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RISK PROFILING AND SURVEILLANCE: PREVIOUS ADENOMAS AND COLORECTAL CANCER

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Abstract

The brief of this issue of *Cancer Forum* is to review information available since the 2005 publication of the National Health and Medical Research Council relating to risk management of individuals with previous adenomas or colorectal cancer. However, this can be abbreviated to the last three years, as Cancer Council Australia commissioned a review of colonoscopy in surveillance for colorectal cancer, which included adenoma and cancer follow-up. This has subsequently been endorsed by the National Health and Medical Research Council. Since then, there have been advances in some areas, although many questions remain and clinical judgement comes into play. In the current era of accountability, economic hardship and increasing demand, surveillance strategies should be proven effective and individualised, based on issues such as fitness, quality of life and personal preferences. International guidelines have aligned, although the simpler strategies specified in European guidelines are noted with interest. Despite clear recommendations, the lack of guideline use in routine practice is concerning and widespread promulgation of simple 'aid-memoirs' could help, along with incentives. Information supports risk related to multiplicity, size and histopathology of adenoma and cancer findings at the index colonoscopy. Quality issues relating to colonoscopy and pathology reporting are being driven through professional fora and training. The paradox of multiplicity and

quality colonoscopy needs addressing in a patient-centred response. Risk-stratification and adjustment over time is likely to gain increasing importance. The serrated pathway, its biology and epidemiology, have attracted attention for the rapid progression and association with interval cancers. Practice points for the management of malignant polyps continue to be topical. The effectiveness of intensive follow-up strategies following curative treatment for colorectal cancer remains unproven, although colonoscopic surveillance is still of value.

Effectiveness of screening or surveillance for colorectal cancer

Before commencing on the issue of risk and what can be done to manage the risk, it is worth pausing to take stock of the evidence that the risk is modifiable. Risk assessment has little clinical relevance unless there are effective ways to modify that risk. Primary prevention, through reducing risk, has a role, and there is increasing evidence around strategies such as aspirin or calcium supplemental chemoprophylaxis, dietary modifications such as for red meat, fibre, cruciferous vegetables, and lifestyle factors such as exercise and healthy weight maintenance.¹ Additionally, following the positive results for polyp burden reduction in familial adenomatous polyposis, Eicosapentaenoic Acid-Free Fatty Acid (EPA-FFA) is currently under study through a randomised control trial (RCT) in high risk adenoma patients.^{2,3} But colonoscopy with polyp detection and removal is the most likely, but not certain, strategy to prevent colorectal cancer.

Many commentators take it for granted that colonoscopic screening or surveillance reduces the incidence of and mortality from colorectal cancer (CRC) without critical evaluation. The non-randomised experience of colonoscopic surveillance in Lynch Syndrome is often quoted.⁴ A recent report from the Nurses Health Study and Health Professionals Observational Follow-up Study also reports reduced CRC incidence in participants having a negative colonoscopy (HR 0.44 95% CI 0.38 to 0.52), as well as a reduced mortality from CRC (0.32 95% CI 0.24 to 0.45). For both incidence and mortality, the benefit included protection from proximal colon cancer.⁵ However, by any good epidemiological standard, the answer would need to come from RCTs, where the intervention is colonoscopy at intervals (perhaps 10 years) versus a control group with no screening or, to be practical, standard screening advice in their setting. Reduced mortality from CRC associated with colonoscopy intervention would be the best endpoint. In fact, there have been no such trials published. Several long-term trials against different randomised control groups are under way: the Veteran's Administration trial in the US is against Faecal Immunochemical Testing (FIT); a large Spanish trial is also against FIT testing; a New York trial against standard US screening advice (measuring participation only of people responding to an initial invitation); and an important Scandinavian trial where the control group has no screening (screening is not implemented or advocated at a population level in Scandinavia).⁶⁻⁹ The Spanish trial has published CRC incidence rates after the initial screening round and there were just as many CRCs detected in the FIT arm as the colonoscopy arm.⁸ This gives pause for thought on cost benefit (poor for colonoscopy) and reach into the population (poor for colonoscopy). Of note, those that did participate in the colonoscopy arm - which were

substantially fewer than in the FIT arm - had as many CRCs as were detected in the larger proportion who accepted FIT testing. The advanced adenoma detection rate, however, was about three times higher in the colonoscopy arm, perhaps pointing to a longer term benefit of colonoscopy in preventing CRC within this trial.

There are RCTs demonstrating reduction in cancer mortality through the faecal occult blood test (FOBT) and in flexible sigmoidoscopy programs.¹⁰ The question is relevant given the complication rate and (albeit low) mortality associated with colonoscopy.

