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Original Article

Quality indicators of Clinical Cancer Care (QC_3) in colorectal cancer

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Running title: Quality indicators of clinical care in colorectal cancer

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ABSTRACT

Objectives: Assessing the quality of cancer care (QoCC) has become increasingly important to providers, regulators and purchasers of care worldwide. Aim of this study was to develop evidence-based quality indicators (QI) for colorectal cancer (CRC) to be applied in a population-based setting.

Design: A comprehensive evidence-based literature search was performed to identify the initial list of QI, which were then selected and developed using a two-step modified Delphi process involving two multidisciplinary expert panels with expertise in colorectal cancer care, quality of care and epidemiology.

Setting: The QC_3 population-based project, which involve all the public and private hospitals and clinics present on the territory of Canton Ticino (South Switzerland).

Participants: Ticino Cancer Registry, The Colorectal Cancer Working Group (CRC-WG) and the external academic Advisory Board (AB).

Main outcome measures: Set of quality indicators (QI) which encompass the whole diagnostic-treatment process of colorectal cancer.

Results: Of the 149 QI emerged from 181 sources of literature, 104 were selected during the in-person meeting of the CRC-WG. During the Delphi process, the CRC-WG shortened the list to 89 QI. The AB finally validated 27 QI according to the phase of care: diagnosis (N=6), pathology (N=3), treatment (N=16), and outcome (N=2).

Conclusions: Using the validated Delphi methodology, including literature review of the evidence and integration of expert opinions from local clinicians and international experts we were able to develop a list of QI to assess QoCC for CRC. This will hopefully guarantee feasibility of data retrieval, acceptance and translation of QI into the daily clinical practice to improve QoCC. Moreover, evidence-based selected QI allow to assess immediate changes and improvements in the diagnostic-therapeutic process that could be translated in a short-term benefit for patients with a possible gaining both in overall and disease-free survival.

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ARTICLE SUMMARY

Article focus

- Quality of Cancer care (QoCC) studies on specific quality indicators (QI) developed worldwide since the late '90s showed both a continuous improvement of oncologic care provided by the clinical structures involved and an increased availability of specialized care in the considered areas.
- This study aims to define evidence-based QI for colorectal cancer care (CRC), in order to favour the evaluation of the oncologic diagnostic-therapeutic process, which can be followed by the definition of standards of care for each QI, in terms of minimum and target requirements.

Key messages

- QI should be defined, developed and tested with scientific evidence-based rigor in a careful and transparent manner, taking into account their degree of relevancy, validity, reliability and feasibility.
- The selected CRC QI can be applied in a population-based setting, implying the inclusion of the elderly, considering age an extremely important determinant of treatment.

Strengths and limitations of this study

- To develop the CRC QI we used a formal iterative process, the RAND/UCLA Appropriateness Methodology widely diffused and validated within other QoCC research. The selected QI are representative of the main steps of the diagnostic-therapeutic process.
- Due to the evidence that research studies demonstrated that single-discipline panels select different indicators than do multidisciplinary panels and to maximize the applicability of CRC QI, we constituted two panels of experts, a local Working Group and an external national/international academic Advisory Board, which could offer a multidisciplinary perspective on practice and who can guarantee that the selected QI and their results will be comparable with national and international data. .

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- The possible limitation of the current work is the level of evidence found in the literature. However this situation is common to many aspects of health care, and it was the reason that the expert panel methodology was developed – specifically, to identify the processes that are most likely to be valid measures of quality when the highest level of evidence is not available

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INTRODUCTION

Research on QoCC performed during the last decade has demonstrated that the increase in knowledge on treatments with proven efficacy do not directly translate into optimal delivery of such treatments to patients. Moreover, accumulating evidence suggests that underuse and overuse of care may occur for patients with cancer.[1-2] In addition to survival analysis, to evaluate and compare quality of care at the population-based level, the assessment of QoCC has become increasingly important to providers, regulators and purchasers of care to growing demand for services, rising costs, constrained resources and evidence of variation in clinical practice.[3]

QoCC studies and structured programmes on specific quality indicators (QI) have been developed worldwide since the late '90s, showing both a continuous improvement of oncologic care provided by the clinical structures involved and an increased availability of specialized care in the considered areas. Most of these studies have been implemented at the regional level on a territory with uniform legislative, health and geographical characteristics, increasing the likelihood of recruitment of involved clinicians.[1, 4-7]

So far, in Switzerland no population-based study on QoCC with a prospective design has been implemented. In addition to the yearly renewed international guidelines for each type of cancer, there is still the need to evaluate the real conditions of care in the community. Population-based Cancer Registry data are therefore essential to describe and reflect real world and routine care as well as to provide regular feedback to healthcare workers and decision makers about the management of a disease in the daily practice and those treatments that are routinely prescribed and/or effective in all patient groups.[8] Moreover, Cancer Registries represent an independent observatory, thus assuring a fair evaluation service, avoiding any conflicts of interest.

We, therefore, implemented the QC_3 project, focusing on QoCC about the diagnosis-treatment process in colon-rectum, prostate, uterus, ovary and lung cancers in the territory of Canton Ticino (South Switzerland).

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Colorectal cancer (CRC) is an important health issue worldwide. It is the most common malignancy in Europe (excluding non-melanoma skin cancers) and the second most common in terms of cancer-related mortality.[9] In Switzerland, CRC is the second and third most frequent tumour in women and men, respectively. About 4000 CRC cases are diagnosed annually, corresponding to a European age-standardized incidence rate equal to 49.4 and 30.6 cases per 100'000 inhabitants in men and women, respectively, and representing the 11% of all tumours.[10-12] CRC is the third leading cancer cause of death in Switzerland, with approximately 1600 deaths/year, corresponding to a European age-standardized mortality rate equal to 18.5 and 10.6 cases per 100'000 inhabitants in men and women, respectively. With a 5-year survival probability equal to 60%, Switzerland is the country with the most favourable prognosis in Europe.[13] A recent Swiss report with follow up to 2009 show an additional 5 year survival increase to 62%.[11]

The aims of the QC_3 study are the following: 1) to define evidence-based QoCC indicators for the tumour localizations above cited, in order to favour an improvement of the short-term oncologic diagnostic-therapeutic process; 2) to define and implement at the regional level standards of care for each QoCC measure, in terms of minimum and target requirements. In the present report we will describe the initial part of the QC_3 project, meaning the process followed to identify the panel of specific QoCC indicators for the CRC, as well as the list of QoCC indicators identified and approved both by a dedicated Working Group of local health care providers and by an external independent academic Advisory Board.

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MATERIAL AND METHODS

The QC_3 project is a prospective, descriptive study on the QoCC to be implemented in a population-based setting; it is performed by the Ticino Cancer Registry on a 3-year time period (2011-2013) on the territory of Canton Ticino (South Switzerland). In this paper we focus on the initial part of the project: the identification of the CRC quality indicators which will be used to evaluate the QoCC about CRC in our region.

Quality indicators (QI) for CRC were developed involving a local expert panel, named QC_3 Colorectal Working Group (CRC-WG). Elected members, selected on the basis of their expertise and on their daily clinical involvement in CRC care, were contacted to have their interest confirmed in being involved. The final QC_3 CRC-WG encompassed two pathologists, four gastroenterologists, two oncologists, three surgeons, two radiologists, two radiation oncologists and one nuclear medicine specialist, for a total of 15 panellists all working in the public or in the private hospitals and clinics of Canton Ticino (see Appendix 1).

Published studies and references were identified through a comprehensive search on PubMed/MEDLINE. For each of the identified candidate indicators, we performed a systematic literature review to identify the highest level of evidence supporting the validity of that quality indicator for articles published from 1990 onwards. The reference list of the included articles were also examined to identify any additional article that had not been identified in the MEDLINE search. We included all the peer-reviewed articles, but case reports, letters, abstracts or editorials. If evidence at the highest level were limited or absent, then lower levels of evidence were evaluated. For example, if data were not available from randomized controlled trials, cohort or case-control studies, case series and expert opinion or clinical guidelines were reviewed.

The initial QI list emerged from 181 sources of literature, and it was proposed to the CRC-WG in the context of an in-person meeting held at the very beginning of the process. The list was then left to the QC_3 CRC-WG's evaluation for a period of two weeks. The participants were asked to provide a whole opinion with written comments about those QI considered pertinent for the assessment of

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CRC care quality, to suggest additional QI not already included in the list and to delete those QI considered not suitable. In order to make the selection and evaluation easier, the QI were subdivided in chapters recalling the Donabedian's and the National Initiative for Cancer Care Quality schemes: diagnosis and staging, pathology, treatment, follow-up, outcome.[2, 14]

Delphi Round 1

The QI selection was done by using a 2-step modified Delphi process.[15] The initial list of QI, re-analyzed by the QC_3 CRC-WG, was formatted as a questionnaire, where for each indicator was specified the numerator, the denominator and the sources of evidence from which it was extracted. The questionnaire was distributed by regular mail to the QC_3 CRC-WG, so to maintain it anonymous, along with a stamped, addressed return envelope and an attached letter with the deadline date of two weeks from the receipt and the instruction for voting. Respondents were asked to rate each QI adopting the RAND Appropriateness Methodology (scale 1 to 9, 1 = extremely inappropriate; 9 = extremely appropriate), according to selection criteria of relevance, scientific soundness (validity, reliability, comparability) and feasibility (precise definition and specification, data feasibility, reliability of data collection).[16-18] Each QI was judged as validated if it reached a strong consensus for acceptance (≥70% of the QC_3 CRC-WG rated the QI with a vote ≥7), discarded if it reached a strong consensus for exclusion (≥70% of the QC_3 CRC-WG rated the QI with a votes ≤ 3) and in stand-by if there was an unclear consensus (4 ≤ votes ≤ 6), which implies an eventual in-person meeting.

Delphi Round 2

The Delphi Round 2 questionnaire was performed with the same modalities of the first round and enclosed the frequency distribution of round 1 votes, allowing the panellists to eventually alter their responses, in the light of colleagues' assessments.[16]

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Advisory Board Review

The list of selected QI derived from the two Delphi rounds was then submitted to an independent external national/international academic multidisciplinary Advisory Board (AB), in order to get an additional evaluation on the suitability of QI as "quality" indexes according to the criteria shown in the previous paragraph. The intent was to achieve at least one health professional for each specialty. The AB included one pathologist, one gastroenterologist, two oncologists, two surgeons, one radiologist, one radiation oncologist, one nuclear medicine specialist and one epidemiologist, for a total of 10 experts in CRC care (see Acknowledgements); all the panellists are daily involved in the CRC care and they had been contacted with the same modalities of the QC_3 CRC WG. The selected QI as well as the corresponding literature sources were distributed to the AB as an electronic form where their opinion about QI were expressed both as megatrends (i.e. response yes/no to the suitability of each QI) and as eventual additional comments. We considered every single QI as finally approved by the AB if it achieved ≥ 70% of the agreement (i.e. ≥ 70% of respondents should have answered "yes") and if no doubtful comments about the QI had been expressed.

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RESULTS

The QI selection process began in January 2011 and ended in December 2011.

Participation of CRC-WG members throughout the process was high: 15 (100%) participated to the in-person meeting, 12 (80%) completed both the Delphi round 1 and 2. The Delphi Round 1 questionnaire respondent time were in the range of 18 to 60 days, while for the Round 2, the delay time was in the range of 8 to 55 days; these delays and the time for recruitment of the AB influence the long time spent for this part of the project.

The Figure 1 summarizes the entire process used to select QI for CRC care. The literature search produces 181 citations dealing with CRC QoCC. From this search, we initially selected a total of 149 QI, which were proposed to the CRC-WG in the context of the initial in-person meeting. The following discussion and revision reduced the list to 104 QI before the modified Delphi process started; these QI were divided into the following areas: diagnosis and staging, pathology, treatment, follow-up and outcome. After the whole Delphi process the list was shortened to 89 QI, distributed as following: diagnosis and staging (N=16), pathology (N=20), treatment (N=38), follow-up (N=10), and outcome (N=5). The QI finally underwent to the AB's evaluation; this last step, according to the procedure described in the Methods, shortened the final list to 27 QI (Tab.1): diagnosis (N=6), pathology (N=3); treatment (N=16), follow-up (N=0), and outcome (N=2).

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DISCUSSION

In the preliminary phase of the QC_3 project shown in this paper we developed a panel of evidence-based CRC QI which are suitable to be implemented in a population-based setting.

To develop the QC_3 QI we used a formal iterative process, the RAND/UCLA Appropriateness Methodology widely diffused and validated within other QoCC research.[16-17] Due to the evidence that research studies demonstrated that single-discipline panels select different indicators than do multidisciplinary panels and to maximize the applicability of QC_3 CRC QI, we constituted a working group which could offer a multidisciplinary perspective on practice, including specialists, professionals, clinicians and researchers coming from both public and private hospitals.[19-25] Moreover, we have used a further validation step enrolling an independent national/international academic AB. This choice was due to the aim of measuring QoCC within a Swiss region, and of obtaining results which will be comparable with national and international data. We believe that the expertise and multidisciplinary representativeness of the QC_3 CRC-WG and of the AB will surely increase quality, acceptance and translation of QI into the daily clinical practice.

