avhengig av rolle og kjennskap til metoden.

Jeg er klar over at skjemaet vil bli publisert i sin helhet på nyemetoder.no (kryss av): ☒
Har du informasjon du mener ikke kan offentliggjøres, ta kontakt med sekretariatet før innsending.

Jeg har fylt ut punkt 11 nedenfor «Interesser og eventuelle interessekonflikter» (kryss av): ☒

1.Hvilken metode gjelder innspillet?	
Metodens ID nummer*:	ID2024_018
Metodens tittel:	Kunstig intelligens-assistert endoskopi for deteksjon av kreft og precancerøse tilstander i tarm

*ID-nummer finner du på metodesiden på nyemetoder.no og har formen ID2020_XXX

2. Opplysninger om den som gir innspill	
Navn	Benny Borgman
Eventuell organisasjon/arbeidsplass	Medtronic AS
Kontaktinformasjon (e-post / telefon)	Benny.Borgman@Medtronic.com +46 72 555 7990

3. Oppsummert innspill til metoden (besvares av alle)

- GI Genius™ is used clinical practice across Europe, but only in a clinical trial in Norway.
- Products/technologies using artificial intelligence to assist endoscopy in the detection of cancer and precancerous conditions in the intestine are not the same. Therefore, clinical evidence from one technology cannot be used to assess the performance of another technology.
- When assessing technologies, the total cost of ownership needs to be considered, including the need for potential initial investments in completely new, or upgraded, colonoscopy columns to access the AI functionality (not relevant for brand agnostic AI solutions).

- As some artificial intelligence technologies include both the capability of detecting colon anomalies (CADe) and lesion characterization (CADx), the health technology assessment should do the same for the resulting recommendations to be actionable by the health care providers.

Nærmere informasjon om metoden og innspill til PICO*

*PICO er et verktøy for å formulere presise problemstillinger i metodevurderingsarbeid. PICO er en forkortelse for Population/Problem – Intervention – Comparison – Outcome. PICO brukes til å presisere hvilken populasjon/problem som skal studeres, hvilke(t) tiltak (metode/behandling) som skal vurderes, hvilket tiltak det er naturlig å sammenligne med, og hvilke utfall/endepunkter det er relevant å måle/vurdere. PICO er viktig for planlegging og gjennomføring av en metodevurdering.

4. Kjenner du til om metoden er i bruk i Norge i dag?
Er metoden i bruk utenom kliniske studier i dag: GI Genius™ is used in clinical practice across Europe but only in a clinical trial in Norway. Diagnostic AI in colonoscopy is used in Norway but limited to one specific supplier offering endoscopy towers with fully integrated AI functionality (CADe only) Fra hvilket tidspunkt har den vært i bruk: - Hvor er eventuelt metoden i bruk: -

5. Hvilken pasientgruppe i den norske spesialisthelsetjenesten er metoden aktuell for? (PICO)
Beskriv kortfattet: Patients that need to undergo a colonoscopy, including patients invited to undergo CRC screening.

6. Er du kjent med behandlingsalternativer til denne metoden og hvordan disse fungerer for pasientgruppen i dag? (PICO)
Beskriv kortfattet: Standard colonoscopy without AI functionality.

7. Har du innspill til hva som vil være viktig for pasienter som er aktuelle for behandling med metoden? (PICO)

Hva kan oppfattes som en fordel for pasienter og brukere med denne metoden sammenlignet med aktuelle alternativer? Hvilke endepunkter/resultater av behandlingen er det aktuelt å måle? Beskriv kortfattet:

- Adenoma miss rate (AMR)
- Adenoma detection rate (ADR)
- Polyp detection rate (PDR)
- Average polyps per colonoscopy (APC)
- Safety
- Sensitivity per frame (low false positive rate)
- Finding polyps easy to be missed to reduce risk of interval cancer.
- By classifying the polyps as adenoma or non-adenoma at above ESGE limit of 90% confidence level to reduce number of removed polyps. And by that minimize risk of complication and reduce cost of removal and/or complications. (using resect & discard or diagnose & leave strategy)
- Patient confidence from being treated with a system that has been proven in clinical studies

8. Spesielt for medisinsk utstyr (besvares av leverandør): CE-merking

Foreligger det CE-merking for bruksområdet som beskrives i metoden? I så fall angi type og tidspunkt:
GI Genius™ system CE marked as class I from 18th Dec 2018
CADx or polyp characterization software CE marked as class IIa from 8 July 2021
GI-Genius™ is to date the only AI colonoscopy device that has received de novo FDA clearance since 8 Sept 2020.