The lack of RCTs addressing cancer incidence and mortality through colonoscopy screening also impinges on the rationale for management of risk for adenoma patients. In adenoma follow-up and indeed in general, the US National Polyp Study is often quoted as demonstrating that colonoscopy with adenoma removal prevents CRC.^{11,12} This trial randomised participants to a more (zero, one and three years) versus a less (zero and three years) intensive surveillance schedule - showing no difference in adenoma or advanced adenoma outcomes. It did not have a control group of 'no colonoscopy'. The initial and later analyses did assess the cancer outcomes in comparison with population incidences of CRC, and historical groups of adenoma patients who did not have colonoscopy - pointing to the possibility that the participants did avoid CRC, as there were statistically fewer that developed within both trial arms compared with those control groups. It should be noted that many other long-term studies of adenoma patients in surveillance programs have not identified a reduced cancer incidence rate below the average incidence - though one assumes that the populations under study were above average risk for CRC to start with, given their propensity to form adenomas.

There is evidence that FIT testing, complementing scheduled colonoscopy in an adenoma and cancer surveillance program, can bring forward the time of detection of advanced adenomas and cancers.¹³ This has not been formally addressed in any national screening guidelines, but is implemented in some organised programs in Australia,¹³ including the authors'.

Setting the scene: new international guidelines on adenoma and cancer follow up

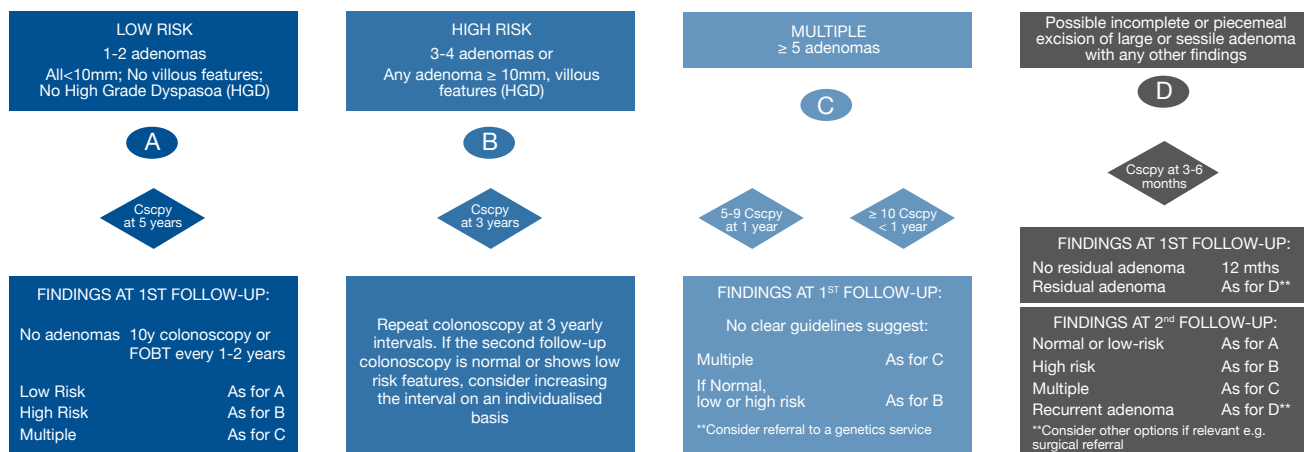
A comparison of the US Multi-Society Task Force on Colorectal Cancer guidelines,¹⁴ with the British Society of Gastroenterology Guidelines,¹⁵ and more recently European guidelines,^{16,17} has recently been published.¹⁸ The greatest deviation from the Australian Guidelines and worthy of note, are the European Society of Gastrointestinal Endoscopy guidelines that recommend returning screenees to the

average-risk national screening program or a colonoscopy after 10 years if no screening program exists, in the low risk group (1-2 small adenomas with low-grade dysplasia), and an increase in interval from three years to five years after a normal follow up colonoscopy in the high risk group (3-4 adenomas, villous features or high grade dysplasia, or ≥ 10 mm in size).¹⁹ Another strong recommendation, although backed only by low quality evidence, is that the endoscopist be responsible for providing a recommendation for the post-polypectomy surveillance schedule. Differences between US and Canadian guidelines have also been published, highlighting the standard of care for average risk (in low risk long-term adenoma follow-up), and differentiating between three or more, and 10 or more adenomas as do the Australian guidelines.^{19, 20} The paper is worthy of review.²⁰

Implementation of the Australian Colonoscopy Guidelines for Adenoma and Cancer Surveillance

