Script for Guideline on Screening for Esophageal Adenocarcinoma in Patients with Chronic Gastroesophageal Reflux Disease

[Slide 1]
The Canadian Task Force on Preventive Health Care - Guideline on screening for esophageal adenocarcinoma in patients with chronic gastroesophageal reflux disease

[Slide 2]
- These slides are made available publicly following the guideline's release as an educational support to assist with the dissemination, uptake and implementation of the guidelines into primary care practice
- Some or all of the slides in this slide deck may be used in educational contexts

[Slide 3]
- The Esophageal adenocarcinoma (EAC) screening Working Group consisted of: Task Force members (Stéphane Groulx (Chair), Scott Klarenbach, Harminder Singh* (non-voting TF member), Brett Thombs, Brenda Wilson,), Non-voting members from the Public Health Agency of Canada (Heather Limburg, Marion Doull) and from the Evidence Review and Synthesis Centre - Ottawa Health Research Institute (OHRI) (Candyce Hamel, Andrew Beck, Nadera Ahmadzai, Micere Thuku, Kusala Pussegoda, Adrienne Stevens, Becky Skidmore, Avijit Chatterjee, Donna E. Maziak, Kristopher Dennis, Lise Bjerre, Lorenzo Ferri, Beverley Shea, Brian Hutton, Julian Little and David Moher)
- Task Force spokespersons are: Stephane Groulx, Brett Thombs and Scott Klarenbach
- Clinical experts were Paul Belletrutti and Laura Targownik

[Slide 4]
- Overview of the Webinar
- Presentation
    - Background on esophageal adenocarcinoma
    - Methods of the CTFPHC
    - Recommendation
    - Results
    - Rationale for recommendations
    - Knowledge gaps and next steps
    - Other national EAC screening recommendations
    - Conclusions
- Questions and Answers

[Slide 5]
- Background

[Slide 6]
- In 2019, an estimated 6 new cases of esophageal cancer were diagnosed per 100,000 Canadians.
    - [In comparison lung and breast cancer were estimated at 62 and 67 cases per 100,000 Canadians in 2019]
- The 5-year net survival rate, estimated at 15%, is among the poorest of all cancer prognoses.
    - [Only pancreatic cancer has a worse prognosis with a 8% five-year net survival rate, while lung cancer has 19% and breast cancer has 88% survival].
- Males have a higher incidence than females with an estimated 9 cases versus 2 cases per 100,000, respectively.

- Esophageal adenocarcinoma is Canada's most common esophageal cancer type, followed by squamous cell carcinoma.
- Incidence has shifted over the past 40 years with rates of adenocarcinoma increasing and squamous cell carcinoma falling (see Figure in next slide). This change may result from increases in adenocarcinoma-related risk factors (e.g., gastroesophageal reflux, obesity) and decreases in risk factors linked to squamous cell carcinoma (e.g., smoking).

[Slide 7]
- Age standardized incidence rates for esophageal adenocarcinoma (EAC) and esophageal squamous cell carcinoma (ESCC), all ages, Canada (excluding Quebec – data unavailable), 1986 to 2015.
    - The rate of esophageal adenocarcinoma has increased while esophageal squamous cell carcinoma has decreased since 1986
    - The largest changes are seen among men with EAC increasing from 2.6 in 1986 to 5.6 in 2015 (red line) and ESCC decreasing from 4.0 in 1986 to 2.1 in 2015 (blue line)

[Slide 8]
- Esophageal adenocarcinoma's most important risk factors are precancerous conditions (e.g., Barrett esophagus, esophageal dysplasia), older age (≥50 years), gastroesophageal reflux disease (GERD), male sex, family history, white race/ethnicity, abdominal obesity and smoking
- GERD is a common condition where reflux of stomach contents (acid regurgitation) causes troublesome symptoms (e.g., heartburn, water brash). It is associated with a 5 to 7 times increased likelihood of developing EAC (35 versus 7 cases per 100 000 males at age 60)
- BE is a pre-cancerous condition where intestinal-type mucosa replaces the normal squamous mucosa. Approximately 5 to 15% of GERD patients develop Barrett esophagus versus 1 to 2% of the general population
- EAC is believed to follow a sequential progression from GERD to BE to low then high grade dysplasia.
- The risk of developing EAC is 0.3% per year with BE (no dysplasia), 0.5% with low grade dysplasia and 6% with high grade dysplasia

[Slide 9]
- The target population in adults with chronic GERD
- This guideline does not apply to people with chronic GERD exhibiting alarm symptoms for esophageal adenocarcinoma (e.g. dysphagia, odynophagia, recurrent vomiting, unexplained weight loss, anemia, loss of appetite or gastrointestinal bleeding) or who were previously diagnosed with Barrett esophagus (with or without dysplasia), as clinicians should evaluate and manage those people accordingly.