The selected QI are representative of the main steps of the diagnostic-therapeutic process. The diagnosis QI reflect the importance of a pre-operative evaluation and staging, reliable evaluation of the tumour localization and local invasion, and particularly for the rectal cancers, of a feasible and effective surgery. The pathology QI reflect the importance of a good communication between clinicians and pathologists in terms of patient's anamnesis and consequent evaluation of the effectiveness of a neo-adjuvant therapy; moreover, there is a need of standardization of the pathologic report following the international guidelines (e.g. take at least three samples of tumour during the macroscopy), not leaving any items unexplained or implicit. The treatment QI cover the general issues of surgery such as emergency, postoperative mortality and a multidisciplinary discussion of the clinical case; furthermore, they focus on the debate of the retrieved lymph nodes, on the timing between radiotherapy and surgery, on the adjuvant chemotherapy and on the attitude towards the metastatic patients. The two main items of the outcome chapter refers to the overall and

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disease free survival. Concerning the QI about follow-up, AB did not finally include any of them. Indeed, although the follow-up procedures are suggested by several international guidelines, they are based on level II-III evidence and controversies remain regarding selection of optimal strategies for following up patients after potentially curative colorectal cancer surgery. [26-29]

The first limitation of the current work is the level of evidence found in the literature. For some indicators, strong evidence of their validity was not available from RCTs. However this situation is common to many aspects of health care, and it was the very reason that the expert panel methodology was developed – specifically, to identify the processes that are most likely to be valid measures of quality when the highest level of evidence is not available.[16, 30-31] Secondly, we may have missed some studies during the literature search and, consequently, some QI has not been proposed to the QC_3 CRC-WG since the beginning of the QI revision process. However, this limitation should have been overcome by the fact that the members of the QC_3 CRC-WG were likely to be very familiar with the literature, and had the opportunity to suggest other QI based on their experience.[7, 19-20, 32] Thus we integrated the best research evidence with clinical expertise, as reported by Sackett et al..[33] A further limit could be the feasibility of measuring QI in terms of data collection and calculation, which is immediately the next step. Actually, the QI selected by both the QC_3 CRC-WG and the AB represent an ideal set of criteria to measure the quality of CRC care; at the same time they both were concerned about the feasibility, validity and reliability of clinical data collection, necessary for the calculation of each single QI. This is the reason why most of the identified QC_3 QI are common to many QoCC studies. In addition, we performed a retrospective preliminary pilot collection on the detailed and necessary incidence data of CRC occurred in 2011, realising that the measurement of most QI is feasible, whereas for some selected QI the retrieving of variables should be additionally tested.[34-35] Only the definitive results will give us the proportion of missing information, whose magnitude will be assessed.

The selected QC_3 CRC QI will be applied in a population-based setting, where age is an extremely important determinant of treatment. The elderly are rarely included in the randomized clinical trials

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with the consequence of a possible "underuse of treatment".[18, 36-37] At a broad European level, national audit registries in surgical oncology have led to improvements with a great impact and they offered the possibility, as for our project, to perform research on patients that are usually excluded from clinical trials such as elderly and co-morbid patients.[38-39] Evidence suggests that the relative benefits of treatment for the elderly are similar to those seen for cancer patients in general, though decision making for treatment becomes more complex as life expectancy, co-existing illnesses, and functional status all need to be considered.[18, 36-37] Applying these QI and if all these items will be satisfied we can affirm to have a real good quality process of CRC care for the whole population. The foreseeable future in quality evaluation and improvement for health care will likely involve more and more frequently the use of QI by regulatory and accrediting agencies, stakeholders, clinicians, individual hospitals and health care providers, as well as patients. This underlines that the QI should be defined, developed and tested with scientific evidence-based rigor in a careful and transparent manner, taking into account their degree of relevancy, validity, reliability and feasibility.[22, 24] Although QI have been defined in several different ways, all authors agreed that the final aim is the improvement of patients outcome.[23, 25, 40]

The systematic trend analysis of QI allows to assess immediate changes and improvements in the diagnostic-therapeutic process that could be translated in a short-term benefit for patient, without waiting for survival analysis typically needed some years to be produced because of the patients' follow-up. Furthermore, this system of evaluation and auto-evaluation could favour the surveillance and monitoring of the comprehensive level of the oncologic care in the region, the clinical performance homogeneity, the possible weakness of the clinical network, and finally the corrective interventions to be adopted to improve the QoCC.

With this study, we hope to increase the awareness of the value of QI in health care so to encourage more uniform practices and improve provider documentation of medical care in our region; moreover, we hope that standardization of QI among different regions will help to define threshold of minimal standard of care.

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COMPETING INTERESTS

The Authors have no competing interests.

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There is no additional data available.

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AUTHORS' CONTRIBUTION

I declare that V. Bianchi, A. Bordoni, A. Spitale and L. Mazzucchelli have directly participated in the planning of the manuscript; that V. Bianchi, A. Bordoni, A. Spitale and the QC_3 Colorectal Working Group have directly participated in the conducting of the project; that V. Bianchi, A. Bordoni, A. Spitale and L. Ortelli have directly participated in the reporting, acquisition of data or analysis and interpretation of data; and that V. Bianchi and A. Bordoni are responsible for the overall content as guarantors of the work. Finally, I declare that all the Authors have drafted and revised the paper critically for important intellectual content, and that they have given final approval of the version published. None of the Authors have competing interests.

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LEGENDS TO FIGURES

FIGURE 1 - Process used to select quality indicators for colorectal cancer care

QI = Quality Indicators; QC_3 CRC-WG = QC3 Colorectal Cancer Working Group; AB = Advisory Board

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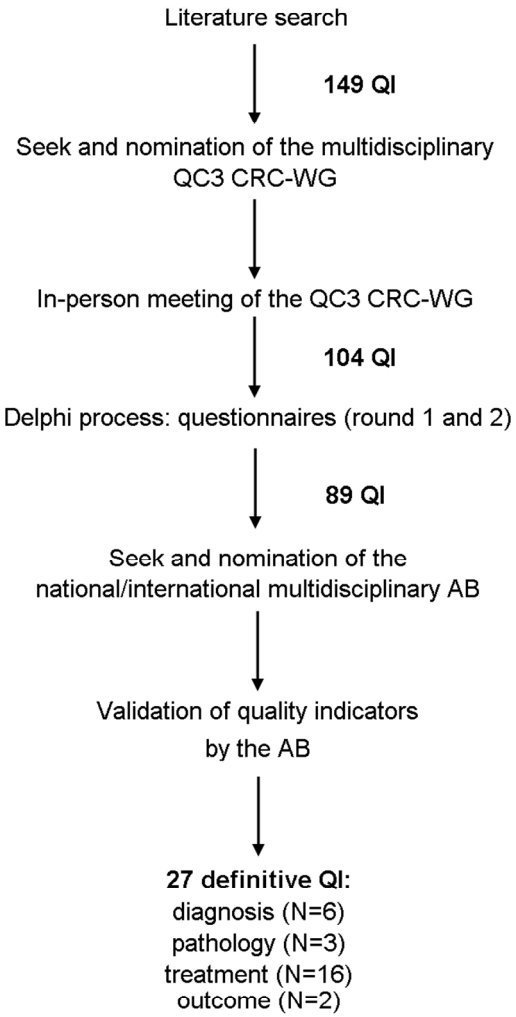
Figure 1. Process used to select quality indicators for colorectal cancer care



QI= Quality Indicators; QC3 CRC-WG: QC3 Colorectal Cancer Working Group; AB: Advisory Board

102x131mm (300 x 300 DPI)

Table 1. Quality indicators of colorectal cancer care according to diagnostic-therapeutic process (diagnosis, pathology, treatment, outcome) and tumour site

TUMOUR SITE	QUALITY INDICATOR	DENOMINATOR	REFERENCES
DIAGNOSIS (n=6)			
C&R	Proportion of patients with colorectal cancer and diagnosis based on symptoms *vs* screening *vs* accidental finding	Patients with colorectal cancer	[41-45]
C&R	Proportion of patients with colorectal cancer, evaluated by preoperative colonoscopy	Patients with colorectal cancer undergoing surgery	[7, 26-27, 46]
R	Proportion of patients with rectal cancer and description of the tumour localization (distance *ab ano*) in the endoscopic/pathologic documentation	Patients with rectal cancer undergoing endoscopy	[1, 47-48]
C&R	Proportion of patients with colorectal cancer and requests for an initial CT and/or a MRI examination completed by clinical information according to the ACR guidelines	Patients with colorectal cancer undergoing initial CT and/or MRI examination	[7, 49]
R	Proportion of patients with low rectal [#] cancer undergoing pelvic MRI of staging	Patients with low rectal cancer	[50-52]
R	Proportion of patients with rectal cancer and a preoperative MRI reporting the description of the radial margin status (mm)	Patients with rectal cancer undergoing preoperative MRI	[53]
PATHOLOGY (n=3)			
R	Proportion of patients with rectal cancer for which the request for the pathological examination includes the information of neo-adjuvant RT±ChT	Patients with rectal cancer undergoing neo-adjuvant RT±ChT and surgery	Proposed by CRC-WG
C&R	Proportion of patients with colorectal cancer and a sufficient number of tumour samples *(≥3)*	Patients with colorectal cancer undergoing surgery	Proposed by CRC-WG
C&R	Proportion of patients with colorectal cancer and a definitive pathological report including the following characteristics: surgical intervention, sample length, tumour localization according to WHO, tumour size, histological type according to WHO, histological grade, resection margins, lympho-vascular invasion, perineural invasion, tumour deposits (discontinuous extramural extension), pathological staging (AJCC pTNM), number of retrieved lymph nodes, treatment effect, macroscopic integrity of the mesorectum (for rectum only)	Patients with colorectal cancer undergoing surgery	[54-55]

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TREATMENT (n=16)			
C&R	Proportion of patients with colorectal cancer operated in emergency[§]	Patients with colorectal cancer undergoing surgery	[56-58]
C&R	Proportion of patients with colorectal cancer and dead within 30 days and 6 months from the surgery (postoperative mortality)	Patients with colorectal cancer undergoing surgery	[59-62]
C&R	Proportion of patients with colorectal cancer and postoperative multidisciplinary discussion	Patients with colorectal cancer undergoing surgery	[63-64]
R	Proportion of patients with malignant rectal polyp (pT1) and complete endoscopic polypectomy	Patients with malignant rectal polyp (pT1)	Proposed by the CRC-WG
R	Proportion of patients with low rectal[#] cancer and surgical intervention with sphincter preservation	Patients with low rectal cancer undergoing surgery	[7, 65-67]
R	Proportion of patients with rectal cancer undergoing TEM with R0 resection	Patients with rectal cancer undergoing TEM	[68-70]
C&R	Proportion of patients with colorectal cancer and a number of resected lymph nodes ≥ 12	Patients with colorectal cancer undergoing surgery, but no neo-adjuvant therapy	[7, 26-27, 46, 71-76]
C&R	Proportion of patients with colorectal cancer operated on with free margins	Patients with colorectal cancer undergoing surgery	[7, 77-78]
C&R	Proportion of patients with colorectal cancer and AJCC TNM clinical stage I (from T2N0M0) to III (any T, N1M0) undergoing a surgical resection with anastomosis	Patients with colorectal cancer and AJCC TNM stage I (from T2N0M0) to III	[26-27, 77-78]
C	Proportion of patients with colon cancer and AJCC TNM stage II (T3N0M0, T4N0M0) high-risk (presence of at least one of the following factors: LN<12, G3, lymph-vascular or perineural invasion, tumour obstruction, tumour perforation, pT4) or III undergoing adjuvant ChT	Patients with colon cancer and AJCC TNM stage II high-risk or III	[26-27, 46, 79-82]
C	Proportion of patients with colon cancer AJCC TNM stage II high-risk or stage III undergoing adjuvant ChT within 8 weeks from surgical resection	Patients with colon cancer and AJCC TNM stage II high-risk or III undergoing adjuvant ChT	[83]
C&R	Proportion of patients with colorectal cancer and histology of the primary tumour or metastases obtained before the beginning of ChT	Patients with colorectal cancer undergoing primary ChT	[26-27]
C&R	Proportion of patients with colorectal cancer and unresectable metastases undergoing first-line ChT or bio-ChT	Patients with colorectal cancer and unresectable metastases	[84-87]
C&R	Proportion of patients with colorectal cancer and hepatic metastases primarily unresectable turned into resectable metastases after neo-adjuvant ChT	Patients with colorectal cancer and unresectable hepatic metastases undergoing neo-adjuvant ChT	[87]

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R	Proportion of patients with locally advanced rectal cancer (T3-4 and/or any T, N+ and M0) undergoing neo-adjuvant RT±ChT	Patients with locally advanced rectal cancer	[88-89]
R	Proportion of patients with rectal cancer and undergoing neo-adjuvant RT±ChT operated within 6-8 weeks after the end of neo-adjuvant RT±ChT	Patients with rectal cancer undergoing neo-adjuvant RT±ChT followed by surgery	[89]
OUTCOME (n=2)			
C&R	Analysis of overall survival at 1, 3, 5 and 10 years from diagnosis	Patients with colorectal cancer	[7, 90]
C&R	Analysis of disease-free survival	Patients with colorectal cancer curatively treated	[7, 90]

Abbreviation:

C&R= colon-rectum; **C**= colon; **R**= rectum; **ACR**= American College of Radiology; **CT**= computed tomography; **MRI**= magnetic resonance imaging; **AJCC**= American Joint Committee on Cancer; **RT**= radiotherapy; **ChT**= chemotherapy; **WHO**= World Health Organization; **TEM**= transanal endoscopic microsurgery.