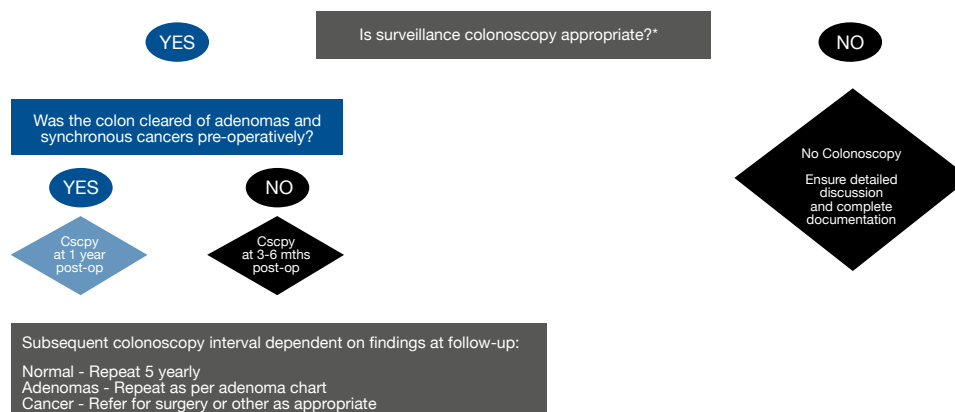
Despite considerable investment in the development of guidelines, numerous groups have shown barriers to their implementation and 'widespread ignorance of guidelines'.¹¹ Most societies or national bodies have provided funding to develop algorithms. The British Society of Gastroenterology published a handy wall chart summarising their guidelines.¹⁵ Recently, such a wall chart presentation of the Australian 2011 Cancer Council/National Health and Medical Research Council (NHMRC) Guidelines for Colonoscopy in Surveillance for adenomas and CRC has been produced and is presented (figure 1 and 2). Although simple strategies such as this have been shown to be effective, barriers to the use of guidelines go beyond this.²¹⁻²³ Access to relevant past information may not be readily available (e.g. previous colonoscopy results, histology and family history) and the current procedure details may be inadequate (colon completely examined, clearance confirmed, exact number and sizes of the polyps noted, histology findings). Clinicians must also deal with patient anxiety and the fear of litigation. Linkage of guideline use to key performance indicators, bonuses and indemnity could enhance wider uptake.

Figure 1: Colonoscopic surveillance intervals - adenomas



NOTES: This algorithm is designed to be used in conjunction with the NHMRC Clinical Practice Guidelines for Surveillance Colonoscopy – in adenoma follow-up; following curative resection of colorectal cancer; and for cancer surveillance in inflammatory bowel disease (December 2011) and is intended to support clinical judgement. Surveillance colonoscopy (cscopy) should be planned based on high-quality endoscopy in a well-prepared colon using most recent and previous procedure information when histology is known. Sessile serrated adenomas and serrated adenomas are followed up as for adenomatous polyps given present evidence, although they may progress to cancer more rapidly. Most patients ≥ 75 y have little to gain from surveillance of adenomas given a 10-20 year lead-time for the progression of adenoma to cancer. The finding of serrated lesions may alter management. Small, pale, distal hyperplastic polyps only do not require follow-up; consider hyperplastic polyposis syndrome if multiple proximal hyperplastic polyps are found. In the absence of a genetic syndrome, family history does not influence surveillance scheduling, which is based on patient factors and adenoma history. Follow-up of an advanced rectal adenoma by digital rectal examination, sigmoidoscopy or endo-rectal ultrasound should be considered independent of colonoscopic surveillance schedules.

Figure 2: Colonoscopic surveillance intervals – following surgery for colorectal cancer



NOTES: This algorithm is designed to be used in conjunction with the NHMRC Clinical Practice Guidelines for Surveillance Colonoscopy – in adenoma follow-up; following curative resection of colorectal cancer; and for cancer surveillance in inflammatory bowel disease (December 2011) and is intended to support clinical judgement. *Surveillance colonoscopy (cscopy) should be offered to those who have undergone curative treatment and are fit for further treatment if disease is detected. Ideally, the colon should be cleared pre-operatively to exclude synchronous cancers and adenomas by either colonoscopy (preferable) or other imaging (in the case of obstructing lesions) unless the proximal bowel is to be included in the resection. Those in whom a familial syndrome is probable or possible, or where there are other indications that the risk of metachronous cancer may be high (e.g. multiple advanced adenomas or cancers at diagnosis, hyperplastic polyposis, age less than 40 years) should be followed up more frequently (see full Clinical Practice Guidelines for Surveillance Colonoscopy). Follow-up of those with known syndromes is recommended in specialist clinics using Clinical Practice Guidelines for Surveillance Colonoscopy. Follow-up of rectal cancers with examination of the rectum by digital examination, sigmoidoscopy or endorectal ultrasound should be considered independent of colonoscopic surveillance.

