Clinical Epidemiology and Global Health 15 (2022) 100997

Contents lists available at ScienceDirect

Clinical Epidemiology and Global Health

journal homepage: www.elsevier.com/locate/cegh

Clinical practice guidelines: Recommendations for CRC screening in Argentinian population with average risk based on iFOBT

Julia Ismael [a,*], María Celeste Díaz [b], Carolina Gabay [a], Luis Ernesto Caro [a], Cecilio Cerisoli [a], Ricardo Figueredo [a], Sandra Canseco [a], Pablo Rodriguez [c], Lucio Criado [d], Ignacio Raffa [e], Juan O'Connor [f], Karin Kopitowsky [g], José Adi [h], Carlos Gonzalez Del Solar [i]

[a] Gedyt Foundation, Argentina
[b] Roffo Institute, Argentina
[c] Chief of the Gastroenterology and Digestive Endoscopy Unit, Cardiology Institute, Cordoba Argentine Medical Association, Argentina
[d] Argentine Society of Medicine, Argentina
[e] CRC Commission Argentine Society of Surgery, Argentina
[f] Argentine Association of Clinical Oncology, Argentina
[g] Argentine Society of Family Medicine, Argentina
[h] Chief of the Gastroenterology Unit, Luis Lagomaggiore Hospital, Argentina
[i] Responsible for the Gastroenterology and Digestive Endoscopy Unit, Mater Dei Clinic, Argentina

ARTICLE INFO

Keywords:
Colorectal cancer screening
Fecal immunochemical test
Guidelines

ABSTRACT

Objectives: Colon cancer (CRC) screening is a cost-effective strategy. A group of experts and methodologists addressed clinical questions to adapt recommendations and provide guidance for health care providers involved in the continuous care of individuals with average-risk for develop CRC. The development group focused on health system resources and implementation issues.

Methods: Following PRISMA guidelines, we carried out a comprehensive systematic review and applied the GRADE-ADOLOPMENT tool. The selected guidelines were appraised through AGREE II tool. The certainty of evidence was rated using GRADE approach.

Finally, we use the Evidence-to-Decision (EtD) frameworks providing by GRADE to discuss benefits and harms, values and preferences, feasibility, acceptability, and equity issues in Argentina to adopt, adapt and make de novo recommendations to the local setting.

Results: Due to the absence of direct evidence, the panel made their recommendations on simulation models to determine how the screening strategies might affect the population outcomes.

The certainty of all the available evidence was very low due to models' assumptions. Since the lack of data about CRC incidence in Argentina and the existing barriers, the panel did not suggest the beginning of screening before 50 years old. The panel highlighted the deficit of colonoscopy availability. Therefore, they suggest that the balance may favor using quantitative over qualitative iFOBT because of the higher specificity to detect CRC and the reduction in colonoscopy required. In our setting and considering adherence, the panel suggests that iFOBT being used annually rather than bi-annual driving an improvement on the loss of follow–up.

Conclusions: The panel the panel did not suggest the beginning of screening before 50 years old, they suggest that the balance may favor using quantitative over qualitative iFOBT and annually iFOBT.

1. Objectives and scope

The aim of these guidelines is to make recommendations on the use of immunochemical fecal occult blood test (iFOBT) for the early detection of precursor lesions (advanced adenomas) and early colorectal cancer (CRC) based on the best evidence available in an average risk population (defined as the absence of either a personal or a family history of CRC, familial adenomatous polyposis, Lynch Syndrome or inflammatory bowel disease, as well as a history of abdominal and/or pelvic radiation therapy) from a population-based clinical perspective

* Corresponding author. Gedyt Foundation, Juncal 2345, C1125ABE, Buenos Aires City, Argentina.
E-mail address: juliaismael@fundaciongedyt.org.ar (J. Ismael).

https://doi.org/10.1016/j.cegh.2022.100997
Received 19 July 2021; Received in revised form 28 January 2022; Accepted 4 February 2022
Available online 10 March 2022

adapted to the local scenario.

The potential benefits and risk of the available options, frequency, feasibility of use and the values and preferences of the users will be considered.

This guide has been designed for Argentinean health care providers involved in the continuous care of patients and individuals with a risk of CRC as well as funding entities and health care decision makers.

2. Introduction

CRC is a potentially curable disease since between 80 and 90% of the cases originate in a polyp. In most cases (around 75%), CRC occurs in individuals with no personal or family history of the disease.