[§]emergency: within 24 hours from the onset of symptoms; [#]low rectum: 4 to 7.5 cm from the dentate line [91]

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Original Article

Quality indicators of Clinical Cancer Care (QC_3) in colorectal cancer

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Running title: Quality indicators of clinical care in colorectal cancer

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ABSTRACT

Objectives: Assessing the quality of cancer care (QoCC) has become increasingly important to providers, regulators and purchasers of care worldwide. Aim of this study was to develop evidence-based quality indicators (QI) for colorectal cancer (CRC) to be applied in a population-based setting.

Design: A comprehensive evidence-based literature search was performed to identify the initial list of QI, which were then selected and developed using a two-step modified Delphi process involving two multidisciplinary expert panels with expertise in colorectal cancer care, quality of care and epidemiology.

Setting: The QC_3 population-based project, which involve all the public and private hospitals and clinics present on the territory of Canton Ticino (South Switzerland).

Participants: Ticino Cancer Registry, The Colorectal Cancer Working Group (CRC-WG) and the external academic Advisory Board (AB).

Main outcome measures: Set of quality indicators (QI) which encompass the whole diagnostic-treatment process of colorectal cancer.

Results: Of the 149 QI emerged from 181 sources of literature, 104 were selected during the in-person meeting of the CRC-WG. During the Delphi process, the CRC-WG shortened the list to 89 QI. The AB finally validated 27 QI according to the phase of care: diagnosis (N=6), pathology (N=3), treatment (N=16), and outcome (N=2).

Conclusions: Using the validated Delphi methodology, including literature review of the evidence and integration of expert opinions from local clinicians and international experts we were able to develop a list of QI to assess QoCC for CRC. This will hopefully guarantee feasibility of data retrieval, acceptance and translation of QI into the daily clinical practice to improve QoCC. Moreover, evidence-based selected QI allow to assess immediate changes and improvements in the diagnostic-therapeutic process that could be translated in a short-term benefit for patients with a possible gaining both in overall and disease-free survival.

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ARTICLE SUMMARY

Article focus

- Quality of Cancer care (QoCC) studies on specific quality indicators (QI) developed worldwide since the late '90s showed both a continuous improvement of oncologic care provided by the clinical structures involved and an increased availability of specialized care in the considered areas.
- This study aims to define evidence-based QI for colorectal cancer (CRC) care, in order to favour a feasible evaluation of the oncologic diagnostic-therapeutic process from a population-based cancer registration and data collection point of view.

Key messages

- QI should be defined, developed and tested with scientific evidence-based rigor in a careful and transparent manner, taking into account their degree of relevancy, validity, reliability and feasibility.
- The selected CRC QI can be applied in a population-based setting, implying the inclusion of the elderly, considering age an extremely important determinant of treatment.

Strengths and limitations of this study

- To develop the CRC QI we used a formal iterative process, the RAND/UCLA Appropriateness Methodology widely diffused and validated within other QoCC research. The selected QI are representative of the main steps of the diagnostic-therapeutic process.
- Due to the evidence that research studies demonstrated that single-discipline panels select different indicators than do multidisciplinary panels and to maximize the applicability of CRC QI, we constituted two panels of experts, a local Working Group and an external national/international academic Advisory Board, which could offer a multidisciplinary perspective on practice and who can guarantee that the selected QI and their results will be comparable with national and international data.
- Possible limitations of the current work are the following:

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- the level of evidence found in the literature. This situation is common to many aspects of health care, and it was the reason that the expert panel methodology was developed – specifically, to identify the processes that are most likely to be valid measures of quality when the highest level of evidence is not available.
- the literature selection could have missed some relevant articles. However, members of the Working Group were likely to be very familiar with the literature, and had the opportunity to suggest other indicators based on their experience and literature search; in this way, we believe to have integrated the best research evidence with clinical expertise.
- the feasibility of measuring indicators in terms of data collection and calculation. However, both the Working Group and the Advisory Board were concerned about the feasibility, validity and reliability of clinical data collection, necessary for the calculation of each single indicator at the population-based level. In fact, in order to warrant an accurate measurement, those indicators reaching more than 70% of the agreement, confirming their scientific and clinical value, but evaluated at least by one of the experts not feasible and difficult to be collected at the population-based level, were definitely excluded. In this way, we have overcome the feasibility limit.

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INTRODUCTION

Research on QoCC performed during the last decade has demonstrated that the increase in knowledge on treatments with proven efficacy do not directly translate into optimal delivery of such treatments to patients. Moreover, accumulating evidence suggests that underuse and overuse of care may occur for patients with cancer.[1-2] In addition to survival analysis, to evaluate and compare quality of care at the population-based level, the assessment of QoCC has become increasingly important to providers, regulators and purchasers of care to growing demand for services, rising costs, constrained resources and evidence of variation in clinical practice.[3]

QoCC studies and structured programmes on specific quality indicators (QI) have been developed worldwide since the late '90s, showing both a continuous improvement of oncologic care provided by the clinical structures involved and an increased availability of specialized care in the considered areas. Most of these studies have been implemented at the regional level on a territory with uniform legislative, health and geographical characteristics, increasing the likelihood of recruitment of involved clinicians.[1 4-7]

So far, in Switzerland no population-based study on QoCC with a prospective design has been implemented. In addition to the yearly renewed international guidelines for each type of cancer, there is still the need to evaluate the real conditions of care in the community. Population-based Cancer Registry data are therefore essential to describe and reflect real world and routine care as well as to provide regular feedback to healthcare workers and decision makers about the management of a disease in the daily practice and those treatments that are routinely prescribed and/or effective in all patient groups.[8] Moreover, Cancer Registries represent an independent observatory, thus assuring a fair evaluation service, avoiding any conflicts of interest.

We, therefore, implemented the QC_3 project, focusing on QoCC about the diagnosis-treatment process in colon-rectum, prostate, uterus, ovary and lung cancers in the territory of Canton Ticino (South Switzerland).

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Colorectal cancer (CRC) is an important health issue worldwide. It is the most common malignancy in Europe (excluding non-melanoma skin cancers) and the second most common in terms of cancer-related mortality.[9] In Switzerland, CRC is the second and third most frequent tumour in women and men, respectively. About 4000 CRC cases are diagnosed annually, corresponding to a European age-standardized incidence rate equal to 49.4 and 30.6 cases per 100'000 inhabitants in men and women, respectively, and representing the 11% of all tumours.[10-12] CRC is the third leading cancer cause of death in Switzerland, with approximately 1600 deaths/year, corresponding to a European age-standardized mortality rate equal to 18.5 and 10.6 cases per 100'000 inhabitants in men and women, respectively. With a 5-year survival probability equal to 60%, Switzerland is the country with the most favourable prognosis in Europe.[13] A recent Swiss report with follow up to 2009 show an additional 5 year survival increase to 62%.[11]

The aims of the QC_3 project are the following: 1) to define and confirm evidence-based QoCC indicators for the tumour localizations above cited, in order to favour a feasible evaluation of the oncologic diagnostic-therapeutic process from a population-based cancer registration and data collection point of view; 2) to define and implement at the regional level standards of care for each QoCC measure, in terms of minimum and target requirements. In the present report we will describe the initial part of the QC_3 project, meaning the process followed to identify the panel of specific QoCC indicators for the CRC, as well as the list of QoCC indicators identified and approved both by a dedicated Working Group of local health care providers and by an external independent Advisory Board, in a perspective of data collection feasibility by a population-based cancer registry.

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MATERIAL AND METHODS

The QC_3 project is a prospective, descriptive study on the QoCC to be implemented in a population-based setting; it is performed by the Ticino Cancer Registry on a 3-year time period (2011-2013) on the territory of Canton Ticino (South Switzerland). In this paper we focus on the initial part of the project: the identification of the CRC quality indicators which will be used to evaluate the QoCC about CRC in our region.

Quality indicators (QI) for CRC were developed involving a local expert panel, named QC_3 Colorectal Working Group (CRC-WG). Elected members, selected on the basis of their expertise and on their daily clinical involvement in CRC care, were contacted to have their interest confirmed in being involved. The final QC_3 CRC-WG encompassed two pathologists, four gastroenterologists, two oncologists, three surgeons, two radiologists, two radiation oncologists and one nuclear medicine specialist, for a total of 15 panellists all working in the public or in the private hospitals and clinics of Canton Ticino (see Appendix 1).

Published studies and references were identified through a comprehensive search on PubMed/MEDLINE, using initially specific strings/expressions, such as the following: “quality of care OR quality indicators AND colorectal cancer”, “diagnosis OR diagnostic AND quality indicators AND colorectal cancer”, “pathology OR pathological AND quality indicators AND colorectal cancer”, “surgery OR surgical AND quality indicators AND colorectal cancer”, “radiation oncology OR radiotherapy AND quality indicators AND colorectal cancer”, “chemotherapy AND quality indicators AND colorectal cancer”, “surveillance OR follow-up OR outcome AND quality indicators AND colorectal cancer”, “preoperative care OR perioperative care OR intraoperative care OR postoperative care AND colorectal cancer”, “population-based AND quality indicators AND colorectal cancer”. For each of the identified candidate indicators, we performed a systematic literature review to identify the highest level of evidence supporting the validity of that quality indicator for articles published from 1990 onwards. The reference list of the included articles were also examined to identify any additional article that had not been identified in

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the MEDLINE search. We included all the peer-reviewed articles, but case reports, letters, abstracts or editorials. If evidence at the highest level were limited or absent, then lower levels of evidence were evaluated. For example, if data were not available from randomized controlled trials, cohort or case-control studies, case series and expert opinion or clinical guidelines were reviewed. A selection of already approved QI provided by the American Society of Clinical Oncology (ASCO), the National Comprehensive Cancer Network (NCCN), the National Initiative on Cancer Care Quality (NICCQ), the Quality Oncology Practice Initiative (QOPI) and the Florida Initiative for Quality Cancer Care (FIQCC), were included in the evaluation list, with the aim to transfer them from the clinical to the population-based setting.[1-2 4 7 14-20]

The initial QI list emerged from 181 sources of literature, and it was proposed to the CRC-WG in the context of an in-person meeting held at the very beginning of the process. The list was then left to the QC_3 CRC-WG's evaluation for a period of two weeks. The participants were asked to provide a whole opinion with written comments about those QI considered pertinent for the assessment of CRC care quality, to suggest additional QI not already included in the list and to delete those QI considered not suitable. In order to make the selection and evaluation easier, the QI were subdivided in chapters recalling the Donabedian's and the National Initiative for Cancer Care Quality schemes: diagnosis and staging, pathology, treatment, follow-up, outcome.[2 21]

Delphi Round 1

The QI selection was done by using a 2-step modified Delphi process.[22] The initial list of QI, re-analyzed by the QC_3 CRC-WG, was formatted as a questionnaire, where for each indicator was specified the numerator, the denominator and the sources of evidence from which it was extracted. The questionnaire was distributed by regular mail to the QC_3 CRC-WG, so to maintain it anonymous, along with a stamped, addressed return envelope and an attached letter with the deadline date of two weeks from the receipt and the instruction for voting. Respondents were asked to rate each QI adopting the RAND Appropriateness Methodology (scale 1 to 9, 1 = extremely

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inappropriate; 9 = extremely appropriate), according to selection criteria of relevance, scientific soundness (validity, reliability, comparability) and feasibility (precise definition and specification, data feasibility, reliability of data collection).[23-25] Each QI was judged as validated if it reached a strong consensus for acceptance (≥70% of the QC_3 CRC-WG rated the QI with a vote ≥7), discarded if it reached a strong consensus for exclusion (≥70% of the QC_3 CRC-WG rated the QI with a votes ≤ 3) and in stand-by if there was an unclear consensus (4 ≤ votes ≤ 6), which implies an eventual in-person meeting.

Delphi Round 2

The Delphi Round 2 questionnaire was performed with the same modalities of the first round and enclosed the frequency distribution of round 1 votes, allowing the panellists to eventually alter their responses, in the light of colleagues' assessments.[23]

Advisory Board Review

The list of selected QI derived from the two Delphi rounds was then submitted to an independent external national/international academic multidisciplinary Advisory Board (AB), in order to get an additional evaluation on the suitability of QI as "quality" indexes according to the criteria shown in the previous paragraph. The intent was to achieve at least one health professional for each specialty. The AB included one pathologist, one gastroenterologist, two oncologists, two surgeons, one radiologist, one radiation oncologist, one nuclear medicine specialist and one epidemiologist, for a total of 10 experts in CRC care (see Acknowledgements); all the panellists are daily involved in the CRC care and they had been contacted with the same modalities of the QC_3 CRC WG. The selected QI as well as the corresponding literature sources were distributed to the AB as an electronic form where their opinion about QI were expressed both as megatrends (i.e. response yes/no to the suitability of each QI) and as eventual additional comments.[26] We considered every single QI as finally approved by the AB if it achieved ≥ 70% of the agreement (i.e. ≥ 70% of respondents should

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have answered “yes”). Besides the vote (“yes” *versus* “no”), the panellists had the chance to comment the single QI from a population-based cancer registration and data collection point of view. Therefore, those QI reaching more than 70% of the agreement, confirming their scientific and clinical value, but evaluated at least by one of the experts “not completely feasible and difficult to be collected at the population-based level”, were definitely excluded.