Barclay Karen, Cancer Council Australia Surveillance Colonoscopy Guidelines Working Party. Algorithm for Colonoscopic Surveillance Intervals – Following Surgery for Colorectal Cancer. 2013. Cancer Council Australia would like to acknowledge and sincerely thank Ms Barclay for developing these algorithms based on the Clinical Practice Guidelines for Surveillance Colonoscopy – in adenoma follow-up; following curative resection of colorectal cancer; and for cancer surveillance in inflammatory bowel disease (December 2011). ©2013 Barclay, Karen. This graphic is licensed under the Creative Commons Attribution-ShareAlike 3.0 Australia license.

Risk related to multiplicity, size and histopathology of adenoma and cancer findings at the index colonoscopy

Multiplicity

The Australian 2011 guidelines had some degree of complexity over frequency of surveillance colonoscopy, derived from the special consideration of risk associated with multiple adenomas. Different risks (and therefore follow-up intervals) were assigned to patients with 1-2 vs 3-4 vs 5 to 9 vs 10 or more adenomas.¹⁹ Whether this needs simplification to enable it to be better accepted in clinical practice, or whether there is sufficient justification to promote that complexity, is a matter for discussion. The logic and data around the complexity is clear, but the complexity in itself may dilute the impact of the guidelines overall.

Multiple adenomas - measured cumulatively or at the last colonoscopy?

A level of uncertainty exists in the literature on this question. The 2011 guidelines recognised the uncertainty, and followed the pragmatic option of accounting for adenomas only at the last colonoscopy, rather than attempting a cumulative history. Further predictive studies need to address this issue. Inherently, one would think that it is the cumulative number of adenomas over time which engages the risk for metachronous CRC most closely, as the timing and frequency of interventions to remove adenomas are somewhat incidental to the biological drive to multiplicity – and presumably its associated metachronous cancer risk.

Nevertheless, this has not been systematically teased out in adenoma follow-up studies.

Cut and discard

The evolving practice to 'cut and discard' small polyps through cold snare guillotine techniques threatens the assessment of metachronous risk which, as we know, is most powerfully associated with multiplicity of adenomas of whatever size, over and above the other histological and polyp characteristics of size, villosity and dysplasia.²⁴ Although we are advocates for 'cut', we are not advocates for 'discard'. In Australian practice, there is no differential rebate for multiple polyp assessment (as there is in the US), so pathology costs are the same.

Multiplicity and adenomatous polyposis syndromes

Multiplicity of adenomas plays very importantly into decisions around mutational analysis of the APC and MUTYH genes, again information lost with a 'discard' policy. In our Familial Cancer Clinic, we carefully record on a spreadsheet the entire colonoscopic history of patients referred, to inform decision-making. We will consider mutational analysis with as few as five documented adenomas. The predictive value of mutational analysis is directly related to the multiplicity.

Size, histology and dysplasia

Size, histology and dysplasia are relatively easily measurable and accessible for the purposes of determining risk. Furthermore, their predictive value is consistent across many studies. The three factors are closely correlated,

so much so that the British guidelines take only size into account, being immediately assessable at the time of colonoscopy. If villosity and high grade dysplasia are not included in prediction algorithms, leaving only size and multiplicity of adenomas to determine high risk for metachronous advanced lesions, it does reduce the size of the high risk group slightly, with a minor shift in Receiver Operator Characteristic curves.¹⁸

Surveillance tailored multifactorial risk

Risk algorithms, not favoured to date in the 2005 or 2011 Guidelines, may yet prove useful with access to easily computed and reliable algorithms even built into endoscopy surveillance management programs. More experience is needed with this approach.²⁵

Quality of colonoscopy

Another important theme relating to risk profiling is the number of adenomas and CRCs detected in relation to the quality of colonoscopy.²⁶ Attention has focused on measurement of quality and surrogates for quality. This includes the time taken to withdraw the colonoscope (during which inspection for polyps takes place),²⁷ adenoma detection rates,²⁸ bowel preparation cleanliness, retroversion of the colonoscope in the right colon and rectum,²⁹ and the thorny issue of missed cancers occurring at an interval after a colonoscopy.²⁷⁻³¹ Whereas quality of colonoscopy is the subject of another paper in this issue, it does bear reinforcement that all of these parameters have a logical connection to quality colonoscopy and point to ways of implementing quality control systems in colonoscopy.³² Perhaps the most compelling data, now from two sources, is that a colonoscopist's adenoma detection rate in routine screening colonoscopy is indirectly but tightly related to the incidence of CRCs occurring in the years after colonoscopy – the interval cancer rate. This has been evident in both Polish and US studies.^{7,31}