In Argentina, 15,692 new cases of CRC were estimated for the year 2018, including 12.2% of the total number of tumors[1] (Graph 1).

Both global patterns and trends in incidence and mortality related to CRC are correlated with the current levels of human development.[38] Therefore, more interventions are needed (dependent on the resources available) to reduce the number of cases of CRC in the coming decades.[2]

In 2018, CRC was responsible for 7349 deaths,[4] which accounted for a mortality rate adjusted for age of 12.6% per 100,000 habitants.[3]

The most important effectiveness measure of a screening strategy is the decrease in mortality due to a specific cause, compared to the equivalent general population not included in the screening.[5,6,7]

Based on the information available, the World Health Organization (WHO)[8] encouraged countries to develop cancer prevention and control programs in a structured, systematic and gradual fashion based on local considerations and needs.[9] However, the most effective strategy has not been identified yet.[12]

Regardless of the testing strategy, most of the evidence in individuals with average risk applies to the 50- to 70-years-old. So, the recommendations are typically based on this target population. Outside this age range, individualized recommendations should be applied.[13] Method selection depends on the quality of performance and also on the resources available in the area where the program is implemented.[14,15]

According to a report drafted by PAHO (Pan American Health Organization) in 2017,[17] many countries in the region introduced CRC population screening based on iFOBT and are at present in different stages (Graph 2).

In our country the National Prevention and Early Detection Program for Colorectal Cancer was created in 2013.[18] It was implemented including the general population and follow up of higher risk groups. The method selected for individuals of both genders in the 50- to 70-year-old group with public health coverage was the yearly qualitative iFOBT, in case of a positive test a colonoscopy is also performed. An assessment of the impact of the CRC screening program in Argentina based on qualitative iFOBT in 50-year-old with public coverage only concluded that this strategy has a positive impact on the healthcare policy selected and on the number of cases and costs for the state.[19]

2.1. Current technologies available for CRC screening

- Stool guaiac test (gFOBT): This test is based on the peroxidation test through the Guaiacum conjugate which turns blue in the presence of hemoglobin. The participant must collect three stool samples and in some cases some diet restrictions and medication are recommended by the manufacturer since the reactive does not react specifically with human hemoglobin.
- iFOBT: This test is used for the detection of occult blood through antibodies (agglutination inhibition) against human hemoglobin present in feces. These measurements are performed using one sample only and do not require diet or drug restrictions. These tests do not react with hemoglobin digestion products. There are qualitative and quantitative FOBT available. Qualitative tests depend on visual interpretation and are associated with inter-observer variability. Quantitative tests require a lab and the use of standardized procedures and therefore the results are more consistent. The cut-off point to define positivity may differ according to implementation.
- Endoscopic methods: A colonoscopy includes visual assessment, requires preparation and sedation.

3. Methodology

The methodology for guideline adaptation from the Ministry of Health[20] was used to design this guideline.

3.1. Research questions

- What is the age when population screening in individuals with average risk of CRC provides a higher reduction in CRC mortality?
- What is the impact of the quantitative vs. the qualitative iFOBT on CRC screening?
- In the population with an average risk exposed to quantitative iFOBT-based screening strategies, which is the most appropriate screening interval?

3.2. Systematic literature review

A systematic review of the literature according to the PRISMA guidelines was conducted in PubMed, TRIP database, Cochrane Library, Epistemonikos and LILACS. The search was complemented with a manual search. Were included Clinical practice guidelines (CPG), Systematic reviews and meta-analyses, CRC screening, Language: English or Spanish, Publication date: until October 2020.

Outcomes selected: a) Target age for the use of CRC screening methods in average risk populations. b) Impact on the CRC-related incidence and mortality of two qualitative and quantitative iFOBT and the potential harms of using these two techniques. c) Impact on the frequency of use of the quantitative iFOBT (Appendix I).

3.3. Assessment of CPGs according to

AGREE II[21] and then the strategy suggested by the National Ministry of Health was used to select the guidelines which might be adapted (Appendix II and III). Evidence was obtained from the guidelines selected in order to answer questions of interest.

3.4. Development of the consensus for recommendations adapted to the local setting

Panel: authorities of the national scientific societies or key opinion leader in the field (Appendix IV).

The appropriate evidence was identified, and the controversial issues were selected for discussion in relation to the proposed topics.