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RESULTS

The QI selection process began in January 2011 and ended in December 2011.

Participation of CRC-WG members throughout the process was high: 15 (100%) participated to the in-person meeting, 12 (80%) completed both the Delphi round 1 and 2. The Delphi Round 1 questionnaire respondent time were in the range of 18 to 60 days, while for the Round 2, the delay time was in the range of 8 to 55 days; these delays and the time for recruitment of the AB influence the long time spent for this part of the project.

The Figure 1 summarizes the entire process used to select QI for CRC care. The literature search produces 181 citations dealing with CRC QoCC, including also already validated QI provided by the ASCO, NCCN, NICCQ, QOPI and FIQCC.[1-2 4 7 14-20] From this search, we initially selected a total of 149 QI, which were proposed to the CRC-WG in the context of the initial in-person meeting. The following discussion and revision reduced the list to 104 QI before the modified Delphi process started; these QI were divided into the following areas: diagnosis and staging, pathology, treatment, follow-up and outcome. After the whole Delphi process the list was shortened to 89 QI, distributed as following: diagnosis and staging (N=16), pathology (N=20), treatment (N=38), follow-up (N=10), and outcome (N=5). The QI finally underwent to the AB's evaluation; this last step, according to the procedure described in the methods, shortened the final list to 27 QI diagnosis (N=6), pathology (N=3); treatment (N=16), follow-up (N=0), and outcome (N=2). Table 1 reports detailed information for each QI: a) QI description; b) criteria for patients inclusion in the numerator and denominator; c) list of the necessary medical documentation that should be collected by the Cancer Registry to extract the needed and relevant information to built the specific QI, such as the report of the endoscopy, the pathology report of the biopsy and/or surgical resection, the preoperative radiological reports (e.g. TAC and MRI), the surgery report, the tumour board documentation, the oncological report, the radiotherapy report and database/documentation of the regional Office of Population Registry Rosters for the assessment of patients vital status (for outcome QI); d) QI rationale; e) related references.

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DISCUSSION

In the preliminary phase of the QC_3 project shown in this paper we developed a panel of evidence-based CRC QI which are suitable to be implemented in a population-based setting.

To develop the QC_3 QI we used a formal iterative process, the RAND/UCLA Appropriateness Methodology widely diffused and validated within other QoCC research.[23-24] Due to the evidence that research studies demonstrated that single-discipline panels select different indicators than do multidisciplinary panels and to maximize the applicability of QC_3 CRC QI, we constituted a working group which could offer a multidisciplinary perspective on practice, including specialists, professionals, clinicians and researchers coming from both public and private hospitals.[27-33] Moreover, we have used a further validation step enrolling an independent national/international academic AB. This choice was due to the aim of measuring QoCC within a Swiss region, with a point of view on the population-based data collection and evaluation, and of obtaining results which will be comparable with national and international data. We believe that the expertise and multidisciplinary representativeness of the QC3 CRC-WG and of the AB will surely increase quality, acceptance and translation of QI into the daily clinical practice.

The selected QI are representative of the main steps of the diagnostic-therapeutic process. The diagnosis QI reflect the importance of a pre-operative evaluation and staging, reliable evaluation of the tumour localization and local invasion, and particularly for the rectal cancers, of a feasible and effective surgery. The first indicator of the "diagnosis" group is important to understand what happens in a territory where there is not an organized screening programme for colorectal cancers, but only an opportunistic screening strategy. If the tumour is detected because the physician submit the patients older than 50 years old to a fecal occult blood test (FOBT) or colonoscopy control or if a patient, being aware of the possible risk, asks his family doctor to undergo screening examinations, is an interesting data to be evaluated, also in the hypothesis of a colorectal cancer screening programme implementation. We, therefore, believe that a higher proportion of patients diagnosed through screening (FOBT or colonoscopy in asymptomatic patients) would represent a

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higher diagnostic quality, since the therapeutic approach and, consequently, the patients outcome (in terms of recurrence and survival) would be more favourable, as reported in the literature.[20 34-39] The pathology QI reflect the importance of a good communication between clinicians and pathologists in terms of patient's clinical history and consequent evaluation of the effectiveness of a neo-adjuvant therapy; moreover, there is a need of standardization of the pathologic report following the international guidelines (e.g. take at least three samples of tumour during the macroscopy), not leaving any items unexplained or implicit. In particular, the third QI reported in Table 1 (pathology section) refers to the surgical pathology report, which derives from the surgical curative intervention and should be as complete as possible to be useful for the future decision about patient's treatment. Our intent is to calculate it for all listed items considered together, but also for each item individually analyzed: e.g. proportion of patients with colorectal cancer and a definitive pathological report including the surgical intervention description; proportion of patients with colorectal cancer and a definitive pathological report including the tumour size; proportion of patients with colorectal cancer and a definitive pathological report including the resection margins; proportion of patients with colorectal cancer and a definitive pathological report including the pathological staging (AJCC pTNM); etc… The treatment QI cover the general issues of surgery, such as emergency, postoperative mortality and a multidisciplinary discussion of the clinical case; furthermore, they focus on the debate of the retrieved lymph nodes, on the timing between radiotherapy and surgery, on the adjuvant chemotherapy and on the attitude towards the metastatic patients. The two main items of the outcome chapter refers to the overall and disease-free survival. Although it is necessary to wait for a certain follow-up period (i.e. 1, 3, 5 to 10 years from the date diagnosis for the calculation of overall survival, and from the date of curative treatment for the calculation of disease-free survival), they will represent the overall resume of the diagnostic and treatment quality of CRC patients. Our intent will be to analyse overall and disease-free survival according to some of the proposed QI (such as QI concerning the pathological characteristics of the tumours, QI of the adjuvant chemotherapy in patients with colon cancer and AJCC TNM stage II

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high-risk or III, QI of colorectal patients operated on with free margins, QI of locally advanced rectal cancer patients undergoing neo-adjuvant radio±chemotherapy, etc…). We will finally compare our results with other regional and national reality, favouring the interpretation of each single QI. Concerning the QI about follow-up, AB did not finally include any of them. Indeed, although the follow-up procedures are suggested by several international guidelines, they are based on level II-III evidence and controversies remain regarding selection of optimal strategies for following up patients after potentially curative CRC surgery.[40-43]

The first limitation of the current work is the level of evidence found in the literature. For some indicators, strong evidence of their validity was not available from RCTs. However this situation is common to many aspects of health care, and it was the very reason that the expert panel methodology was developed – specifically, to identify the processes that are most likely to be valid measures of quality when the highest level of evidence is not available.[19 23 44] Secondly, we may have missed some studies during the literature search and, consequently, some QI has not been proposed to the QC_3 CRC-WG since the beginning of the QI revision process. However, this limitation should have been overcome by the fact that the members of the QC_3 CRC-WG were likely to be very familiar with the literature, and had the opportunity to suggest other QI based on their experience and literature search.[7 27-28 45] Thus we integrated the best research evidence with clinical expertise, as reported by Sackett *et al*..[46] A further limit could be the feasibility of measuring QI in terms of data collection and calculation, which is immediately the next step. Actually, the QI selected by both the QC_3 CRC-WG and the AB represent an ideal set of criteria to measure the quality of CRC care; at the same time they both were concerned about the feasibility, validity and reliability of clinical data collection, necessary for the calculation of each single QI at the population-based level. This is the reason why most of the identified QC_3 QI are common to many QoCC studies.[1-2 4 7 14-20] Besides the traditional Delphi process, the panellists had the chance to comment the single QI from a population-based cancer registration and data collection point of view. Therefore, in order to warrant an accurate measurement, those QI reaching more than

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70% of the agreement, confirming their scientific and clinical value, but evaluated at least by one of the experts not feasible and difficult to be collected at the population-based level, were definitely excluded. In addition, we performed a retrospective preliminary pilot collection on the detailed and necessary incidence data of CRC occurred in 2011, realising that the measurement of most QI is feasible, whereas for some selected QI the retrieving of variables would need additional efforts; some preliminary results were presented in national and international conferences and congresses, receiving positive feedback by both the clinical and epidemiological setting.[47-50] Only the definitive results will give us the proportion of missing information, whose magnitude will be assessed.

The selected QC_3 CRC QI will be applied in a population-based setting, where age is an extremely important determinant of treatment. The elderly are rarely included in the randomized clinical trials with the consequence of a possible "underuse of treatment".[25 51-52] At a broad European level, national audit registries in surgical oncology have led to improvements with a great impact and they offered the possibility, as for our project, to perform research on patients that are usually excluded from clinical trials such as elderly and co-morbid patients.[53-54] Evidence suggests that the relative benefits of treatment for the elderly are similar to those seen for cancer patients in general, though decision making for treatment becomes more complex as life expectancy, co-existing illnesses, and functional status all need to be considered.[25 51-52] Applying these QI and if all these items will be satisfied we can affirm to have a real good quality process of CRC care for the whole population. The foreseeable future in quality evaluation and improvement for health care will likely involve more and more frequently the use of QI by regulatory and accrediting agencies, stakeholders, clinicians, individual hospitals and health care providers, as well as patients. This underlines that the QI should be defined, developed and tested with scientific evidence-based rigor in a careful and transparent manner, taking into account their degree of relevancy, validity, reliability and feasibility.[30 32] Although QI have been defined in several different ways, all authors agreed that the final aim is the improvement of patients outcome.[31 33 55]

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The systematic trend analysis of QI allows to assess immediate changes and improvements in the diagnostic-therapeutic process that could be translated in a short-term benefit for patient, without waiting for survival analysis typically needed some years to be produced because of the patients' follow-up. Furthermore, this system of evaluation and auto-evaluation could favour the surveillance and monitoring of the comprehensive level of the oncologic care in the region, the clinical performance homogeneity, the possible weakness of the clinical network, and finally the corrective interventions to be adopted to improve the QoCC.

With this study, we hope to increase the awareness of the value of QI in health care so to encourage more uniform practices and improve provider documentation of medical care in our region; moreover, we hope that standardization of QI among different regions will help to define threshold of minimal standard of care.

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APPENDIX (List of Collaborators)

Members of the QC_3 CRC Working Group are listed as following:

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COMPETING INTERESTS

The Authors have no competing interests.

DATA SHARING

no additional data available.

AUTHORS' CONTRIBUTION

I declare that V. Bianchi, A. Bordoni, A. Spitale and L. Mazzucchelli have directly participated in the planning of the manuscript; that V. Bianchi, A. Bordoni, A. Spitale and the QC_3 Colorectal Working Group have directly participated in the conducting of the project; that V. Bianchi, A. Bordoni, A. Spitale and L. Ortelli have directly participated in the reporting, acquisition of data or analysis and interpretation of data; and that V. Bianchi and A. Bordoni are responsible for the overall content as guarantors of the work. Finally, I declare that all the Authors have drafted and revised the paper critically for important intellectual content, and that they have given final approval of the version published. None of the Authors have competing interests.

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LEGENDS TO FIGURES

FIGURE 1 - Process used to select quality indicators for colorectal cancer care

QI = Quality Indicators; QC_3 CRC-WG = QC3 Colorectal Cancer Working Group; AB = Advisory Board

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Table 1. Quality indicators of colorectal cancer care according to diagnostic-therapeutic process (diagnosis, pathology, treatment - surgery, chemotherapy and radiotherapy - and outcome) and tumour site.