[Slide 10]
- Methods

[Slide 11]
- The Canadian Task Force on Preventive Health Care is an independent body of up to 15 clinicians and methodologists
- The mandate is to develop evidence-based clinical practice guidelines that support primary care providers in the delivery of preventive healthcare
- Ultimately the goal of the Task Force is to improve the health of Canadians by making sure that primary care providers have access to clinical prevention guidelines which are based on the best available evidence.

[Slide 12]
- The CTFPHC works with Evidence Review and Synthesis Centres (ERSCs) who independently review the evidence.
- The ERSCs undertake a systematic review of the literature based on the analytical framework and prepare the final report and GRADE tables
- They also participate in working group and CTFPHC meetings (non-voting)

[Slide 13]
- The TF review process includes:
- Internal review by the guideline working group and all other CTFPHC members
- External review is undertaken at 3 key stages:
    - Protocol, systematic review(s) and guideline
- External stakeholder reviewer groups include:
    - Generalist and disease specific stakeholders
    - Federal and Provincial/Territorial stakeholders
    - Academic peer reviewers
- CMAJ undertakes an independent peer review process to review guidelines before accepting for publication

[Slide 14]
The guideline is based on three reviews:

1. Screening for esophageal adenocarcinoma and precancerous conditions (dysplasia and Barrett esophagus) in patients with chronic gastroesophageal reflux disease with or without other risk factors: Systematic review
2. Patient values and preferences in relation to screening for esophageal adenocarcinoma and precancerous conditions (dysplasia and Barrett esophagus) in patients with chronic gastroesophageal reflux disease with or without other risk factors: Systematic review
3. Benefits and Harms of Treatment Options for Esophageal Adenocarcinoma and precancerous Conditions: An Overview of Systematic Review

[Slide 15]
- All three guidelines are published together in the journal "Systematic reviews" and can also be found on the TF website

[Slide 16]
Analytical framework shows the KQs
- KQ1: What are the benefits and harms of screening?
- KQ2: How do adults weight the benefits and harms of screening (patient preferences)
- KQ3: What are the benefits and harms of treatment for BE, dysplasia and stage 1 EAC?

Outcomes include:
- Mortality (all-cause and EAC)
- Survival
- Quality of life
- Incidence of EAC by stage, incidence of BE and low or high grade dysplasia
- Medical consequences of screening (e.g. hospitalization, injury)
- Psychological effects of screening (e.g. anxiety)
- Major or minor medical procedures following screening

- Overdiagnosis

[Slide 17]
- The Task Force uses GRADE to develop recommendations.

[Slide 18]
The GRADE process involves:
- Defining questions in terms of populations, alternative management strategies and patient-important outcomes.
- Characterising outcomes as critical or important to developing recommendations.
- Completing a systematic search for relevant studies
- Developing a pre-defined criteria for eligible studies generate best estimate of the effect of the intervention on each critical and important outcome
- Assessing the certainty of evidence associated with the effect estimate.

[Slide 19]
The GRADE Approach:
- RCTs start as high-certainty evidence and observational studies as low-certainty evidence
- RCT data is prioritized over observational
- Rating of certainty is modified downward for each outcome across studies in relation to:
    - Study limitations (Risk of Bias)
    - Imprecision
    - Inconsistency of results
    - Indirectness of evidence
    - Publication bias likely (part of the upgrading criteria below)
- Rating of certainty is modified upward for each outcome across studies in relation to:
    - Publication bias (undetected)
    - Large magnitude of effect
    - Dose response
    - No evidence for plausible confounders likely minimizing the effect

[Slide 20]
What are we grading?
1. Certainty of Evidence

Degree of confidence that the available evidence correctly reflects the theoretical true effect of the intervention or service *(High, moderate, low, very low)*

2. Strength of Recommendation

The balance between the certainty of supporting evidence; the certainty about the balance between desirable and undesirable effects; the certainty/variability in values and preferences of individuals; and the certainty about whether the intervention represents a wise use of resources *(strong and conditional)*

[Slide 21]
- Ideally, direct evidence should be examined which consists of studies examining the effects of screening versus no screening among chronic GERD patients.
- When direct evidence is unavailable the task force may also examine indirect evidence.