Methodology for consensus: First, the GRADE® system and the corresponding framework for decision making was presented at a virtual meeting (Appendix VI). The strength of the system is based on the explicit and transparent recommendations obtained from the assessment of the body of evidence (Appendix VII). At the same meeting, the structured summary of evidence found for each question based on accurate evidence was also described. Also, the members of the panel discussed the validation of topics for analysis, the modification or inclusion of relevant questions not included in the original proposal.

At the second virtual meeting, recommendations adapted to the local scenario were made by implementing the decision framework and related domains as provided by GRADEpro.

Finally, a preliminary document was drafted and e-mailed to the members of the panel for revision and underwriting of the final document. The external revision was conducted by Dr. Linda Rabeneck.

All the members of the working group and participants of the consensus declared their conflicts of interest (Appendix V).

This document was funded by *Fundación Gedyt.*

4. Results

A) The selected guidelines were 4 (Table 1)[25]
B) Questions

4.1. What is the age when population screening in individuals with average risk for CRC provides a larger reduction in CRC mortality?

There is no direct evidence of the impact of screening strategies for critical outcome such as CRC-related incidence and mortality in the 45–49 age group. Three European studies initiated in the 80s and 90s included individuals older than 45, gFOBT was used as a screening test and no age subgroup analysis was reported, probably because of the absence of statistical significant power.[26]

CRC caused a total of 7349 deaths in Argentina in 2018 (Table 2),[27] most of them occurs in adults older than 60 years old (Table 3).

Two guidelines include a weak recommendation to conduct screening in the population between the ages of 45 and 50.[22,24] These recommendations are based only on the opinion of the panel members in relation to the increased number of CRC cases in this age group in the territory in question (USA) and used simulation models to support their recommendations.

One guideline[23] use MISCAN model to determine how screening might affect this population. The MISCAN model considers the following: 100% compliance rate; 132 screening strategies; increased incidence adjusted rate in young adults in the USA between 1974 and 2013 according as reported by SEER,[28] and supposing an increased risk as the cohort ages. The endpoint was a balance between the benefits, i.e., years gained and the potential burden and harms, defined as the number of colonoscopies needed. As a reference, strategies including colonoscopy and meeting the effectiveness limit or 98% of this limit as defined by the working group were selected.

The rate between the increase in burden compared to the benefit was (Efficiency Ratio, ER) estimated for the different strategies. The threshold for the strategy recommended by the model was an ER below 39 (as defined by USPSTF) for colonoscopy, while for methods not using colonoscopy the ER was supposed to be under that obtained by the colonoscopy as well as years of life gained equal or under 90% as compared to the colonoscopy.

The most effective strategies by the model were: colonoscopy every 10 years from the age of 45 to the age of 75, for as compared to the 50–75 age group 6.2% more years of life were gained and a 17% of colonoscopies per 1000 adults during a “lifetime” for screening.

In this particular model, the initiation of screening at the age of 40 with colonoscopy every 10 years led to a slight increase in the years of life gained (438 vs. 429) as compared to the initiation at the age of 45 but with the same number of preventable deaths[37] per 1000 adults; so it was not considered a recommended strategy (Table 4).

This model has several limitations: The burden of tools other than colonoscopy was not considered. There is no consensus about the threshold to measure efficacy for the increased number of colonoscopies over the years of life gained. Adherence to screening, follow up and diagnosis is not 100%. There is uncertainty as to whether “test performance” between the ages of 45 and 49 is similar, supposing a lower prevalence, as that observed in older individuals.

It is important to consider that the panel and the model in this selected guideline did not consider costs or the appropriate use of resources for recommendations.

The use of annual iFOBT starting at age 45 vs. 50 prevented one death (11 vs. 12) every 1000 individuals screened, and 3225 more iFOBTs and 296 colonoscopy were needed. Years of life gained were 403 vs. 377, respectively. The 2-year interval also helped prevent one death every 1000 screened individuals (16 vs. 17), a larger number of tests (2134) and colonoscopy (232) were needed every 1000 individuals screened.

The summary of evidence were judged following the GRADE guidelines by Brozek J. et al. (2020)[29] to assess certainty in evidence. Confidence of estimates was very low due to imprecision and indirect evidence (Appendix VIII).