CLINICAL DOMAIN	SITE	QUALITY INDICATOR	NUMERATOR	DENOMINATOR	MEDICAL DOCUMENTATION	RATIONALE	REF
DIAGNOSIS (n=6)	C&R	Proportion of patients with colorectal cancer and diagnosis based on symptoms *vs* screening *vs* accidental finding	Number of patients with colorectal cancer whose diagnosis is based on symptoms, defined as appearance or persistence of clinical events and signs, such as rectal bleeding, occult blood in stool, weight loss with no apparent cause, general abdominal discomfort, bowel obstruction, change in bowel habits, constant tiredness, anaemia Number of patients with colorectal cancer whose diagnosis is based on screening, defined as regular examination, such as faecal occult blood test (FOBT) or colonoscopy in asymptomatic patients Number of patients with colorectal cancer whose diagnosis is an accidental finding following examinations or therapies for other diseases (e.g. hospital admission for other causes…)	Number of patients with colorectal cancer	Request form of endoscopic examination Endoscopy and surgical pathology reports Reports/discharge letters coming from all hospital units/department (i.e. surgery, medicine, radiation oncology, medical oncology)	Assessment of the patient's take charge	[18 34-38]
	C&R	Proportion of patients with colorectal cancer, evaluated by preoperative colonoscopy	Number of patients with colorectal cancer who have been evaluated by a preoperative colonoscopy	Number of patients with colorectal cancer undergoing surgery	Endoscopy report Request form of pathology examination Pathology report of endoscopy	Planning of further diagnostic procedures and treatments Comprehensiveness of diagnostic and staging evaluation	[7 16 18 40-41]
	R	Proportion of patients with rectal cancer and description of the tumour localization (distance *ab ano*) in the endoscopic/pathologic documentation	Number of patients with rectal cancer who have the description of the tumour localization, in terms of distance *ab ano*, in the endoscopic/pathologic documentation	Number of patients with rectal cancer undergoing endoscopy	Endoscopy report Request form of pathology examination Pathology report of endoscopy	Planning of further diagnostic procedures and treatments Comprehensiveness of diagnostic and staging evaluation	[1 19 56-57]
	C&R	Proportion of patients with colorectal cancer and requests for an initial CT and/or a MRI examination completed by clinical information according to the ACR guidelines	Number of patients with colorectal cancer for which the request of an initial CT and/or a MRI examination is completed by clinical information according to the ACR guidelines	Number of patients with colorectal cancer undergoing initial CT and/or MRI examination	Radiology (CT and/or MRI examination) report	Providing the necessary information for a comprehensive radiological examination Assessment of the quality of the flux of clinical information	[7 58]

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	R	Proportion of patients with low rectal[a] cancer undergoing pelvic MRI of staging	Number of patients with low rectal[a] cancer who have undergone a pelvic MRI of staging	Number of patients with low rectal cancer	Radiology (MRI examination) report Discharge letters coming from all hospital units/department (i.e. surgery, medicine, medical oncology, radiation oncology)	Planning of further diagnostic procedures and treatments Comprehensiveness of diagnostic and staging evaluation	[19 59-61]
	R	Proportion of patients with rectal cancer and a preoperative MRI reporting the description of the radial margin status (mm)	Number of patients with rectal cancer who have undergone a preoperative MRI reporting the description of the radial margin status (mm)	Number of patients with rectal cancer undergoing preoperative MRI	Radiology (MRI examination) report	Planning of further diagnostic procedures and treatments Comprehensiveness of diagnostic and staging evaluation	[62]
PATHOLOGY (n=3)	R	Proportion of patients with rectal cancer for which the request for the pathological examination includes the information of neo-adjuvant RT±ChT	Number of patients with rectal cancer for which the request for the pathological examination includes the information of neo-adjuvant RT±ChT	Number of patients with rectal cancer undergoing neo-adjuvant RT±ChT and surgery [a]	Request form of pathology examination Surgical pathology report	Providing the necessary information for a comprehensive pathological examination Assessment of the quality of the flux of clinical information	Proposed by CRC-WG
	C&R	Proportion of patients with colorectal cancer and a sufficient number of tumour samples *(≥3)*	Number of patients with colorectal cancer for which 3 or more tumour sample were processed for the pathological analysis	Number of patients with colorectal cancer undergoing surgery [a]	Surgical pathology report	Comprehensiveness of pathology examination	Proposed by CRC-WG
	C&R	Proportion of patients with colorectal cancer and a surgical pathology report including the following characteristics: - surgical intervention description - sample length - tumour localization according to WHO - tumour size - histological type according to WHO - histological grade - resection margins - lymph-vascular invasion - perineural invasion - tumour deposits (discontinuous extramural extension)	Number of patients with colorectal cancer whose pathological report includes the following characteristics: - surgical intervention description - sample length - tumour localization according to WHO - tumour size - histological type according to WHO - histological grade - resection margins - lymph-vascular invasion - perineural invasion - tumour deposits (discontinuous extramural extension) - pathological staging (AJCC pTNM) - number of retrieved lymph nodes - treatment effect -macroscopic integrity of the mesorectum	Number of patients with colorectal cancer undergoing surgery [a]	Surgical pathology report	Comprehensiveness and standardisation of surgical pathology report Comprehensiveness of staging evaluation Planning of further treatments	[18-19 63-64]

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		- pathological staging (AJCC pTNM) - number of retrieved lymph nodes - treatment effect -macroscopic integrity of the mesorectum (for rectum only) (this quality indicator should be provided for each characteristic)	(for rectum only)				
TREATMENT (n=16)	C&R	Proportion of patients with colorectal cancer operated in emergency [b]	Number of patients with colorectal cancer who have been operated in emergency [b]	Number of patients with colorectal cancer undergoing surgery [a]	Radiology and surgery report/discharge letter Surgical pathology report	Assessment of the patient's take charge	[65-67]
	C&R	Proportion of patients with colorectal cancer and dead within 30 days and 6 months from the surgery (postoperative mortality)	Number of patients with colorectal cancer and dead within 30 days from the surgery Number of patients with colorectal cancer and dead within 6 months from the surgery	Number of patients with colorectal cancer undergoing surgery [a]	Surgery report/discharge letter Surgical pathology report Access to regional Office of Population Registry Rosters for the assessment of patients vital status	Assessment of the quality of surgical procedure	[68-71]
	C&R	Proportion of patients with colorectal cancer and postoperative multidisciplinary discussion	Number of patients with colorectal cancer for which there have been a multidisciplinary discussion after surgery	Number of patients with colorectal cancer undergoing surgery [a]	Surgery, Oncology, Radiation Oncology reports/discharge letters Multidisciplinary discussion documentation	Planning of further diagnostic procedures and treatments	[72-73]
	R	Proportion of patients with malignant rectal polyp (pT1) and complete endoscopic polypectomy	Number of patients with malignant rectal polyp (pT1) who have undergone a complete endoscopic polypectomy	Number of patients with malignant rectal polyp (pT1)	Endoscopy report, Endoscopic pathology reports	Assessment of the quality of surgical procedure	Proposed by the CRC-WG
	R	Proportion of patients with low rectal [c] cancer and surgical intervention with sphincter preservation	Number of patients with low rectal [c] cancer who have undergone a surgical intervention with sphincter preservation	Number of patients with low rectal cancer undergoing surgery [a]	Surgical pathology report Surgery report/discharge letter	Assessment of the quality of surgical procedure	[7 74-76]
	R	Proportion of patients with rectal cancer undergoing TEM with R0 resection	Number of patients with rectal cancer who had undergone TEM with R0 resection	Number of patients with rectal cancer undergoing TEM	Surgical pathology report Surgery report/discharge letter	Assessment of the quality of surgical procedure	[77-79]
	C&R	Proportion of patients with colorectal cancer and a number of resected lymph nodes ≥ 12	Number of patients with colorectal cancer with a number of resected lymph nodes ≥ 12	Number of patients with colorectal cancer undergoing surgery [a], but no neo-adjuvant therapy	Surgical pathology report Surgery report/discharge letter	Assessment of the quality of surgical procedure and pathology examination	[7 14 16 40-41 80-85]
	C&R	Proportion of patients with colorectal cancer operated on with free margins	Number of patients with colon cancer who have undergone surgery and have free margins	Number of patients with colorectal cancer undergoing surgery [a]	Surgical pathology report Surgery report/discharge	Assessment of the quality of surgical procedure	[7 86-87]

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					letter		
	C&R	Proportion of patients with colorectal cancer and AJCC TNM clinical stage I (from T2N0M0) to III (any T, N1M0) undergoing a surgical resection with anastomosis	Number of patients with colon cancer and AJCC TNM clinical stage I (from T2N0M0) to III (any T, N1M0) who have undergone a surgical resection with anastomosis	Number of patients with colorectal cancer and AJCC TNM stage I (from T2N0M0) to III	Radiology report Surgical pathology report Surgery report/discharge letter	Assessment of the quality of surgical procedure	[40-41 86-87]
	C	Proportion of patients with colon cancer and AJCC TNM stage II (T3N0M0, T4N0M0) high-risk (presence of at least one of the following factors: LN<12, G3, lymph-vascular or perineural invasion, tumour obstruction, tumour perforation, pT4) or III undergoing adjuvant ChT	Number of patients with colon cancer and AJCC TNM stage II (T3N0M0, T4N0M0) high-risk (presence of at least one of the following factors: LN<12, G3, lymph-vascular or perineural invasion, tumour obstruction, tumour perforation, pT4) or III, who have undergone adjuvant ChT	Number of patients with colon cancer and AJCC TNM stage II high-risk or III, undergoing surgery [a]	Radiology report Surgical pathology report Surgery, oncology reports/discharge letters	Assessment of the quality of oncologic treatment	[16 18 40-41 88-91]
	C	Proportion of patients with colon cancer AJCC TNM stage II high-risk or stage III undergoing adjuvant ChT within 8 weeks from surgical resection	Number of patients with colon cancer and AJCC TNM stage II high-risk or III, who have undergone adjuvant ChT within 8 weeks from surgical resection	Number of patients with colon cancer and AJCC TNM stage II high-risk or III undergoing surgery [a] and adjuvant ChT	Radiology report Surgical pathology report Surgery, oncology reports/discharge letters	Assessment of the quality of oncologic treatment	[18 92]
	C&R	Proportion of patients with colorectal cancer and histology of the primary tumour or metastases obtained before the beginning of ChT	Number of patients with colorectal cancer and histology of the primary tumour or metastases obtained before the beginning of ChT	Number of patients with colorectal cancer undergoing primary ChT	Radiology and pathology reports Oncology report/discharge letter	Assessment of the quality of oncologic treatment	[40-41]
	C&R	Proportion of patients with colorectal cancer and unresectable metastases undergoing first-line ChT or bio-ChT	Number of patients with colorectal cancer and unresectable metastases who have undergone a first-line ChT or bio-ChT	Number of patients with colorectal cancer and unresectable metastases	Radiology and pathology reports Oncology report/discharge letter	Assessment of the quality of oncologic treatment	[93-96]
	C&R	Proportion of patients with colorectal cancer and hepatic metastases primarily unresectable turned into resectable metastases after neo-adjuvant ChT	Number of patients with colorectal cancer and hepatic metastases primarily unresectable turned into resectable metastases after neo-adjuvant ChT	Number of patients with colorectal cancer and unresectable hepatic metastases undergoing neo-adjuvant ChT	Radiology report Oncology report/discharge letter	Assessment of the quality of oncologic treatment	[96]
	R	Proportion of patients with locally advanced rectal cancer (T3-4 and/or any T, N+ and M0) undergoing neo-adjuvant RT±ChT	Proportion of patients with locally advanced rectal cancer (T3-4 and/or any T, N+ and M0) who have undergone neo-adjuvant RT±ChT	Number of patients with locally advanced rectal cancer undergoing surgery [a]	Endoscopic pathology report Radiology report Radiation Oncology and oncology reports/discharge letters	Assessment of the quality of oncologic and radio-oncologic treatment	[97-98]
	R	Proportion of patients with	Number of patients with rectal cancer who	Number of patients with rectal	Endoscopic pathology	Assessment of the quality	[18 98]

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		rectal cancer and undergoing neo-adjuvant RT±ChT operated within 6-8 weeks after the end of neo-adjuvant RT±ChT	have undergone neo-adjuvant RT±ChT and were operated within 6-8 weeks after the end of neo-adjuvant RT±ChT	cancer undergoing neo-adjuvant RT±ChT followed by surgery [a]	report Radiology report Radiation Oncology and oncology reports/discharge letters Surgical pathology report	of oncologic and radio-oncologic treatment	
OUTCOME (n=2)	C&R	Analysis of overall survival at 1, 3, 5 and 10 years from diagnosis	Number of patients with colorectal cancer who survive at 1, 3, 5 and 10 years from diagnosis	Number of patients with colorectal cancer	Access to regional Office of Population Registry Rosters for the assessment of patients vital status	Assessment of overall survival	[7 99]
	C&R	Analysis of disease-free survival at 1, 3, 5 and 10 years from the curative treatment	Number of patients with colorectal cancer who are disease-free at 1, 3, 5 and 10 years from the curative treatment	Number of patients with colorectal cancer curatively treated	Reports/discharge letters coming from all hospital units/department (i.e. surgery, medicine, oncology, radio-oncology)	Assessment of disease-free survival	[7 99]

Abbreviation:

C&R= colon-rectum; **C**= colon; **R**= rectum; **FOBT**= Faecal Occult Blood Test; **ACR**= American College of Radiology; **CT**= computed tomography; **MRI**= magnetic resonance imaging; **AJCC**= American Joint Committee on Cancer; **RT**= radiotherapy; **ChT**= chemotherapy; **WHO**= World Health Organization; **TEM**= transanal endoscopic microsurgery.

[a] surgery excludes endoscopic resection and colostomy

[b] emergency: within 24 hours from the onset of symptoms;

[c] low rectum: 4 to 7.5 cm from the dentate line [100]

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Original Article

Quality indicators of Clinical Cancer Care (QC_3) in colorectal cancer

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Running title: Quality indicators of clinical care in colorectal cancer

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ABSTRACT

Objectives: Assessing the quality of cancer care (QoCC) has become increasingly important to providers, regulators and purchasers of care worldwide. Aim of this study was to develop evidence-based quality indicators (QI) for colorectal cancer (CRC) to be applied in a population-based setting.

Design: A comprehensive evidence-based literature search was performed to identify the initial list of QI, which were then selected and developed using a two-step modified Delphi process involving two multidisciplinary expert panels with expertise in colorectal cancer care, quality of care and epidemiology.

Setting: The QC_3 population-based project, which involve all the public and private hospitals and clinics present on the territory of Canton Ticino (South Switzerland).

Participants: Ticino Cancer Registry, The Colorectal Cancer Working Group (CRC-WG) and the external academic Advisory Board (AB).

Main outcome measures: Set of quality indicators (QI) which encompass the whole diagnostic-treatment process of colorectal cancer.

Results: Of the 149 QI emerged from 181 sources of literature, 104 were selected during the in-person meeting of the CRC-WG. During the Delphi process, the CRC-WG shortened the list to 89 QI. The AB finally validated 27 QI according to the phase of care: diagnosis (N=6), pathology (N=3), treatment (N=16), and outcome (N=2).