- Indirect evidence is either linked to the outcome (e.g. treatment) or related to the intervention (e.g. different screening interventions) but this indirectness decreases the certainty of evidence

[Slide 22]
Recommendation

[Slide 23]
- The TF recommends not screening adults (≥18 years) with chronic GERD, for esophageal adenocarcinoma or precursor conditions (Barrett esophagus or dysplasia) (strong recommendation; very low-certainty evidence).
- This recommendation does not apply to people with chronic GERD exhibiting alarm symptoms or to those diagnosed with Barrett esophagus (with or without dysplasia)
- Although risk factors such as age (≥50 yr), male sex, family history, white race/ethnicity, abdominal obesity and smoking may increase the risk for esophageal adenocarcinoma, relevant trials and cohort studies did not include sufficient data within each category to support modifying our screening recommendation based on these factors, alone or in combination.

[Slide 24]
Other considerations for implementation:
- Clinicians should be aware of alarm symptoms for esophageal adenocarcinoma and evaluate, refer and manage patients accordingly.
- They should also apply clinical judgement for the investigation and management of those unresponsive to GERD treatment or with symptoms suggestive of other upper gastrointestinal disorders (e.g., dyspepsia).

[Slide 25]
Results

[Slide 26]
Benefits of screening for EAC were analysed in the systematic review. These included:
- All-cause mortality or survival
    - Direct evidence from one retrospective cohort study indicates no statistically significant difference in survival (all cause) as a result of screening (very low certainty evidence)
- Incidence of EAC (by stage), BE and dysplasia
    - Direct evidence from one retrospective cohort study indicates statistically significant absolute effect of 156 more per 1,000 diagnosed with a lower stage of esophageal adenocarcinoma (stage 1 versus stages 2-4) (very low certainty evidence). There was no evidence on the incidence of BE and/or dysplasia.
- EAC mortality
    - No data
- Quality of life
    - No data

[Slide 27]
Harms of screening for EAC were analysed in the systematic review, these included:

- Life threatening or severe medical consequences of screening

- Indirect evidence from two trials comparing sedated esophagogastroduodenoscopy (sEGD) versus unsedated transnasal esophagoscopy (uTNE) (N = 209) and uTNE versus unsedated transoral esophagogastroduodenoscopy (uEGD) (N = 59) reported one serious adverse event (following uTNE)
- Psychological effects
    - Indirect evidence from three RCTs comparing uTNE was associated with statistically significant higher anxiety compared to sEGD (during procedure) or swallowed VCE (before and during procedure).
    - However, the mild additional discomfort seems to be well tolerated, given that 70 to 95% of participants stated they would undergo it again

[Slide 28]
Harms (continued)
- Overdiagnosis
    - No data
- Additional major and minor medical procedures
    - No data

Subgroup analysis
- A priori-defined subgroup analysis variables included age, sex, body mass index (BMI), smoking history, duration of chronic GERD, definition of chronic GERD, groupings of risk factors, and various ethnic groups. Due to the poor reporting of variables, we were not able to perform our a priori-defined subgroup analysis.

[Slide 29]
Direct evidence on the benefits of EAC screening among chronic GERD patients was found in 2 retrospective cohort studies
- Rubenstein, 2008: Compared GERD patients with prior EGD versus no prior EDG
    - Initiated from 1995-2003 in the US.
    - 155 veterans (99% male)
- Hammad, 2018: Compared GERD patients with prior EGD versus no prior EDG
    - Initiated from 2005-2017 in the US.
    - 153 patients (99% male)
- Certainty of the evidence from these studies was assessed as being very low due to serious concerns around risk of bias, indirectness, and imprecision.
- Both studies presented insufficient data to permit subgroup analyses by risk factors
- There was no direct evidence on the incidence of BE and/or dysplasia.

[Slide 30]
Benefits of EAC screening among chronic GERD patients:
- Rubenstein et al., reported no statistical difference in long-term survival between those who had received a prior EGD and those who had not (HR 0.82, 95% CI 0.52-1.29). Adjustment for age, comorbidities, and year of diagnosis yielded similar results (HR 0.93, 95% CI, 0.58-1.50).
- Rubenstein et al., also showed a statistically significant lower stage at diagnosis for those with a prior EDG (screening). 156 per 1,000 more had a lower stage (stage 1 vs stage 2-4) at diagnosis with prior EGD (5 more to 486 more). This represents a risk ratio of 2.27 (Confidence interval of 1.04 to 4.95) and an absolute increase of 15.7%.