The multiplicity paradox

The integration of the themes of risk associated with multiple adenomas, and the logical training and practice goal to increase adenoma detection rates, brings us to a paradox: those patients who are under the care of high quality colonoscopists with high adenoma detection rates will likely be found to have more polyps and adenomas, driving them under current guidelines (which are themselves, as noted, determined by multiplicity) to have even more frequent colonoscopies, inevitably towards points of diminishing return. On the other hand, individuals who are under the care of poor quality colonoscopists with low adenoma detection rates will be found to have few (or no) polyps, placing them in a 'lower' risk group, requiring less frequent colonoscopies on current guidelines – yet we know these people are the ones who develop the interval cancers. An anecdotal impression is that low quality colonoscopists compensate by offering frequent colonoscopies, outside guidelines. The answer to this dilemma must be to introduce quality control systems across all colonoscopy practices, including monitoring adenoma detection rates. With time, we may be able to introduce colonoscopy quality parameters into the guidelines such that the interval between

colonoscopies can be discounted (lengthened) where good quality colonoscopy has been documented through a range of parameters relating to the procedure and the colonoscopist. Notwithstanding that a colonoscopist's adenoma detection rate in US studies is calculated from the relatively homogeneous population of average risk patients undergoing screening colonoscopy (a population which is not within current Australian guidelines for clinical practice and is not reimbursable through Medicare), adenoma detection rates in other Australian settings can be used with some reliability. At the same time, there would need to be an economic incentive for the proceduralist to meet these standards (or disincentive if not). This should surely be in the patient's interests and attractive to the payers. This would then address the paradox.

Longer term surveillance: Does risk attenuate over time, where sequential colonoscopies are clear of polyps?

The 2011 NHMRC guidelines are equivocal regarding the need to maintain surveillance at the interval determined by the polyp and patient characteristics at the time of the index (the last) colonoscopy. With follow up colonoscopies showing no further polyps, can the interval be relaxed? In some situations the answer is clearly 'no'. This would include the serrated polyposis syndrome discussed below, perhaps serrated polyps short of the syndrome, and the well characterised genotypically defined syndromes of Lynch Syndrome, familial adenomatous polyposis, MUTYH associated polyposis, Peutz Jeghers Syndromes (polyps grow quicker than adenomatous polyposis in the author's experience) and juvenile polyposis. Debate on the velocity of carcinogenesis in MUTYH associated polyposis has been engaging.³³ However, in the common adenoma patient, follow-up interval is less certain. In the Royal Melbourne Hospital-Flinders long-term experience (submitted for publication), there is a relatively high risk for advanced adenomas to be found within 18 months of an index colonoscopy, where an advanced adenoma is also identified and removed (we carefully reviewed the data to exclude patients from the analysis where the index advanced adenoma was not completely removed). With time, the risk did attenuate, but still there was a long tail of advanced adenoma detection that continued at a stable rate, suggesting an intrinsic continuing risk that needs to be addressed through a fixed frequency of colonoscopy – arguably three yearly from our data. This is supported from US experience. For small adenomas, the risk is small as reported in many series, such that the risk for metachronous cancer reverts to average risk or below average risk.^{6, 7, 27, 34}

Sessile serrated polyps and serrated polyposis

The serrated pathway

The discovery and understanding of the serrated polyp pathway to CRC has been the focus of much attention since the last guidelines. There is now some evidence that identifies interval cancers in adenoma and other surveillance programs as being more likely to be associated with the serrated pathway, either through methylation of the MLH1 promotor, or more generally, having high CpG Island

Methylator Phenotype status.^{35,36} Studies on antecedent polyps in these patients, especially as to their serrated architecture, are needed. Some evidence suggests that polyps pass through this pathway more rapidly than the more conventional microsatellite stable, APC gate-controlled pathway. Importantly, it would point to the need for more frequent surveillance in patients who have shown a propensity to develop sessile serrated polyps.³⁷ A consensus meeting dedicated to serrated lesions recommended particular attention (increased frequency) to patients with three or more sessile serrated adenomas/polyps or traditional serrated adenomas, especially if large (every two years) and any with dysplasia.³⁸ This question needs more data before implementing a change to the guidelines. The 2011 guidelines signalled an issue relating to this question, but did not spell out any alteration to the frequency of colonoscopy in follow-up for these patients, which are determined, as in conventional adenoma follow-up, by multiplicity and size of adenomas, with villosity and dysplasia also implicated through the definition of an advanced adenoma. Advanced adenomas in the current guidelines attract a three year interval for colonoscopy.