Conclusions: Using the validated Delphi methodology, including literature review of the evidence and integration of expert opinions from local clinicians and international experts we were able to develop a list of QI to assess QoCC for CRC. This will hopefully guarantee feasibility of data retrieval, acceptance and translation of QI into the daily clinical practice to improve QoCC. Moreover, evidence-based selected QI allow to assess immediate changes and improvements in the diagnostic-therapeutic process that could be translated in a short-term benefit for patients with a possible gaining both in overall and disease-free survival.

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ARTICLE SUMMARY

Article focus

- Quality of Cancer care (QoCC) studies on specific quality indicators (QI) developed worldwide since the late '90s showed both a continuous improvement of oncologic care provided by the clinical structures involved and an increased availability of specialized care in the considered areas.
- This study aims to define evidence-based QI for colorectal cancer (CRC) care ~~(CRC)~~, in order to favour ~~the~~ a feasible evaluation of the oncologic diagnostic-therapeutic process ~~, which can be followed by the definition of standards of care for each QI, in terms of minimum and target requirements.~~ from a population-based cancer registration and data collection point of view.

Key messages

- QI should be defined, developed and tested with scientific evidence-based rigor in a careful and transparent manner, taking into account their degree of relevancy, validity, reliability and feasibility.
- The selected CRC QI can be applied in a population-based setting, implying the inclusion of the elderly, considering age an extremely important determinant of treatment.

Strengths and limitations of this study

- To develop the CRC QI we used a formal iterative process, the RAND/UCLA Appropriateness Methodology widely diffused and validated within other QoCC research. The selected QI are representative of the main steps of the diagnostic-therapeutic process.
- Due to the evidence that research studies demonstrated that single-discipline panels select different indicators than do multidisciplinary panels and to maximize the applicability of CRC QI, we constituted two panels of experts, a local Working Group and an external national/international academic Advisory Board, which could offer a multidisciplinary

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perspective on practice and who can guarantee that the selected QI and their results will be comparable with national and international data. ~~.~~

- ~~The p~~Possible limitations of the current work are the following:
  - ~~is~~ the level of evidence found in the literature. ~~However t~~This situation is common to many aspects of health care, and it was the reason that the expert panel methodology was developed – specifically, to identify ~~-~~the processes that are most likely to be valid measures of quality when the highest level of evidence is not available.
  - the literature selection could have missed some relevant articles. However, members of the Working Group were likely to be very familiar with the literature, and had the opportunity to suggest other indicators based on their experience and literature search; in this way, we believe to have integrated the best research evidence with clinical expertise.
  - the feasibility of measuring indicators in terms of data collection and calculation. However, both the Working Group and the Advisory Board were concerned about the feasibility, validity and reliability of clinical data collection, necessary for the calculation of each single indicator at the population-based level. In fact, in order to warrant an accurate measurement, those indicators reaching more than 70% of the agreement, confirming their scientific and clinical value, but evaluated at least by one of the experts not feasible and difficult to be collected at the population-based level, were definitely excluded. In this way, we have overcome the feasibility limit.

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INTRODUCTION

Research on QoCC performed during the last decade has demonstrated that the increase in knowledge on treatments with proven efficacy do not directly translate into optimal delivery of such treatments to patients. Moreover, accumulating evidence suggests that underuse and overuse of care may occur for patients with cancer.[1-2]~~[1–2]~~ In addition to survival analysis, to evaluate and compare quality of care at the population-based level, the assessment of QoCC has become increasingly important to providers, regulators and purchasers of care to growing demand for services, rising costs, constrained resources and evidence of variation in clinical practice.[3]~~[3]~~ QoCC studies and structured programmes on specific quality indicators (QI) have been developed worldwide since the late '90s, showing both a continuous improvement of oncologic care provided by the clinical structures involved and an increased availability of specialized care in the considered areas. Most of these studies have been implemented at the regional level on a territory with uniform legislative, health and geographical characteristics, increasing the likelihood of recruitment of involved clinicians.[1 4-7]~~[1, 4–7]~~

So far, in Switzerland no population-based study on QoCC with a prospective design has been implemented. In addition to the yearly renewed international guidelines for each type of cancer, there is still the need to evaluate the real conditions of care in the community. Population-based Cancer Registry data are therefore essential to describe and reflect real world and routine care as well as to provide regular feedback to healthcare workers and decision makers about the management of a disease in the daily practice and those treatments that are routinely prescribed and/or effective in all patient groups.[8]~~[8]~~ Moreover, Cancer Registries represent an independent observatory, thus assuring a fair evaluation service, avoiding any conflicts of interest.

We, therefore, implemented the QC_3 project, focusing on QoCC about the diagnosis-treatment process in colon-rectum, prostate, uterus, ovary and lung cancers in the territory of Canton Ticino (South Switzerland).

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Colorectal cancer (CRC) is an important health issue worldwide. It is the most common malignancy in Europe (excluding non-melanoma skin cancers) and the second most common in terms of cancer-related mortality.[9]~~[9]~~ In Switzerland, CRC is the second and third most frequent tumour in women and men, respectively. About 4000 CRC cases are diagnosed annually, corresponding to a European age-standardized incidence rate equal to 49.4 and 30.6 cases per 100'000 inhabitants in men and women, respectively, and representing the 11% of all tumours.[10-12]~~[10-12]~~ CRC is the third leading cancer cause of death in Switzerland, with approximately 1600 deaths/year, corresponding to a European age-standardized mortality rate equal to 18.5 and 10.6 cases per 100'000 inhabitants in men and women, respectively. With a 5-year survival probability equal to 60%, Switzerland is the country with the most favourable prognosis in Europe.[13]~~[13]~~ A recent Swiss report with follow up to 2009 show an additional 5 year survival increase to 62%.[11]~~[11]~~ The aims of the QC_3 ~~study~~ project are the following: 1) to define and confirm evidence-based QoCC indicators for the tumour localizations above cited, in order to favour a feasible evaluation of the oncologic diagnostic-therapeutic process from a population-based cancer registration and data collection point of view~~an improvement of the short-term oncologic diagnostic-therapeutic process~~; 2) to define and implement at the regional level standards of care for each QoCC measure, in terms of minimum and target requirements. In the present report we will describe the initial part of the QC_3 project, meaning the process followed to identify the panel of specific QoCC indicators for the CRC, as well as the list of QoCC indicators identified and approved both by a dedicated Working Group of local health care providers and by an external independent Advisory Board, in a perspective of data collection feasibility by a population-based cancer registry.

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MATERIAL AND METHODS

The QC_3 project is a prospective, descriptive study on the QoCC to be implemented in a population-based setting; it is performed by the Ticino Cancer Registry on a 3-year time period (2011-2013) on the territory of Canton Ticino (South Switzerland). In this paper we focus on the initial part of the project: the identification of the CRC quality indicators which will be used to evaluate the QoCC about CRC in our region.

Quality indicators (QI) for CRC were developed involving a local expert panel, named QC_3 Colorectal Working Group (CRC-WG). Elected members, selected on the basis of their expertise and on their daily clinical involvement in CRC care, were contacted to have their interest confirmed in being involved. The final QC_3 CRC-WG encompassed two pathologists, four gastroenterologists, two oncologists, three surgeons, two radiologists, two radiation oncologists and one nuclear medicine specialist, for a total of 15 panellists all working in the public or in the private hospitals and clinics of Canton Ticino (see Appendix 1).

Published studies and references were identified through a comprehensive search on PubMed/MEDLINE, using initially specific strings/expressions, such as the following: "quality of care OR quality indicators AND colorectal cancer", "diagnosis OR diagnostic AND quality indicators AND colorectal cancer", "pathology OR pathological AND quality indicators AND colorectal cancer", "surgery OR surgical AND quality indicators AND colorectal cancer", "radiation oncology OR radiotherapy AND quality indicators AND colorectal cancer", "chemotherapy AND quality indicators AND colorectal cancer", "surveillance OR follow-up OR outcome AND quality indicators AND colorectal cancer", "preoperative care OR perioperative care OR intraoperative care OR postoperative care AND colorectal cancer", "population-based AND quality indicators AND colorectal cancer". For each of the identified candidate indicators, we performed a systematic literature review to identify the highest level of evidence supporting the validity of that quality indicator for articles published from 1990 onwards. The reference list of the included articles were also examined to identify any additional article that had not been identified in

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the MEDLINE search. We included all the peer-reviewed articles, but case reports, letters, abstracts or editorials. If evidence at the highest level were limited or absent, then lower levels of evidence were evaluated. For example, if data were not available from randomized controlled trials, cohort or case-control studies, case series and expert opinion or clinical guidelines were reviewed. A selection of already approved QI provided by the American Society of Clinical Oncology (ASCO), the National Comprehensive Cancer Network (NCCN), the National Initiative on Cancer Care Quality (NICCQ), the Quality Oncology Practice Initiative (QOPI) and the Florida Initiative for Quality Cancer Care (FIQCC), were included in the evaluation list, with the aim to transfer them from the clinical to the population-based setting.[1-2 4 7 14-20]

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The initial QI list emerged from 181 sources of literature, and it was proposed to the CRC-WG in the context of an in-person meeting held at the very beginning of the process. The list was then left to the QC_3 CRC-WG's evaluation for a period of two weeks. The participants were asked to provide a whole opinion with written comments about those QI considered pertinent for the assessment of CRC care quality, to suggest additional QI not already included in the list and to delete those QI considered not suitable. In order to make the selection and evaluation easier, the QI were subdivided in chapters recalling the Donabedian's and the National Initiative for Cancer Care Quality schemes: diagnosis and staging, pathology, treatment, follow-up, outcome.[2 21]~~[2, 14]~~

Delphi Round 1

The QI selection was done by using a 2-step modified Delphi process.[22]~~[15]~~ The initial list of QI, re-analyzed by the QC_3 CRC-WG, was formatted as a questionnaire, where for each indicator was specified the numerator, the denominator and the sources of evidence from which it was extracted. The questionnaire was distributed by regular mail to the QC_3 CRC-WG, so to maintain it anonymous, along with a stamped, addressed return envelope and an attached letter with the deadline date of two weeks from the receipt and the instruction for voting. Respondents were asked to rate each QI adopting the RAND Appropriateness Methodology (scale 1 to 9, 1 = extremely

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inappropriate; 9 = extremely appropriate), according to selection criteria of relevance, scientific soundness (validity, reliability, comparability) and feasibility (precise definition and specification, data feasibility, reliability of data collection).[23-25]~~[16-18]~~ Each QI was judged as validated if it reached a strong consensus for acceptance (≥70% of the QC_3 CRC-WG rated the QI with a vote ≥7), discarded if it reached a strong consensus for exclusion (≥70% of the QC_3 CRC-WG rated the QI with a votes ≤ 3) and in stand-by if there was an unclear consensus (4 ≤ votes ≤ 6), which implies an eventual in-person meeting.

Delphi Round 2

The Delphi Round 2 questionnaire was performed with the same modalities of the first round and enclosed the frequency distribution of round 1 votes, allowing the panellists to eventually alter their responses, in the light of colleagues' assessments.[23]~~[16]~~

Advisory Board Review

The list of selected QI derived from the two Delphi rounds was then submitted to an independent external national/international academic multidisciplinary Advisory Board (AB), in order to get an additional evaluation on the suitability of QI as "quality" indexes according to the criteria shown in the previous paragraph. The intent was to achieve at least one health professional for each specialty. The AB included one pathologist, one gastroenterologist, two oncologists, two surgeons, one radiologist, one radiation oncologist, one nuclear medicine specialist and one epidemiologist, for a total of 10 experts in CRC care (see Acknowledgements); all the panellists are daily involved in the CRC care and they had been contacted with the same modalities of the QC_3 CRC WG. The selected QI as well as the corresponding literature sources were distributed to the AB as an electronic form where their opinion about QI were expressed both as megatrends (i.e. response yes/no to the suitability of each QI) and as eventual additional comments.[26] We considered every single QI as finally approved by the AB if it achieved ≥ 70% of the agreement (i.e. ≥ 70% of respondents should

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have answered “yes”). Besides the vote (“yes” *versus* “no”), the panellists had the chance to comment the single QI from a population-based cancer registration and data collection point of view. Therefore, those QI reaching more than 70% of the agreement, confirming their scientific and clinical value, but evaluated at least by one of the experts “not completely feasible and difficult to be collected at the population-based level”, were definitely excluded.

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RESULTS

The QI selection process began in January 2011 and ended in December 2011.

Participation of CRC-WG members throughout the process was high: 15 (100%) participated to the in-person meeting, 12 (80%) completed both the Delphi round 1 and 2. The Delphi Round 1 questionnaire respondent time were in the range of 18 to 60 days, while for the Round 2, the delay time was in the range of 8 to 55 days; these delays and the time for recruitment of the AB influence the long time spent for this part of the project.