- The other study (Hammad et al., 2018) only had one patient fit our criteria (i.e. not under surveillance for BE and was screened in the previous five years). An additional 15 had received an EGD more than five years ago, with no details on timing. This one patient was diagnosed with "unknown stage" of EAC.

[Slide 31]
- There was no direct evidence on harms of EAC screening (i.e. comparing screening vs no screening)
- However, indirect evidence on harms (life threatening, severe or medically significant consequences of screening) was found in 2 RCTs comparing different screening modalities
    - Sami, 2015: Compared screening with sedated EGD versus hospital based unsedated transnasal endoscopy (uTNE) and mobile based uTNE among GERD patients
        - Initiated from 2011-2013 in the US.
        - 209 patients (46% male) with a one time test.
- Zaman 1999: Compared screening with uTNE versus unsedated EGD among GERD patients
        - Study dates not reported. Performed in the US.
        - 105 patients (58% male) with one time test.
- Certainty of the evidence from these trials was assessed as being very low due to very serious concerns around risk of bias and serious concerns around indirectness and imprecision (Sami, 2015) and serious concerns around risk of bias, indirectness and imprecision (Zaman, 1999).
- Both studies presented insufficient data to permit subgroup analyses by risk factors

[Slide 32]
Harms of screening (life threatening, severe, or medically significant consequences)
- In Sami et al, serious adverse events were assessed 1 and 30 days after the procedure. No serious adverse events were reported in any of the study arms (sEGD versus uTNE).
- In Zaman et al., 1 of 25 participants had serious, or medically significant consequences with uTNE and 0 of 34 with uEGD.

[Slide 33]
- There was no direct evidence on harms of EAC screening (i.e. comparing screening vs no screening)
- However, indirect evidence on harms (psychological harms) was found in 4 RCTs comparing different screening modalities
    - Chak, 2014: Compared screening with uTNE versus swallowed video capsule endoscopy (VCE) among GERD patients
        - Study dates not reported. Performed in the US.
        - 184 patients (96% male) with a one time test.
    - Jobe, 2006: Randomized crossover study. Compared screening with sEGD + biopsy versus uTNE among GERD patients
        - Initiated from 2004-2005 in the US.
        - 134 patients (80% male) with a one time test for each modality (crossover).

    - Sami, 2015: Compared screening with sEGD versus hospital based uTNE and mobile based uTNE among GERD patients
        - Initiated from 2011-2013 in the US.
        - 209 patients (46% male) with a one time test.

[Slide 34]
- Zaman 1999: Compared screening with uTNE versus uEGD among GERD patients
    - Study dates not reported. Performed in the US.
    -105 patients (58% male) with one time test.
- Certainty of the evidence from these trials was assessed as being very low due to very serious concerns around risk of bias and serious concerns around indirectness and imprecision (Chak, 2014, Jobe, 2006, Sami, 2015, and Zaman, 1999).
- All studies presented insufficient data to permit subgroup analyses by risk factors

[Slide 35]
Harms of screening (psychological harms)
- In Chak et al, there was a statistically significant increase in anxiety before the procedure associated with unsedated TNE compared to swallowed VCE (RR=2.28, CI 1.33-3.88). 213 per 1,000 more experienced anxiety with uTNE (55 more to 480 more) compared to swallowed VCE. This represents an absolute increase of 21.3%.
- In Jobe et al., there was no difference in anxiety rates before the procedure between sedated EGD and unsedated TNE
- Sami et al, reported no statistically significant difference between uTNE and unsedated EGD in terms of anxiety before the procedure

[Slide 36]
Harms of screening (psychological harms)
- In Jobe et al, There was statistically more anxiety during insertion reported with uTNE compared to sedated EGD
- In Zaman et al., there was no statistically significant difference between uTNE and unsedated EGD for anxiety during insertion.