Serrated polyposis syndrome

Serrated polyposis Syndrome (previously known as Hyperplastic polyposis) is increasingly being recognised by colonoscopists. It is defined by five serrated polyps proximal to the sigmoid colon, with two one cm or over in size, or 20 (some say 30) serrated polyps spread throughout the colon. The third definition is any serrated polyps in a first degree relative of a patient with serrated polyposis. This remains tantalisingly without a genetic predisposition identified, whereas all other multiple polyposis syndromes have had their germline predisposition identified. Perhaps this is not surprising, as Mendelian inheritance is not commonly seen in the families of patients with serrated polyposis syndrome. The colonoscopist needs to treat this syndrome respectfully: although the absolute risk of CRC is not well defined, it is undoubtedly high.³⁹ Most colonoscopists have experienced interval CRCs occurring during surveillance of these patients, even within the recommended two year interval. Although this could be due to the inherent difficulty in detecting the subtle, flat and sessile serrated polyps with their indiscernible margins in the right colon (though perhaps flagged through its mucus cap), the evidence around the real possibility of a rapid pathway through diffuse methylation of suppressor genes or other mechanisms needs constant scrutiny. The high risk of CRC in the first degree relatives of patients with the serrated polyposis syndrome needs addressing in surveillance.⁴⁰

Management of the malignant polyp

Little new information has emerged to change the recommendations for management of malignant polyps, which balances the risk of surgical intervention (after malignant polypectomy) versus the risk of nodal metastases with ultimate progression within the lifetime of the patient.⁴¹ Attention has been given to the importance of pathology reporting for decision-making. The recent publication by the Royal College of Pathologists of Australia of a structured reporting protocol for polypectomy and local resections of the colon and rectum are likely to be beneficial.

Follow-up and surveillance: CRC patients

This section addresses the risk of metachronous CRC in patients who have already developed CRC and the role that colonoscopy plays in managing this. A more comprehensive analysis of the contemporary literature is available, which points to the limited benefit of surveillance after CRC resection, duration of follow-up, intensity and methods of follow-up, cost-effectiveness, and identifying RCTs in progress further addressing the question.⁴² Colonoscopies should be done with the same quality in cancer follow-up as in adenoma follow-up.

The main change introduced in the 2011 guidelines was the introduction of a colonoscopy at one year after resection. Although the need for peri-operative total colonoscopy to seek synchronous cancers overlooked either due to incomplete index colonoscopy due to obstructing lesions, or other considerations, has long been recognised, the importance of a routine colonoscopy at 12 months from follow-up studies was brought to the fore in the 2011 guidelines. This holds true and may, incidentally, have a message for patients with advanced adenomas at index colonoscopy as well – notwithstanding the National Polyp Study noted above. Perhaps not surprisingly, the risk of metachronous adenomas and cancers is generally lower after cancer resection, than in adenoma follow-up. Counterintuitive? Probably not, as the resection reduces the epithelial mass available for adenomas and cancers to develop.

The metachronous risk of CRC after segmental oncological resection in Lynch Syndrome is now very clear: it is high - up to 60% at 40 years. Thus there is a strong rationale for suspecting, then diagnosing (preferably molecularly) and counselling patients with Lynch Syndrome to undergo extensive colonic surgical resection prior to resection of the index cancer or other advanced lesion in the colon. At a minimum, in the appropriate circumstance such as an early age onset index colon cancer, immunohistochemistry on the cancer should be done as part of the diagnostic work up. This information should usefully help decision-making around the surgical approach. Family history of cancer and the pattern of loss of expression in the cancer would all play into this decision-making.

Conclusion

Evidence is accumulating on risks for metachronous adenomas and cancers in patients with adenomas or CRC. Risk reduction through appropriate colonoscopic surveillance has been described in the 2011 NHMRC Clinical Practice Guidelines for Surveillance Colonoscopy. However, implementation of these guidelines has been limited by lack of resources to promote the guidelines in clinical practice, except for their publication on the NHMRC website. This will be addressed in part by the algorithmic depiction of the guidelines now available, and published here, for dissemination at points of service, be it general practice, endoscopy services in private and practice and through dedicated and managed follow-up programs. Further, the need and implications of quality practice in colonoscopy, especially with respect to adenoma detection

rates, will need leadership and buy in by the endoscopic community and professional bodies.

Points of continuing clinical research attention include systems to integrate cumulative adenoma detection in

patients into risk and surveillance planning, the biology of the serrated pathway with its implications for surveillance scheduling, and further attention to early follow-up risk in patients with advanced adenomas.