9. Spesielt for legemidler (besvares av leverandør): Markedsføringstillatelse (MT)

Har legemiddelet MT for indikasjonen som omfattes av metoden? Angi i så fall tidspunkt eller ventet tidspunkt for MT:

10. Andre kommentarer

Introduction: The assessment of artificial intelligence-assisted endoscopy for the detection of cancer and precancerous conditions in the intestine is announced as a full technology appraisal. However, currently available products do not form a homogenous body of solutions. They are based on different algorithms, distinct set of pre-loaded images that drive the AI interpretation, have different evidence bases and different solutions in terms of interoperability. This needs to be accounted for in the evaluation for the resulting recommendations to be optimized for the Norwegian health care system and for the patients.

Clinical evidence: The algorithms that drive the AI guidance can be compared to a standard algorithm and depending on how you set it up, you will arrive at different outcomes. Therefore, results from one AI solution cannot automatically be transferred to another product. Instead, each producer needs to prove the clinical benefit of their specific product. The GI Genius™ intelligent endoscopy module is the first commercially available AI-assisted colonoscopy module, being FDA-cleared and CE-marked with more than 20 publications to date (ref 1-21) supporting the clinical value of GI Genius™.

This evidence includes multiple randomized controlled trials (RCTs) published in world renowned scientific journals demonstrating that physicians using GI Genius™ can improve the quality of CC procedures and the detection of heterogenous colon lesions (ref 1,3,9,14,15,18). GI Genius™ is to date the most studied device with proven clinical and economic benefit.

The recently performed Danish HTA of artificial intelligence-assisted endoscopy even found that only GI Genius™ had the evidence needed to perform a cost-effectiveness analysis, stating that "The evidence base for the meta-analysis is limited to examining the effect of one CADe technology (GI-genius, Medtronic)." (ref 22, page 58).

A selection of performance highlights only proven for GI Genius™ in clinical studies include: In a randomized controlled trial (RCT) performed in an expert endoscopist setting GI Genius™ contributed to a 14% absolute increase in ADR vs standard high-definition white light colonoscopy. (ref 15)

Another RCT performed in a non-expert setting showed that the use of GI Genius™ CADe was associated with a 22% relative increase in ADR. This was also the case for the adenoma per colonoscopy (APC) rate which increased by 21%. (ref 14)

In a tandem RCT performed in 8 centers across Europe and US, the adoption of GI Genius™ was associated with a reduction in the risk of adenoma miss rate (AMR) by approximately 50%, when compared with a standard colonoscopy. (ref 1)

In the first validation study the proportion of the frames with a False Positive (FP) over the total number of frames in a colonoscopy was measured to be less than 1%. (ref 10)

Results from several studies confirmed that the clinical relevance of GI Genius's FP rate is negligible and that it was associated with an insignificant time of additional inspection. (ref 13, 19)

Moreover, the clinical performance of GI Genius™ characterization (CADx) module (version 3) was assessed in a prospective study (ref 12) that demonstrated its effectiveness in meeting the international thresholds for adopting leave in situ strategies for diminutive rectosigmoid polyps.

The prospective study (ref 12) on GI Genius CADx performance showed:

• a 97.6% Negative Predictive Value (NPV) for GI Genius™, exceeding the 90% NPV threshold for adenomatous histology required for the leave-in-situ strategy in standard white light endoscopy
• more than 95% agreement on surveillance intervals
• 44% of the removed polyps were amenable for leave in situ strategy

Image base: Just like different algorithms can give different end results, so can the quality and quantity of the in-data. For example, a regression analysis with only one or two explaining factors and a limited data set will have a large error-term. As more accurate variables and date are added to the regression the smaller explanatory value is left in the residual. The amount, quality and representativeness of images loaded into the AI module is in a similar way important for the end result when using artificial intelligence-assisted endoscopy for the detection of cancer and precancerous conditions in the intestine.