[Slide 37]
Harms of screening (psychological harms)
- In Chak et al, there was a statistically significant increase in anxiety during the procedure associated with unsedated TNE compared to swallowed VCE (RR=2.14, CI 1.22-3.77). 177 per 1,000 more experienced anxiety with uTNE (34 more to 421 more) compared to swallowed VCE. This represents an absolute increase of 17.7%.
- In Jobe et al., and Sami et al., both studies reported statistically significant differences with those randomized uTNE experiencing more anxiety during the procedure than sedated EGD
- Zaman et al, reported that mean anxiety did not differ between the uTNE and unsedated EGD groups in terms of anxiety during the procedure

[Slide 38]
Patient Values and Preferences on Screening for Esophageal Adenocarcinoma

[Slide 39]
A systematic review by Hamel et al., 2019 assessed
(a) how adults with chronic GERD weigh the benefits and harms of screening for EAC
(b) what factors contribute to these preferences and to their decision to undergo screening

- The SR identified two RCTs and one cohort study

[Slide 40]
The included studies were:

- Chak, 2014: Patients asked to participate in RCT compared screening with uTNE versus swallowed VCE among GERD patients
    - Study dates not reported. Performed in the US.
    - Patient characteristics providing outcome data not reported
- Zaman 1999: Patients asked to participate in RCT compared screening with uTNE versus uEGD among GERD patients
    - Study dates not reported. Performed in the US.
    - Patient characteristics providing outcome data not reported
- Zaman 1998: Patients asked to participate in cohort study compared screening with uEGD versus sEGD among GERD patients
    - Study dates not reported. Performed in the US.
    - Patient characteristics providing outcome data not reported

-Risk of bias for these studies for the outcome "uptake of screening" was assessed as high risk due to issues with randomization, blinding of participants, missing protocols, selective outcome reporting and sources of funding.

[Slide 41]

- The systematic review of patient values and preferences found no evidence on how patients weigh the benefits and harms of screening. However, evidence on factors that contribute to willingness to be screened (acceptability) was found in three studies comparing endoscopic screening strategies
- Zaman, et al., 1999 and Zaman et al., 1998 showed high "stated or intended" refusal rates (45 of 105; 43% and 19 of 62; 31% respectively) due to anxiety, lack of interest, fear of gagging, unwilling to be study subjects, or reluctance to undergo transnasal procedures. Chak et al., showed that among 1,210 invited participants, 52% did not respond to the letter, 32% refused (no reason provided), 1% were ineligible, and 0.2% cited difficulty attending.

[Slide 42]
Patient values and preferences: Focus groups

- The Task Force engaged patients in guideline development through two phases conducted by the Knowledge Translation group at St. Michael's Hospital, Toronto.
- Each phase recruited 17 men and women (aged ≥18 years) with chronic GERD.
- Phase 1 included online surveys and telephone focus groups to obtain patient ratings of relevant outcomes.
- Phase 2 asked participants to reconsider outcome ratings when presented with synthesized evidence from the systematic reviews.
- Results indicated that chronic GERD participants had a moderate desire to be screened (median rating = 6 out of 9; where 1 = not at all willing and 9 = very much willing).

[Slide 43]
Summary of patient values and preferences

- Acceptability of screening was variable due to individual values and preferences; some people consistently favoured screening because of individual and familial risk factors, personal beliefs, or fear of missing an early diagnosis (e.g. focus group response (moderate intention to screen))

- While others were concerned about the invasiveness and risks of screening (e.g. reluctance to participate in screening trials due to anxiety or fear of gagging (low actual participation found in SR))

Based on this range of observations from trials and within focus groups, values and preferences for screening are judged to be variable.

[Slide 44]
Treatment of Barrett esophagus, dysplasia and stage I EAC

[Slide 45]
Treatment of Barrett esophagus, dysplasia or stage 1 EAC

- Given the limited availability of direct evidence on screening effectiveness, the Task Force also examined the effectiveness of treatment options for stage 1 EAC and precancerous conditions (BE and/or dysplasia).

A review of systematic reviews identified 11 systematic reviews

- Pandey, 2018: Patients diagnosed with BE and low grade dysplasia (LGD). Comparison of radiofrequency ablation (RFA) versus endoscopic surveillance.
    - Date of last search: May 2017. Conducted in the UK
    - 2 RCTs; 619 patients
- Codipilly, 2018: Patients diagnosed with BE. Comparison of endoscopic surveillance versus no surveillance.
    - Date of last search: September 2017. Conducted in the US
    - 1 ongoing RCT; 3,400 patients

[Slide 46]