Table 1: Recommendations

Summary of 2011 NHMRC recommendations for patients with previous adenomas or CRC	Practice recommendation	Status	Considerations for updated recommendations based on current evidence – if applicable
<p>Patients with adenomas and risk of developing CRC Determination of risks for patients with adenomas must clearly distinguish between:</p> <ol style="list-style-type: none"> Variables that relate to the likelihood of any particular adenoma having a malignant focus and Variables that relate to patient, pathological and epidemiological characteristics which predict metachronous adenomas and cancers. <p>Patients whose only polyps are small, pale, distal, hyperplastic polyps require no colonoscopic follow-up.</p>	Practice Point: Recommend	No change	N/A
Patients whose only polyps are small, pale, distal, hyperplastic polyps require no colonoscopic follow-up.	Practice Point: Recommend	No change	N/A
<p>Location of adenomas and cancer: protection against right sided cancer in adenoma follow-up Proximal location of adenomas may be a risk factor for metachronous neoplasia.</p>	Practice Point: Strongly recommend	Upgrade	Further attention to issues relating to the biology of right sided lesions, especially CIMP status, and the interface with quality of colonoscopy, especially relating to right sided colonoscopy, imaging and documentation of same.
<p>Models of risk assessment Because of the complexity of multivariate analyses to predict individual patient risk of metachronous polyps, their use currently is difficult to apply to day to day practice.</p>	Practice Point: Recommend	Upgrade	The feasibility of these needs assessment through academic programs such as the NHMRC Centre for Research Excellence: Reducing the Burden of Colorectal Cancer by Optimising Screening - Evidence to Clinical Practice
<p>General considerations relating to polypectomy All polyps should be considered for removal. Diminutive polyps may be too numerous to be cleared completely. In patients with small polyps, a sample should be taken for histological study. However, if syndromic diagnosis is under consideration, then sampling of many polyps is important, to guide decisions on which gene should be subjected to mutational analysis.</p>	Practice Point: Recommend	No change	The 'cut and discard' policy gaining credibility in colonoscopy practice needs to be modified to take into consideration syndromic diagnoses – which are becoming increasingly broader (less polyps) in consideration.
<p>Tattooing polypectomy sites Tattooing any polyp site where there is a possibility of surgical resection will be needed is important at the primary colonoscopy if at all possible. This is necessary even for conventional surgery, as the site of polypectomy may well be impalpable, but particularly important where follow-up treatment may be laparoscopic, as the surgeon has no capacity to palpate the area.</p>	Practice Point: Recommend	No change	Raising a preliminary bleb with saline and injecting into the bleb helps to localize the tattoo to the site of injection.
<p>Malignant polyps In general, malignant polyps which:</p> <ol style="list-style-type: none"> Have a clear margin of excision pathologically Are well or moderately well differentiated Lack lymphatic or venous invasion Are endoscopically judged totally removed. <p>They can be managed without subsequent surgery, but the decision needs to be individualised with respect to patient comorbidities and age.</p>	Practice Point: Strongly recommend	No change	N/A