The Figure 1 summarizes the entire process used to select QI for CRC care. The literature search produces 181 citations dealing with CRC QoCC, including also already validated QI provided by the ASCO, NCCN, NICCQ, QOPI and FIQCC.[1-2 4 7 14-20] From this search, we initially selected a total of 149 QI, which were proposed to the CRC-WG in the context of the initial in-person meeting. The following discussion and revision reduced the list to 104 QI before the modified Delphi process started; these QI were divided into the following areas: diagnosis and staging, pathology, treatment, follow-up and outcome. After the whole Delphi process the list was shortened to 89 QI, distributed as following: diagnosis and staging (N=16), pathology (N=20), treatment (N=38), follow-up (N=10), and outcome (N=5). The QI finally underwent to the AB's evaluation; this last step, according to the procedure described in the methods, shortened the final list to 27 QI ~~(Tab.1):~~ diagnosis (N=6), pathology (N=3); treatment (N=16), follow-up (N=0), and outcome (N=2). Table 1 reports detailed information for each QI: a) QI description; b) criteria for patients inclusion in the numerator and denominator; c) list of the necessary medical documentation that should be collected by the Cancer Registry to extract the needed and relevant information to built the specific QI, such as the report of the endoscopy, the pathology report of the biopsy and/or surgical resection, the preoperative radiological reports (e.g. TAC and MRI), the surgery report, the tumour board documentation, the oncological report, the radiotherapy report and database/documentation of the regional Office of Population Registry Rosters for the assessment of patients vital status (for outcome QI); d) QI rationale; e) related references.

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DISCUSSION

In the preliminary phase of the QC_3 project shown in this paper we developed a panel of evidence-based CRC QI which are suitable to be implemented in a population-based setting.

To develop the QC_3 QI we used a formal iterative process, the RAND/UCLA Appropriateness Methodology widely diffused and validated within other QoCC research.[23-24]~~[16-17]~~ Due to the evidence that research studies demonstrated that single-discipline panels select different indicators than do multidisciplinary panels and to maximize the applicability of QC_3 CRC QI, we constituted a working group which could offer a multidisciplinary perspective on practice, including specialists, professionals, clinicians and researchers coming from both public and private hospitals.[27-33]~~[19-25]~~ Moreover, we have used a further validation step enrolling an independent national/international academic AB. This choice was due to the aim of measuring QoCC within a Swiss region, with a point of view on the population-based data collection and evaluation, and of obtaining results which will be comparable with national and international data. We believe that the expertise and multidisciplinary representativeness of the QC3 CRC-WG and of the AB will surely increase quality, acceptance and translation of QI into the daily clinical practice~~.~~.

The selected QI are representative of the main steps of the diagnostic-therapeutic process. The diagnosis QI reflect the importance of a pre-operative evaluation and staging, reliable evaluation of the tumour localization and local invasion, and particularly for the rectal cancers, of a feasible and effective surgery. The first indicator of the "diagnosis" group is important to understand what happens in a territory where there is not an organized screening programme for colorectal cancers, but only an opportunistic screening strategy. If the tumour is detected because the physician submit the patients older than 50 years old to a fecal occult blood test (FOBT) or colonoscopy control or if a patient, being aware of the possible risk, asks his family doctor to undergo screening examinations, is an interesting data to be evaluated, also in the hypothesis of a colorectal cancer screening programme implementation. We, therefore, believe that a higher proportion of patients diagnosed through screening (FOBT or colonoscopy in asymptomatic patients) would represent a

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higher diagnostic quality, since the therapeutic approach and, consequently, the patients outcome (in terms of recurrence and survival) would be more favourable, as reported in the literature.[20 34-39] The pathology QI reflect the importance of a good communication between clinicians and pathologists in terms of patient's clinical history and consequent evaluation of the effectiveness of a neo-adjuvant therapy; moreover, there is a need of standardization of the pathologic report following the international guidelines (e.g. take at least three samples of tumour during the macroscopy), not leaving any items unexplained or implicit. In particular, the third QI reported in Table 1 (pathology section) refers to the surgical pathology report, which derives from the surgical curative intervention and should be as complete as possible to be useful for the future decision about patient's treatment. Our intent is to calculate it for all listed items considered together, but also for each item individually analyzed: e.g. proportion of patients with colorectal cancer and a definitive pathological report including the surgical intervention description; proportion of patients with colorectal cancer and a definitive pathological report including the tumour size; proportion of patients with colorectal cancer and a definitive pathological report including the resection margins; proportion of patients with colorectal cancer and a definitive pathological report including the pathological staging (AJCC pTNM); etc… The treatment QI cover the general issues of surgery, such as emergency, postoperative mortality and a multidisciplinary discussion of the clinical case; furthermore, they focus on the debate of the retrieved lymph nodes, on the timing between radiotherapy and surgery, on the adjuvant chemotherapy and on the attitude towards the metastatic patients. The two main items of the outcome chapter refers to the overall and disease-free survival. Although it is necessary to wait for a certain follow-up period (i.e. 1, 3, 5 to 10 years from the date diagnosis for the calculation of overall survival, and from the date of curative treatment for the calculation of disease-free survival), they will represent the overall resume of the diagnostic and treatment quality of CRC patients. Our intent will be to analyse overall and disease-free survival according to some of the proposed QI (such as QI concerning the pathological characteristics of the tumours, QI of the adjuvant chemotherapy in patients with colon cancer and AJCC TNM stage II

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high-risk or III, QI of colorectal patients operated on with free margins, QI of locally advanced rectal cancer patients undergoing neo-adjuvant radio±chemotherapy, etc…). We will finally compare our results with other regional and national reality, favouring the interpretation of each single QI. Concerning the QI about follow-up, AB did not finally include any of them. Indeed, although the follow-up procedures are suggested by several international guidelines, they are based on level II-III evidence and controversies remain regarding selection of optimal strategies for following up patients after potentially curative CRC~~colorectal cancer~~ surgery.~~.~~[40-43]~~[26-29]~~

The first limitation of the current work is the level of evidence found in the literature. For some indicators, strong evidence of their validity was not available from RCTs. However this situation is common to many aspects of health care, and it was the very reason that the expert panel methodology was developed – specifically, to identify ~~-~~the processes that are most likely to be valid measures of quality when the highest level of evidence is not available.[19 23 44]~~[16, 30-31]~~

Secondly, we may have missed some studies during the literature search and, consequently, some QI has not been proposed to the QC_3 CRC-WG since the beginning of the QI revision process. However, this limitation should have been overcome by the fact that the members of the QC_3 CRC-WG were likely to be very familiar with the literature, and had the opportunity to suggest other QI based on their experience and literature search.[7 27-28 45]~~[7, 19-20, 32]~~ Thus we integrated the best research evidence with clinical expertise, as reported by Sackett *et al*..[46]~~[33]~~ A further limit could be the feasibility of measuring QI in terms of data collection and calculation, which is immediately the next step. Actually, the QI selected by both the QC_3 CRC-WG and the AB represent an ideal set of criteria to measure the quality of CRC care; at the same time they both were concerned about the feasibility, validity and reliability of clinical data collection, necessary for the calculation of each single QI at the population-based level. This is the reason why most of the identified QC_3 QI are common to many QoCC studies.[1-2 4 7 14-20] Besides the traditional Delphi process, the panellists had the chance to comment the single QI from a population-based cancer registration and data collection point of view. Therefore, in order to warrant an accurate

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measurement, those QI reaching more than 70% of the agreement, confirming their scientific and clinical value, but evaluated at least by one of the experts not feasible and difficult to be collected at the population-based level, were definitely excluded. In addition, we performed a retrospective preliminary pilot collection on the detailed and necessary incidence data of CRC occurred in 2011, realising that the measurement of most QI is feasible, whereas for some selected QI the retrieving of variables ~~should~~ would need ~~be~~ additional efforts~~ly tested~~,~~.~~ some preliminary results were presented in national and international conferences and congresses, receiving positive feedback by both the clinical and epidemiological setting.[47-50]~~[34-35]~~ Only the definitive results will give us the proportion of missing information, whose magnitude will be assessed.

The selected QC_3 CRC QI will be applied in a population-based setting, where age is an extremely important determinant of treatment. The elderly are rarely included in the randomized clinical trials with the consequence of a possible "underuse of treatment".[25 51-52]~~[18, 36-37]~~ At a broad European level, national audit registries in surgical oncology have led to improvements with a great impact and they offered the possibility, as for our project, to perform research on patients that are usually excluded from clinical trials such as elderly and co-morbid patients.[53-54]~~[38-39]~~ Evidence suggests that the relative benefits of treatment for the elderly are similar to those seen for cancer patients in general, though decision making for treatment becomes more complex as life expectancy, co-existing illnesses, and functional status all need to be considered.[25 51-52]~~[18, 36-37]~~ Applying these QI and if all these items will be satisfied we can affirm to have a real good quality process of CRC care for the whole population. The foreseeable future in quality evaluation and improvement for health care will likely involve more and more frequently the use of QI by regulatory and accrediting agencies, stakeholders, clinicians, individual hospitals and health care providers, as well as patients. This underlines that the QI should be defined, developed and tested with scientific evidence-based rigor in a careful and transparent manner, taking into account their degree of relevancy, validity, reliability and feasibility.[30 32]~~[22, 24]~~ Although QI have been

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defined in several different ways, all authors agreed that the final aim is the improvement of patients outcome.[31 33 55]~~[23, 25, 40]~~

The systematic trend analysis of QI allows to assess immediate changes and improvements in the diagnostic-therapeutic process that could be translated in a short-term benefit for patient, without waiting for survival analysis typically needed some years to be produced because of the patients' follow-up. Furthermore, this system of evaluation and auto-evaluation could favour the surveillance and monitoring of the comprehensive level of the oncologic care in the region, the clinical performance homogeneity, the possible weakness of the clinical network, and finally the corrective interventions to be adopted to improve the QoCC.

With this study, we hope to increase the awareness of the value of QI in health care so to encourage more uniform practices and improve provider documentation of medical care in our region; moreover, we hope that standardization of QI among different regions will help to define threshold of minimal standard of care.

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COMPETING INTERESTS

The Authors have no competing interests.

DATA SHARING

There is no additional data available.

AUTHORS' CONTRIBUTION

I declare that V. Bianchi, A. Bordoni, A. Spitale and L. Mazzucchelli have directly participated in the planning of the manuscript; that V. Bianchi, A. Bordoni, A. Spitale and the QC_3 Colorectal Working Group have directly participated in the conducting of the project; that V. Bianchi, A. Bordoni, A. Spitale and L. Ortelli have directly participated in the reporting, acquisition of data or analysis and interpretation of data; and that V. Bianchi and A. Bordoni are responsible for the overall content as guarantors of the work. Finally, I declare that all the Authors have drafted and revised the paper critically for important intellectual content, and that they have given final approval of the version published. None of the Authors have competing interests.

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LEGENDS TO FIGURES

FIGURE 1 - Process used to select quality indicators for colorectal cancer care

QI = Quality Indicators; QC_3 CRC-WG = QC3 Colorectal Cancer Working Group; AB = Advisory Board

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Table 1. Quality indicators of colorectal cancer care according to diagnostic-therapeutic process (diagnosis, pathology, treatment - surgery, chemotherapy and radiotherapy - and outcome) and tumour site.

CLINICAL DOMAIN	SITE	QUALITY INDICATOR	NUMERATOR	DENOMINATOR	MEDICAL DOCUMENTATION	RATIONALE	REF
DIAGNOSIS (n=6)	C&R	Proportion of patients with colorectal cancer and diagnosis based on symptoms *vs* screening *vs* accidental finding	Number of patients with colorectal cancer whose diagnosis is based on symptoms, defined as appearance or persistence of clinical events and signs, such as rectal bleeding, occult blood in stool, weight loss with no apparent cause, general abdominal discomfort, bowel obstruction, change in bowel habits, constant tiredness, anaemia Number of patients with colorectal cancer whose diagnosis is based on screening, defined as regular examination, such as faecal occult blood test (FOBT) or colonoscopy in asymptomatic patients Number of patients with colorectal cancer whose diagnosis is an accidental finding following examinations or therapies for other diseases (e.g. hospital admission for other causes…)	Number of patients with colorectal cancer	Request form of endoscopic examination Endoscopy and surgical pathology reports Reports/discharge letters coming from all hospital units/department (i.e. surgery, medicine, radiation oncology, medical oncology)	Assessment of the patient's take charge	[18 34-38]
	C&R	Proportion of patients with colorectal cancer, evaluated by preoperative colonoscopy	Number of patients with colorectal cancer who have been evaluated by a preoperative colonoscopy	Number of patients with colorectal cancer undergoing surgery	Endoscopy report Request form of pathology examination Pathology report of endoscopy	Planning of further diagnostic procedures and treatments Comprehensiveness of diagnostic and staging evaluation	[7 16 18 40-41]
	R	Proportion of patients with rectal cancer and description of the tumour localization (distance *ab ano*) in the endoscopic/pathologic documentation	Number of patients with rectal cancer who have the description of the tumour localization, in terms of distance *ab ano*, in the endoscopic/pathologic documentation	Number of patients with rectal cancer undergoing endoscopy	Endoscopy report Request form of pathology examination Pathology report of endoscopy	Planning of further diagnostic procedures and treatments Comprehensiveness of diagnostic and staging evaluation	[1 19 56-57]
	C&R	Proportion of patients with colorectal cancer and requests for an initial CT and/or a MRI examination completed by clinical information according to the ACR guidelines	Number of patients with colorectal cancer for which the request of an initial CT and/or a MRI examination is completed by clinical information according to the ACR guidelines	Number of patients with colorectal cancer undergoing initial CT and/or MRI examination	Radiology (CT and/or MRI examination) report	Providing the necessary information for a comprehensive radiological examination Assessment of the quality of the flux of clinical information	[7 58]