- Almond, 2014: Patients diagnosed with LGD. Comparison of photodynamic therapy (PDT) vs argon plasma coagulation (APC).
    - Date of last search: January 2013. Conducted in the UK
    - 6 RCTs (3 providing data); 90 patients
- Chadwick, 2014: Patients diagnosed with BE and high grade dysplasia (HGD) or intramucosal cancer. Comparison of (a) complete endoscopic mucosal resection (EMR) + triple therapy (proton pump inhibitors (PPIs), Histamine type 2 Receptor Antagonist (HR2A) and sucralfate) vs RFA + triple therapy and (b) RFA + PPI vs sham + PPI.
    - Date of last search: January 2013. Conducted in the UK
    - 3 RCTs; 47 patients
- De Souza, 2014: Patients diagnosed with BE comparing; (a) PDT vs APC (b) multipolar electrocoagulation (MPEC) vs APC (c) PDT vs PPI, (d) APC vs PPI, (e) RFA vs PPI
    - Date of last search: Not reported. Conducted in Brazil
    - 9 RCTs; 649 patients

[Slide 47]

- Desai, 2017: Patients diagnosed with BE-related neoplasia (HGD/EAC). Comparison of focal EMR + RFA vs stepwise (complete) EMR.
    - Date of last search: June 2016. Conducted in the USA
    - 1 RCT; 47 patients

- Fayter, 2010: Patients diagnosed with BE or EAC. Comparison of (a) 5-aminolevulinic acid (5-ALA)-PDT vs placebo PDT (b) 5-ALA-PDT vs APC (c) PDT with porfimer sodium vs APC (d) PDT with porfimer sodium + PPI vs PPI alone (e) PDT delivery comparisons
    - Date of last search: October 2008. Conducted in the UK
    - 11 RCTs; 594 patients
- Fujii-Lau, 2017: Patients who achieved complete eradication of intestinal metaplasia after treatment with endoscopic eradication therapies. Comparison of (a) Stepwise complete EMR vs RFA (b) RFA vs sham
    - Date of last search: May 2016. Conducted in the USA
    - 2 RCTs; 22 patients

[Slide 48]

- Li, 2008: Patients with BE. Comparison of (a) anti-reflux surgery (ARS) vs Omeprazole (b) PPI vs H2RA (c) PDT vs PPI (d) ARS+APC vs ARS+ endoscopic surveillance (e) APC vs PDT
    - Date of last search: Not reported. Conducted in China
    - 13 RCTs (12 providing data); 747 patients
- Qumseya, 2017: Patients with BE and LGD. Comparison of RFA vs surveillance.
    - Date of last search: December 2015. Conducted in the USA
    - 2 RCT; 199 patients
- Rees, 2010: Patients with BE (with or without dysplasia). Comparison of (a) PPI vs H2RA (b) Celecoxib vs placebo (c) ARS vs PPI/H2RA (d) APC vs endoscopic surveillance (e) APC + PPI vs MPEC + PPI (f) APC + PPI vs PDT (g) PDT + PPI vs PPI (h) 5-ALA-PDT vs PDT (Porfimer sodium) (i) RFA+PPI vs PPI
    - Date of last search: June 2008. Conducted in the UK
    - 16 RCTs (15 providing data); 1074 patients

[Slide 49]

An AMSTAR rating (assessment of methodological quality) for these systematic reviews was assessed as being critically low (Pandey, 2018, Codipilly, 2018, Almond, 2014, Chadwick, 2014, De Souza, 2014, Desai, 2017, Fayter, 2010, Fujii-Lau, 2017, Li, 2008) to low (Qumseya, 2017, Rees, 2010).

[Slide 50]

Results:

- There were few studies, all with small sample sizes by outcome, and for many outcomes, only one study provided results, thereby providing little information with which to gauge the certainty of the evidence.
    - PDT, RFA and EMR of BE (with or without PPI) provided a statistically significant increase in eradication or clearance of dysplasia (very low to low-certainty evidence)
    - Harms included increased stenosis and strictures for EMR compared to RFA and increased stricture formation with PDT plus omeprazole compared to omeprazole alone (very low-certainty evidence).
- No data was available for quality of life, psychological effects, additional medical procedures or overdiagnosis.

[Slide 51]

Rationale for recommendation

[Slide 52]

- One small retrospective cohort study compared screening to no screening and reported that, although patients with a prior EGD were statistically more likely to have a lower stage of adenocarcinoma at time of diagnosis, there were no statistically significant - survival differences (very low-certainty evidence).
- Preferences among chronic GERD patients appear variable. The systematic review indicated hesitancy to participate, while focus groups showed a moderate willingness to be screened.
- Some endoscopic techniques may eradicate dysplasia but the overview of reviews showed a range of possible evidence certainty from very low to low.