The 2020 USPSTF Update used 3 models (Sim-CRC, CRC-Spin and MISCAN) to assess 239 screening strategies.[22] These models considered epidemiological data from the USA considering a 100% adherence among the individuals screened. The strategies related to the management of CRC were considered for the analysis.

The aim was to determine the best strategy within each modality. This was different from the model proposed by the American Cancer Society (ACS) 2018, where according to the threshold some strategies were recommended by the model or not. The proportion in the increased incidence between both models was also different. (Appendix IX).

The results obtained in two of the three models (Sir-CRC and CRC-spin models), the use of iFOBT starting at age 50 both with an annual interval or an interval every two or three years were strategies characterized by the initiation at the age of 45.

The initiation of quantitative iFOBT at the age of 45 as compared to the age of 50 resulted in one less death (7 vs. 6 for Sim-CRC and CRC-Spin; 11 vs. 10 MISCAN) with more than 3000 iFOBT and 170 colonoscopy needed per 1000 individuals with average risk screened (Appendix X). Noticeably, the cut-off value for iFOBT was under 20 mcg/g.

No direct evidence providing values and preferences of patients on this question has been found (What is the magnitude of benefits and harms accepted to start testing at the age of 45 vs. 50?). The guidelines used to answer this question only mentions high variability in terms of methods and intervals.[30,31]

Another guideline comes to the same conclusion as for the variability in values and preferences about CRC screening, so the members of the panel are asked rounds of questions to indirectly estimate the likely preferences of the target population.[3233]

According to the opinion of the panel, the local epidemiological data of the 45–49 age group should be available.

Recommendation (Table 5).

The guideline panel does not recommend the use of screening in individuals between 45 and 50 years of age with an average risk for CRC (conditional based on very low certainty in the evidence). This decision should be considered within the context of shared decision making.

4.2. What is the impact of quantitative vs. qualitative iFOBT in CRC screening?

Due to the absence of direct evidence in the guidelines selected and given that they only include the quantitative iFOBT, an advisory group (Raguza M and Izcovich A) was asked to assess the impact of both sensitivity and specificity of both tests on CRC incidence and mortality as well as the use of videocolonoscopy and related complications.

A decision tree with 100% adherence and two screening strategies (qualitative and quantitative iFOBT) was selected. For the quantitative tests, different cut off points were selected ($\leq$10 mcg/g, 10–20 mcg/g, 20–30 mcg/g and >30 mcg/g). Incidence and mortality data adjusted for age in Argentina, other sources of mortality were taken from systematic reviews, the prevalence was obtained from the meta-analysis of selected diagnostic studies and the colonoscopy-related complications were obtained from a systematic review (Reumkens, 2016).

The threshold defined as non-trivial or clinically relevant was the detection of 10 new cases or deaths for CRC every 1,000,000 individuals screened, an 8% difference between both methods for sensitivity to detect adenomas and 1% for CRC, and a difference in specificity of 18% and 17% for adenoma and CRC, respectively.

The body of evidence from comparative and non-comparative studies was assessed separately, the certainty was selected in the highest evidence. To answer this question, 42 primaries studies were found, 32 including quantitative iFOBT and 14 qualitative gFOBT. Four studies compared these strategies directly only.

The qualitative method was more sensitive than the quantitative method in the meta-analysis, except for a cut-off point of >30 mcg/g to detect CRC. The quantitative method was more specific except for the detection of CRC at cut off values of 10–20 mcg/g and >30 mcg/g, which showed no differences. Certainty in evidence was from very low to moderate. (Appendix XI).

No differences were seen between false negatives for CRC between the quantitative and the qualitative method except when considering cut off values of >30 mcg/g, when 2 cases less were detected than when using the qualitative method. As for the false positives no differences were reported for CRC for cut off points of >30 mcg/g to 10–20 mcg/g; a difference of 60 less cases was seen when the <10 mcg/g threshold was used. Estimate certainty was from very low to moderate. (Appendix XII). As for the incidence for a cut off value of ≤10 mcg/g, the use of the quantitative test detects 22 cases more, and for a cut off value of >30 mcg/g it is able to detect 15 cases more with very low certainty level in the evidence.

In the case of mortality with a cut off value of ≤10 mcg/g 80 deaths could be obtained, at a range of 10–20 mcg/g, 124 more and at a cut-off point of >30 mcg/g, 253 less with very low level of certainty in the evidence.