It is essential to transparently report on the architecture of AI algorithms, as well as on the data that are used for training and the method that is used for testing, in order to address the concerns over the black-box nature of AI and its potential biases. The manufacturer of the GI Genius™ is a strong believer of this type of transparency and has shared the details of the patient demographics and dataset subdivision used in the GI Genius™ CADe v1 module. These data are summarized in figure 2 and table 1 of the Cherubini et al paper (ref 27). The total number of the frames that were used for training and testing of the CADe v1 device was over 13 million. (ref 27)

Total cost of ownership: Medtronic GI Genius™ technology is brand agnostic. It comes in the form of an external box that can be used with any current colonoscopy column, regardless of manufacturer. Other solutions on the market requires AI module and colonoscopy column to be from the same manufacturer and they are sold as an integrated system. This leads to significant threshold costs for investments in artificial intelligence-assisted endoscopy. Even in the cases when the hospital has a column of the "right" brand there could be significant costs for software upgrades to ensure compatibility with the same brand AI module. The assumption of compatibility with existing colonoscopy columns is only trivial for the brand agnostic GI Genius™ technology, not for the brand specific technologies.

This dynamic also impacts the freedom manufacturers have when it comes to pricing of the AI module. Some companies with brand requirement may sell the AI module at a low cost but make up the revenue by demanding costly software upgrades to the colonoscopy column. Only focusing on the AI module acquisition cost and service agreement may therefore be misleading and total cost may be underestimated both in the cost-effectiveness analysis and budget impact for modules that are not brand agnostic.

Cost-effectiveness and CADx: CADe, the ability for artificial intelligence-assisted detection of polyps, has been found to be a cost-effective, even dominant (cost saving) strategy to further prevent colorectal cancer (CRC) incidence and mortality (ref 23,28, 29). A cost-utility model from an Italian healthcare perspective estimated that the GI Genius™ CADe system, on a cohort of 100.000 patients, could prevent 155 CRC cases (-2.7%), 77 CRC-related deaths (-2.8%), and could improve quality of life (+0.027QALY) compared to colonoscopy alone. The increase in screening cost (+€10.50) and care for adenoma (+€3.53) was offset by the savings in cost of care for CRC (-€28.37) leading to a total saving of €14.34 per patient. (ref 28)

However, development of the GI Genius™ artificial intelligence module now also allows for polyp characterization (CADx). With this technology it is possible to implement a "Resect & discard" or "Diagnose & Leave"-strategy (Ref 30). As GI Genius™ is meeting the criteria required to implement cost-saving strategies in colonoscopy (ref 32), the system may

substantially reduce the polypectomy-related burden for patients (through the reduction of unnecessary resections), as well as the burden for healthcare systems (through the reduction of pathology costs). (ref 30) Evidence exists showing the cost-saving potential with this approach (ref 25, 33).

Interviewed clinicians in the Danish HTA report (ref 22, section 9.1.4.5) agreed that characterization adds value. Leaving out CADx and its potential to optimize the patient pathway via diagnose and leave strategies from the analysis will thus not provide an accurate description of current solutions. Furthermore, only including CADe capabilities in the evaluation will also lead to ambiguity in the final recommendations. Learnings can be taken from the Danish HTA that only evaluated CADe and excluded CADx, but in the final recommendation highlighted that: “The professional committee draws attention to the fact that, due to further development of the technology, CADe systems may no longer be marketed which do not simultaneously contain a characterization function (CADx).” (ref 26, page 2). The resulting question from the health care providers are then what products are included in the recommendation from the evaluation.

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11. Interesser og eventuelle interessekonflikter

Beskriv dine relasjoner eller aktiviteter som kan påvirke, påvirkes av eller oppfattes av andre å ha betydning for den videre håndteringen av metoden som det gis innspill på (for eksempel: økonomiske interesser i saken, oppdrag eller andre bindinger).

Beskriv kortfattet:
This document has been filled in by employees of Medtronic that is the distributor of the GI Genius™.