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	R	Proportion of patients with low rectal[a] cancer undergoing pelvic MRI of staging	Number of patients with low rectal[a] cancer who have undergone a pelvic MRI of staging	Number of patients with low rectal cancer	Radiology (MRI examination) report Discharge letters coming from all hospital units/department (i.e. surgery, medicine, medical oncology, radiation oncology)	Planning of further diagnostic procedures and treatments Comprehensiveness of diagnostic and staging evaluation	[19 59-61]
	R	Proportion of patients with rectal cancer and a preoperative MRI reporting the description of the radial margin status (mm)	Number of patients with rectal cancer who have undergone a preoperative MRI reporting the description of the radial margin status (mm)	Number of patients with rectal cancer undergoing preoperative MRI	Radiology (MRI examination) report	Planning of further diagnostic procedures and treatments Comprehensiveness of diagnostic and staging evaluation	[62]
PATHOLOGY (n=3)	R	Proportion of patients with rectal cancer for which the request for the pathological examination includes the information of neo-adjuvant RT±ChT	Number of patients with rectal cancer for which the request for the pathological examination includes the information of neo-adjuvant RT±ChT	Number of patients with rectal cancer undergoing neo-adjuvant RT±ChT and surgery [a]	Request form of pathology examination Surgical pathology report	Providing the necessary information for a comprehensive pathological examination Assessment of the quality of the flux of clinical information	Proposed by CRC-WG
	C&R	Proportion of patients with colorectal cancer and a sufficient number of tumour samples *(≥3)*	Number of patients with colorectal cancer for which 3 or more tumour sample were processed for the pathological analysis	Number of patients with colorectal cancer undergoing surgery [a]	Surgical pathology report	Comprehensiveness of pathology examination	Proposed by CRC-WG
	C&R	Proportion of patients with colorectal cancer and a surgical pathology report including the following characteristics: - surgical intervention description - sample length - tumour localization according to WHO - tumour size - histological type according to WHO - histological grade - resection margins - lymph-vascular invasion - perineural invasion - tumour deposits (discontinuous extramural extension)	Number of patients with colorectal cancer whose pathological report includes the following characteristics: - surgical intervention description - sample length - tumour localization according to WHO - tumour size - histological type according to WHO - histological grade - resection margins - lymph-vascular invasion - perineural invasion - tumour deposits (discontinuous extramural extension) - pathological staging (AJCC pTNM) - number of retrieved lymph nodes - treatment effect -macroscopic integrity of the mesorectum	Number of patients with colorectal cancer undergoing surgery [a]	Surgical pathology report	Comprehensiveness and standardisation of surgical pathology report Comprehensiveness of staging evaluation Planning of further treatments	[18-19 63-64]

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		- pathological staging (AJCC pTNM) - number of retrieved lymph nodes - treatment effect -macroscopic integrity of the mesorectum (for rectum only) (this quality indicator should be provided for each characteristic)	(for rectum only)				
TREATMENT (n=16)	C&R	Proportion of patients with colorectal cancer operated in emergency [b]	Number of patients with colorectal cancer who have been operated in emergency [b]	Number of patients with colorectal cancer undergoing surgery [a]	Radiology and surgery report/discharge letter Surgical pathology report	Assessment of the patient's take charge	[65-67]
	C&R	Proportion of patients with colorectal cancer and dead within 30 days and 6 months from the surgery (postoperative mortality)	Number of patients with colorectal cancer and dead within 30 days from the surgery Number of patients with colorectal cancer and dead within 6 months from the surgery	Number of patients with colorectal cancer undergoing surgery [a]	Surgery report/discharge letter Surgical pathology report Access to regional Office of Population Registry Rosters for the assessment of patients vital status	Assessment of the quality of surgical procedure	[68-71]
	C&R	Proportion of patients with colorectal cancer and postoperative multidisciplinary discussion	Number of patients with colorectal cancer for which there have been a multidisciplinary discussion after surgery	Number of patients with colorectal cancer undergoing surgery [a]	Surgery, Oncology, Radiation Oncology reports/discharge letters Multidisciplinary discussion documentation	Planning of further diagnostic procedures and treatments	[72-73]
	R	Proportion of patients with malignant rectal polyp (pT1) and complete endoscopic polypectomy	Number of patients with malignant rectal polyp (pT1) who have undergone a complete endoscopic polypectomy	Number of patients with malignant rectal polyp (pT1)	Endoscopy report, Endoscopic pathology reports	Assessment of the quality of surgical procedure	Proposed by the CRC-WG
	R	Proportion of patients with low rectal [c] cancer and surgical intervention with sphincter preservation	Number of patients with low rectal [c] cancer who have undergone a surgical intervention with sphincter preservation	Number of patients with low rectal cancer undergoing surgery [a]	Surgical pathology report Surgery report/discharge letter	Assessment of the quality of surgical procedure	[7 74-76]
	R	Proportion of patients with rectal cancer undergoing TEM with R0 resection	Number of patients with rectal cancer who had undergone TEM with R0 resection	Number of patients with rectal cancer undergoing TEM	Surgical pathology report Surgery report/discharge letter	Assessment of the quality of surgical procedure	[77-79]
	C&R	Proportion of patients with colorectal cancer and a number of resected lymph nodes ≥ 12	Number of patients with colorectal cancer with a number of resected lymph nodes ≥ 12	Number of patients with colorectal cancer undergoing surgery [a], but no neo-adjuvant therapy	Surgical pathology report Surgery report/discharge letter	Assessment of the quality of surgical procedure and pathology examination	[7 14 16 40-41 80-85]
	C&R	Proportion of patients with colorectal cancer operated on with free margins	Number of patients with colon cancer who have undergone surgery and have free margins	Number of patients with colorectal cancer undergoing surgery [a]	Surgical pathology report Surgery report/discharge	Assessment of the quality of surgical procedure	[7 86-87]

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					letter		
	C&R	Proportion of patients with colorectal cancer and AJCC TNM clinical stage I (from T2N0M0) to III (any T, N1M0) undergoing a surgical resection with anastomosis	Number of patients with colon cancer and AJCC TNM clinical stage I (from T2N0M0) to III (any T, N1M0) who have undergone a surgical resection with anastomosis	Number of patients with colorectal cancer and AJCC TNM stage I (from T2N0M0) to III	Radiology report Surgical pathology report Surgery report/discharge letter	Assessment of the quality of surgical procedure	[40-41 86-87]
	C	Proportion of patients with colon cancer and AJCC TNM stage II (T3N0M0, T4N0M0) high-risk (presence of at least one of the following factors: LN<12, G3, lymph-vascular or perineural invasion, tumour obstruction, tumour perforation, pT4) or III undergoing adjuvant ChT	Number of patients with colon cancer and AJCC TNM stage II (T3N0M0, T4N0M0) high-risk (presence of at least one of the following factors: LN<12, G3, lymph-vascular or perineural invasion, tumour obstruction, tumour perforation, pT4) or III, who have undergone adjuvant ChT	Number of patients with colon cancer and AJCC TNM stage II high-risk or III, undergoing surgery [a]	Radiology report Surgical pathology report Surgery, oncology reports/discharge letters	Assessment of the quality of oncologic treatment	[16 18 40-41 88-91]
	C	Proportion of patients with colon cancer AJCC TNM stage II high-risk or stage III undergoing adjuvant ChT within 8 weeks from surgical resection	Number of patients with colon cancer and AJCC TNM stage II high-risk or III, who have undergone adjuvant ChT within 8 weeks from surgical resection	Number of patients with colon cancer and AJCC TNM stage II high-risk or III undergoing surgery [a] and adjuvant ChT	Radiology report Surgical pathology report Surgery, oncology reports/discharge letters	Assessment of the quality of oncologic treatment	[18 92]
	C&R	Proportion of patients with colorectal cancer and histology of the primary tumour or metastases obtained before the beginning of ChT	Number of patients with colorectal cancer and histology of the primary tumour or metastases obtained before the beginning of ChT	Number of patients with colorectal cancer undergoing primary ChT	Radiology and pathology reports Oncology report/discharge letter	Assessment of the quality of oncologic treatment	[40-41]
	C&R	Proportion of patients with colorectal cancer and unresectable metastases undergoing first-line ChT or bio-ChT	Number of patients with colorectal cancer and unresectable metastases who have undergone a first-line ChT or bio-ChT	Number of patients with colorectal cancer and unresectable metastases	Radiology and pathology reports Oncology report/discharge letter	Assessment of the quality of oncologic treatment	[93-96]
	C&R	Proportion of patients with colorectal cancer and hepatic metastases primarily unresectable turned into resectable metastases after neo-adjuvant ChT	Number of patients with colorectal cancer and hepatic metastases primarily unresectable turned into resectable metastases after neo-adjuvant ChT	Number of patients with colorectal cancer and unresectable hepatic metastases undergoing neo-adjuvant ChT	Radiology report Oncology report/discharge letter	Assessment of the quality of oncologic treatment	[96]
	R	Proportion of patients with locally advanced rectal cancer (T3-4 and/or any T, N+ and M0) undergoing neo-adjuvant RT±ChT	Proportion of patients with locally advanced rectal cancer (T3-4 and/or any T, N+ and M0) who have undergone neo-adjuvant RT±ChT	Number of patients with locally advanced rectal cancer undergoing surgery [a]	Endoscopic pathology report Radiology report Radiation Oncology and oncology reports/discharge letters	Assessment of the quality of oncologic and radio-oncologic treatment	[97-98]
	R	Proportion of patients with	Number of patients with rectal cancer who	Number of patients with rectal	Endoscopic pathology	Assessment of the quality	[18 98]

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		rectal cancer and undergoing neo-adjuvant RT±ChT operated within 6-8 weeks after the end of neo-adjuvant RT±ChT	have undergone neo-adjuvant RT±ChT and were operated within 6-8 weeks after the end of neo-adjuvant RT±ChT	cancer undergoing neo-adjuvant RT±ChT followed by surgery [a]	report Radiology report Radiation Oncology and oncology reports/discharge letters Surgical pathology report	of oncologic and radio-oncologic treatment	
OUTCOME (n=2)	C&R	Analysis of overall survival at 1, 3, 5 and 10 years from diagnosis	Number of patients with colorectal cancer who survive at 1, 3, 5 and 10 years from diagnosis	Number of patients with colorectal cancer	Access to regional Office of Population Registry Rosters for the assessment of patients vital status	Assessment of overall survival	[7 99]
	C&R	Analysis of disease-free survival at 1, 3, 5 and 10 years from the curative treatment	Number of patients with colorectal cancer who are disease-free at 1, 3, 5 and 10 years from the curative treatment	Number of patients with colorectal cancer curatively treated	Reports/discharge letters coming from all hospital units/department (i.e. surgery, medicine, oncology, radio-oncology)	Assessment of disease-free survival	[7 99]

Abbreviation:

C&R= colon-rectum; **C**= colon; **R**= rectum; **FOBT**= Faecal Occult Blood Test; **ACR**= American College of Radiology; **CT**= computed tomography; **MRI**= magnetic resonance imaging; **AJCC**= American Joint Committee on Cancer; **RT**= radiotherapy; **ChT**= chemotherapy; **WHO**= World Health Organization; **TEM**= transanal endoscopic microsurgery.

[a] surgery excludes endoscopic resection and colostomy

[b] emergency: within 24 hours from the onset of symptoms;

[c] low rectum: 4 to 7.5 cm from the dentate line [100]

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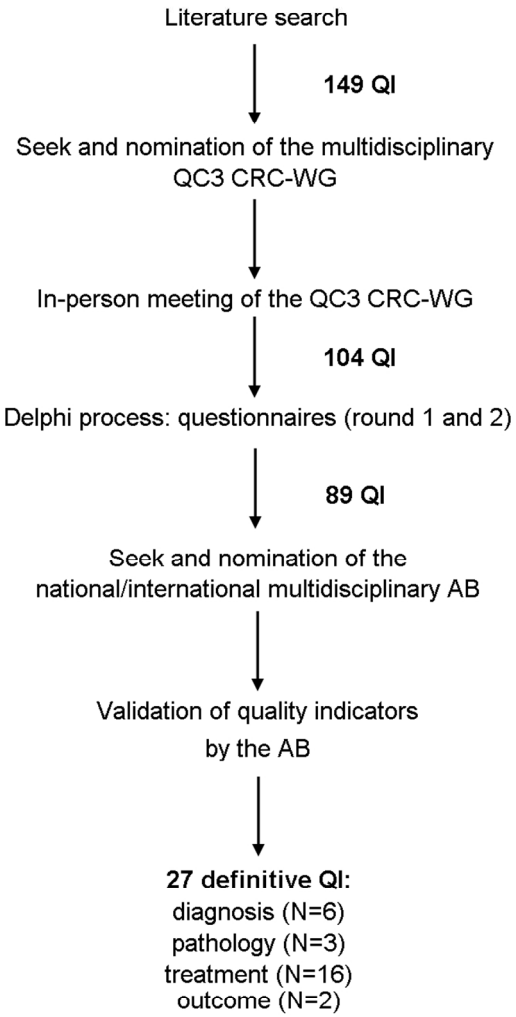
Figure 1. Process used to select quality indicators for colorectal cancer care



QI= Quality Indicators; QC3 CRC-WG: QC3 Colorectal Cancer Working Group; AB: Advisory Board

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