The number of colonoscopy and related complications (bleeding, perforations) is lower when using the quantitative method in the cut off points with low certainty in the level of evidence. No comparisons were found for the cut -off point of 20–30 mcg/g (Appendix XIII).

An important limitation of the model is that neither the variability in the adoption of methods or the frequency in follow-up nor the barriers for access are considered.

No evidence related to values and preferences on the use of one method or the other were found either.

4.3. Recommendation

Guideline panel suggests the use of quantitative iFOBT to screen patients with average risk for CRC between the ages of 50 and 70 (conditional based on very low certainty in the evidence). (Table 6).

4.4. In the population with average risk undergoing screening with quantitative iFOBT, what is the most appropriate testing interval?

Due to absence of direct evidence to select the most appropriate interval, the simulation model in the guideline by Helsingen L.M et al. (2019) was used.[23]

The authors used the MISCAN-colon model with epidemiological data from the Norwegian population between the ages of 50 and 79. Four strategies were assessed: colonoscopy, sigmoidoscopy, annual iFOBT and iFOBT every two years.

The cut -off value for the iFOBT test was 20mcg/g. The role of these strategies was simulated in the following outcomes: incidence of CRC, CRC specific mortality and number of colonoscopies per 1000 individuals screened. Other outcomes assessed were global mortality, number of tests used and procedure-related complications.

As reported in the literature, most of the Western individuals over the age of 50 have a 1–2% risk of developing CRC in the next 15 years; so, seven hypothetical cohorts were used with a baseline risk for CRC in 15 years of between 1% and 7%. This risk was estimated using an online tool (Qcancer) which may predict the individual risk of developing CRC based on different variables such as ethnicity.

To estimate the risk for colonoscopy-related complications the data from SEER-Medicare were used. The 2013 European Guidelines on gastrointestinal endoscopy were used for the follow up according to the findings.[34] 100% adherence was estimated for the cohorts both in screening and for follow up.

The authors considered certainty in evidence was low due to the uncertainty observed in: All CRCs derive from an adenoma; differences in CRC risk are caused by differences in the incidence of adenomas and length of time of adenoma.

The tables with the summary of the evidence (Appendix XIV) were designed based on the results of the model to compare the use of annual iFOBT or iFOBT every two years. The level of the evidence went down to very low due to indirect evidence available. The burden was measured considering the number of colonoscopies and the number of tests.

The impact of both strategies is higher when the individual risk is higher; the reduction in the number of cases and mortality with the use of the annual test is higher but associated with the need for a larger number of tests and colonoscopies.

It should be underscored that the perspective for recommendations in this guide is individual so, all the options are supposed to be available and are accessible.

No direct evidence providing estimates about the values and preferences of patients in this field have been found. The analyzed guide concludes that variability is high in terms of values and preferences, so it includes rounds of questions for the panel members to indirectly estimate the probable preferences of the target population[3536]

4.5. Recommendation

The guideline panel suggests the use of quantitative iFOBT with the annual (conditional based on very low certainty in evidence) (Table 7).

Considering that certainty of evidence is very low to estimate the number of preventable deaths with both intervals and even considering the annual use may lead to increased costs, the panel considers the annual interval is more feasible to improve adherence and reduce the loss to follow-up rate.

5. Conclusion

This work provides unprecedented and essential information for Argentina in relation to CRC screening in an average-risk population.

We answer three crucial common practice questions and we hope it can be a critical decision-making tool.

At present, based on the available evidence, the guideline panel does not recommend the use of screening in individuals between 45 and 50 years of age with an average risk for CRC and this decision should be considered within the context of shared decision making; guideline panel suggests the use of quantitative iFOBT to screen patients with average risk for CRC between the ages of 50 and 70 and considering that certainty of evidence is very low to estimate the number of preventable deaths with both intervals and even considering the annual use may lead to increased costs, the panel considers the annual interval is more feasible to improve adherence and reduce the loss to follow-up rate.

Declaration of competing interest

Authors declare that they have no competing interests.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cegh.2022.100997.