[Slide 53]
- One serious adverse event from screening was reported across two small trials, which compared screening modalities (very low-certainty).
- Screening all adults with chronic GERD would require substantial resources. Given the limited and uncertain evidence of effectiveness, we believe screening all patients with chronic GERD would not be feasible or acceptable and that it could inappropriately divert substantial health resources
- In light of:
- No direct evidence of benefit from screening on any critical or important outcome other than a statistically improved stage at diagnosis, without a difference in survival:

- The Task Force recommends against screening all chronic GERD patients

[Slide 54]
- A strong recommendation is used when:
    - The WG is confident that the undesirable effects outweigh the desirable effects or
    - The WG is confident that the desirable effects outweigh the undesirable effects
- The recommendation is strong because in its evidence to decision framework the Task Force placed a high value on the system-wide resources required to screen all chronic GERD patients without evidence of benefit

[Slide 55]
Knowledge gaps and next steps

[Slide 56]
Knowledge gaps
- Screening trials
    -There is a lack of well designed screening trials due to the low prevalence of esophageal adenocarcinoma and limited probability that GERD patients will progress to cancer.
    - Future RCTs should examine screening among chronic GERD subgroup populations to help predict who will progress to EAC
    -A standard definition of what is considered chronic GERD should be agreed upon and employed in trials

[Slide 57]
    - Alternative screening modalities
    - High quality evidence on less invasive screening modalities is needed (e.g. Cytosponge or other swallowed devices)

- Treatment:
    - More and better designed trials are needed

- Interpretation of data was limited due to poorly reported low-quality SRs, unclear or high risk of bias trials with small sample sizes and few studies per treatment modality

[Slide 58]
Harms of screening
- Increased research and understanding of the risk of overdiagnosis and other harms of screening is needed

Patient values and preferences
- Additional studies on patient values and preferences for screening are needed

[Slide 59]
Knowledge translation (KT) tools

[Slide 60]
Knowledge Translation
- A KT tool has been developed to help clinicians and individuals understand the esophageal cancer screening guideline
- After the public release, this tool will be freely available for download in both French and English on the website: http://canadiantaskforce.ca

[Slide 61]
Other national EAC screening recommendations

[Slide 62]
Other national EAC screening recommendations:
- American College of Gastroenterology, 2015
  - Screening for Barrett esophagus may be considered in men with chronic (>5 years) and/or frequent (weekly or more) symptoms of gastroesophageal reflux disease and two or more risk factors for Barrett esophagus or esophageal adenocarcinoma. (Strong recommendation, moderate level of evidence).
- American Society for Gastrointestinal Endoscopy, 2015
  - We suggest that endoscopy be considered in patients with multiple risk factors for Barrett esophagus. (Very low quality)
- National Institute for Health Care Excellence (NICE), 2014
  - Do not routinely offer endoscopy to diagnose Barrett esophagus, (strong recommendation) but consider it if the person has gastroesophageal reflux disease (conditional recommendation). Discuss the person's preferences and their individual risk factors

[Slide 63]
- British Society of Gastroenterology, 2013
  - Screening with endoscopy is not feasible or justified for an unselected population with gastro-oesophageal reflux symptoms (Recommendation grade B).
- American Gastroenterological Association (AGA), 2011
  - We recommend against screening the general population with gastroesophageal reflux disease for Barrett esophagus (strong recommendation, low-quality evidence).
  - In patients with multiple risk factors associated with esophageal adenocarcinoma, we suggest screening for Barrett esophagus (weak recommendation, moderate-quality evidence).

[Slide 64]
Conclusions

[Slide 65]
- The Task Force recommends not screening adults with chronic GERD for EAC and precursor conditions (BE or dysplasia), because available evidence did not demonstrate benefit, and there are uncertain harms, important resource implications and variable patient values and preferences.
- This strong recommendation indicates that clinicians should not offer screening to adults ≥18 years with chronic GERD*

**Excludes those who are exhibiting alarm symptoms or those diagnosed with BE (with or without dysplasia)*

[Slide 66]
For more information on the details of this guideline please see:
Canadian Task Force for Preventive Health Care website: http://canadiantaskforce.ca

[Slide 67]
Questions & Answers
Thank you