References

1 Ministry of Health. National cancer institute, Argentina [En línea] 12 de July de 2020 https://www.argentina.gob.ar/salud/instituto-nacional-del-cancer/estadisticas/incidencia.
2 Arnold M, Sierra MS, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global patterns and trends in colorectal cancer incidence and mortality. *Gut.* 2017;66(4): 683–691. https://doi.org/10.1136/gutjnl-2015-310912.
3 Ministry of Health. National cancer institute. Mortality trends [En línea] [Citado el: 12 de July de 2020 https://www.argentina.gob.ar/salud/instituto-nacional-del-cancer/estadisticas/mortalidad.
4 IARC. Estimated age-standardized mortality rates in 2020, colorectum, both sexes, all ages. Mortality. [En línea] [Citado el: 12 de July de 2020.] https://gco.iarc.fr

/today/online-analysis-map?v=2020&mode=population&mode_population=continents&population=900&populations=900&key=asr&sex=0&cancer=41&type=1&statistic=5&prevalence=0&population_group=0&ages_group%5B%5D=0&ages_group%5B%5D=17&nb_items=10&gr.
5 Sharp L, Tilson L, Whyte S, et al. Cost-effectiveness of population-based screening for colorectal cancer: a comparison of guaiac-based faecal occult blood testing, faecal immunochemical testing and flexible sigmoidoscopy. *Br J Cancer*. 2012 Feb;106(5):805–816. https://doi.org/10.1038/bjc.2011.580.
6 Lansdorp-Vogelaar I, Kuntz KM, Knudsen AB, Wilschut JA, Zauber AG, van Ballegooijen M. Stool DNA testing to screen for colorectal cancer in the Medicare population: a cost-effectiveness analysis. *Ann Intern Med*. 2010;153(6):368–377. https://doi.org/10.7326/0003-4819-153-6-201009210-00004.
7 Telford JJ, Levy AR, Sambrook JC, Zou D, Enns RA. The cost-effectiveness of screening for colorectal cancer. *CMAJ (Can Med Assoc J)*. 2010;182(12):1307–1313. https://doi.org/10.1503/cmaj.090845.
8 WHO. WHA 58 [En línea] [Citado el: 12 de July de 2020.] https://www.who.int/cancer/media/news/WHA58_22-sp.pdf?ua=1.
9 WHO. WHA 58 [En línea] [Citado el: 12 de July de 2020.] https://apps.who.int/iris/bitstream/handle/10665/44022/9789243547114_spa.pdf;jsessionid=9822B0BA03C1D05F93922A78C57DCC3A?sequence=1.
12 Lauby-Secretan B, Vilahur N, Bianchini F, Guha N, Straif K, International Agency for Research on Cancer Handbook Working Group. The IARC Perspective on colorectal cancer screening. *N Engl J Med*. 2018;378(18):1734–1740.
13 Qaseem ADT, Hopkins RH, Humphrey LL, Levine J, Sweet DE, Shekelle P. Clinical guidelines committee of the American college of physicians. Screening for colorectal cancer: a guidance statement from the American college of physicians. *s.l. : Ann Intern Med*. 2012;156:378–386.
14 *International Digestive Cancer Alliance Practice Guidelines: Colorrectal Cancer Screening*. World Gastroenterology Association; 2007.
15 Levin BLD, McFarland B, Andrews KS, et al. *US Multi-Society Task Force, American College, Committee. oRCC. Screening and Surveillance for the Early Detection of Colorectal Cancer and Adenomatous Polyps*vol. 134. American Cancer Society Colorectal Cancer Advisory Group. s.l. : Gastroenterology; 2008:1570–1595, 2008: a joint guideline from the American Cancer Society, the US Multi-Society Task Force.
17 PAHO. Colorectal cancer screening landscape [En línea], [Citado el: 12 de July de 2020 https://www.paho.org/hq/dmdocuments/2016/Colorectal-Cancer-Screening-Landscape-English.pdf; 2017.
18 Ministry of Health. Argentine national cancer institute [En línea] [Citado el: 12 de July de http://servicios.infoleg.gob.ar/infolegInternet/anexos/225000-229999/225414/norma.htm; 2020.
19 Ministry of Health. Argentine National Cancer Institute [En línea] [Citado el: 12 de July de 2020.] http://www.msal.gob.ar/images/stories/bes/graficos/0000001555cnt-tamizaje-ccr-diagramada.pdf.
20 Ministry of Health. Argentine National Cancer Institute Guia de adpatación de GPC [En línea] [Citado el: 12 de July de 2020 https://www.argentina.gob.ar/sites/default/files/guia-adaptacion-gpc.pdf.
21 The AGREE Collaboration. AGREE Instrument Spanish version [En línea] [Citado el: 12 de July de 2020 http://www.agreecollaboration.org.
22 US preventive service task force [En línea] [Citado el: 10 de October de 2020 https://www.uspreventiveservicestaskforce.org/uspstf/document/draft-evidence-review/colorectal-cancer-screening.
23 Helsingen LM, Vandvik PO, Jodal HC, et al. Colorectal cancer screening with faecal immunochemical testing, sigmoidoscopy or colonoscopy: a clinical practice guideline. *BMJ*. 2019 Oct 2;367:l5515. https://doi.org/10.1136/bmj.l5515. PMID: 31578196.
24 Colorectal cancer screening for average-risk adults: 2018 guideline update from the American Cancer Society. Wolf, A.M., Fontham, E.T., Church, T.R., et al. s.l. : CA A Cancer J Clin, Vols. 68: 250-281. doi:10.3322/caac.21457.
25 Cubiella Joaquín, Marzo-Castillejo Mercè, Mascort-Roca Juan José, et al. Guía de práctica clínica. Diagnóstico y prevención del cáncer colorrectal. Actualización, 2018 *Gastroenterología y Hepatología*. 2018;41(9):585–596. https://doi.org/10.1016/j.gastrohep.2018.07.012. ISSN 0210-5705.
26 Lin JS, Piper MA, Perdue LA, et al. Screening for colorectal cancer: updated evidencereport and systematic review for theUS Preventive Services Task Force. *JAMA*. 2016;315, 2576-259.
27 Ministry of Health. DEIS (Dirección de Estadísticas e Información de la Salud) [En línea], [Citado el: 10 de Oct de 2020.] http://www.deis.msal.gov.ar/wp-content/uploads/2020/01/Serie5-Nro62.pdf; 2020.
28 Siegel RL, Fedewa SA, Anderson WF, et al. Colorectal cancer incidence patterns in the United States, 1974-2013. *J Natl Cancer Inst*. 2017;109(8).
29 GRADE guidelines 30: the GRADE approach to assessing the certainty of modeled evidence—an overview in the context of health decision-making. Brozek, Jan L. et al. J Clin Epidemiol, Volume 0, Issue 0.
30 Dolan JG, Boohaker E, Allison J, Imperiale TF. Patients' preferences and priorities regarding colorectal cancer screening. *Med Decis Making*. 2013;33(1):59–70. https://doi.org/10.1177/0272989X12453502.
31 Ely JW, Levy BT, Daly J, Xu Y. Patient beliefs about colon cancer screening. *J Cancer Educ : Off. J. Am. Assoc. Canc. Edu.* 2016 Mar;31(1):39–46. https://doi.org/10.1007/s13187-015-0792-5.
32 Hol L, de Bekker-Grob EW, van Dam L, et al. Preferences for colorectal cancer screening strategies: a discrete choice experiment. *Br J Cancer*. 2010;102:972–980. https://doi.org/10.1038/sj.bjc.6605566. pmid:20197766.
33 Kistler CE, Hess TM, Howard K, et al. Older adults' preferences for colorectal cancer-screening test attributes and test choice. *Patient Prefer Adherence*. 2015;9:1005–1016. https://doi.org/10.2147/ppa.S82203. pmid:26203233.
34 Hassan 1 Cesare, Quintero Enrique, Dumonceau Jean-Marc, et al. Post-polypectomy colonoscopy surveillance: European Society of gastrointestinal endoscopy (ESGE) guideline. *Endoscopy*. 2013 Oct;45(10):842–851. https://doi.org/10.1055/s-0033-1344548.
35 Hol L, de Bekker-Grob EW, van Dam L, et al. Preferences for colorectal cancer screening strategies: a discrete choice experiment. *Br J Cancer*. 2010;102:972–980. https://doi.org/10.1038/sj.bjc.6605566. pmid:20197766.
36 Kistler CE, Hess TM, Howard K, et al. Older adults' preferences for colorectal cancer-screening test attributes and test choice. *Patient Prefer Adherence*. 2015;9:1005–1016. https://doi.org/10.2147/ppa.S82203. pmid:26203233.
37 Rutter CM, Johnson EA, Feuer EJ, Knudsen AB, Kuntz KM, Schrag D. Secular trends in colon and rectal cancer relative survival. *J Natl Cancer Inst*. 2013;105:1806–1813.
38 IARC [En línea] 12 de July de 2020 https://gco.iarc.fr.