<p>Quality of colonoscopy High quality colonoscopy is critically important for good practice and patient safety. Adenoma detection rates (ADRs) should be monitored, though they will be influenced by patient mix (e.g. age, indications). ADRs within the NBCSP provide a sound basis for bench marking.</p>	Practice Point: Strongly recommend	No change	N/A
<p>Approach to adenoma follow-up in surveillance Colonoscopy surveillance intervals should be planned when the colonoscopist is satisfied that the colon has been completely cleared of polyps and the polyp histology is known.</p>	Practice Point: Recommend	No change	N/A
<p>Follow-up for patients with low risk adenomas Patients with one or two small (<10mm) tubular adenomas can be scheduled for follow up colonoscopy at five years. If that colonoscopy is normal, then that patient can be considered as at average risk, with colonoscopy at 10 years or by FIT at least every two years.</p>	Grade B: Strongly recommend	Upgrade	These patients are considered at average risk on follow up evidence. This patient might simply continue within the National Bowel Cancer Screening Program.
<p>Follow-up of patients with high risk adenomas Surveillance colonoscopy should take place at a three year interval for patients with high risk adenomas (three or more adenomas, >9mm, or with tubulo-villous or villous histology or high grade dysplasia).</p>	Grade A: Strongly recommend	No change	Surveillance intervals after a clear colonoscopy needs further research.
<p>Follow-up of patients with sessile adenomas and laterally spreading adenomas If large and sessile adenomas are removed piecemeal, follow-up should be at three to six months to ensure complete removal. If removal is complete, subsequent surveillance should be based on histological findings, size and number of adenomas.</p>	Grade B: Recommend	No change. Consideration for update	Consideration should be given to referring these patients to centres of endoscopic excellence, experienced in managing these polyps. The first attempt to remove the polyp is the best attempt.
<p>Follow-up following resection of serrated adenomas (SAs and sessile serrated adenomas (SSAs) At present, there is not enough evidence to differentiate follow-up protocols for sessile serrated adenomas from standard follow-up guidelines. Follow-up should be determined as for adenomatous polyps, taking into account size, number and presence of high grade dysplasia.</p>	Practice Point: Recommend	Update to strong recommendation	Anecdotal experience and biological studies have highlighted these polyps may progress rapidly, elevating an early metachronous risk.
<p>Follow-up of patients with multiple adenomas As multiplicity of adenomas strongly determines risk of metachronous advanced and non-advanced neoplasia, follow up should be at 12 months for those with five or more adenomas and, because the likelihood of missed synchronous polyps being present, sooner in those with 10 or more adenomas. If a polyposis syndrome accounts for the findings, follow-up should be within one year for patients with five or more adenomas at one examination. FAP and MUTYH associated polyposis should be considered with as few as 10 adenomas and referred to a Familial Cancer Clinic (FCC).</p>	Grade B: Strongly recommend	No change. Consideration for update Change	Complexity versus utility in practice of this guideline needs evaluation in practice. Further studies needed on whether the 'count' is cumulative needed. FAP and MUTYH patients should have annual flexible sigmoidoscopy or colonoscopy regardless of findings at any one examination. The number of adenomas generating a referral for mutational analysis differs across FCCs and is resource dependent. It should be noted that 30% of MUTYH associated colorectal cancer patients have no synchronous adenomas.
<p>Interaction of age and family history Family history should be considered separately when planning colonoscopy surveillance. Intervals should be predominantly determined by the adenoma characteristics, unless a syndromic risk mandates more frequent surveillance</p>	Equivocal	No change	N/A
<p>Follow up based on two or more examinations If advanced adenomas are found during subsequent surveillance, maintaining a three yearly schedule is prudent but the choice should be individualised. The interval can be lengthened if advanced adenomas are not found.</p>	Grade B: Strongly recommend		Further evidence on attenuation of risk with time, or not, such as the Royal Melbourne Hospital Flinders data, needs to be sourced.

<p>Cumulative adenoma counts Endoscopists should be encouraged to assess not only the current colonoscopy findings but those of any previous colonoscopies.</p>	Practice Point: Recommend	Consideration for update	Reporting systems and endoscopy databases need to be developed to take account of cumulative findings to facilitate decision making, and decisions on referral to familial cancer clinics.
<p>Hyperplastic polyposis Risk of cancer in hyperplastic polyposis is still being defined, however there is sufficient evidence to identify these patients as being at high risk. Colonoscopy, with the aim of complete polyp removal, including the right sided sessile serrated polyps, should be the aim. Risks of polypectomy, notable because of the number and sessile nature of polyps, should be explained. Surgery is an acceptable alternative in patients with well defined hyperplastic polyposis.</p>	Practice Point: Recommend	No change. Consideration for update	Now called Sessile Serrated Polyposis, or Jass Syndrome. Consideration should be given to referring these patients to centres of endoscopic excellence, experienced in managing these large sessile polyps. The first attempt to remove the polyp is the best attempt. Referral to FCC if the patient has a mixed adenoma/serrated polyposis phenotype, as MUTYH mutations can be found in this subset

Summary of 2011 NHMRC recommendations for patients or CRC	Practice Recommendation	Status	Considerations for updated recommendations based on current evidence – if applicable
<p>Role of pre and peri operative colonoscopy in CRC patients A peri-operative colonoscopy should be attempted in all patients with a newly diagnosed CRC. Colonoscopy should be performed three to six months after resection with obstructive XCRC in whom complete perioperative colonoscopy was not performed and in whom there is residual colon proximal to the obstructing cancer.</p>	Grade B: Strongly recommend Grade B: Strongly recommend	No change	N/A
<p>Risk factors for metachronous neoplasia following resection for CRC Patients with Lynch Syndrome should continue to have annual surveillance performed post operatively because of the apparent rapid progression of neoplasia from adenoma to carcinoma.</p>	Practice Point	Upgrade to recommend	N/A
<p>Surveillance of the residual colonic mucosa in patients with cancer in FAP Should follow recommendations elsewhere in the 2005 NHMRC guidelines.</p>	Practice Point	No change	
<p>Patients including those</p> <ol style="list-style-type: none"> whose initial diagnosis was made younger than 40 years of age with probable or possible HNPCC (ie. Patients whose tumours are MSI-High and less 50 years old at the time of initial cancer diagnosis but not proved by genetic testing to have Lynch Syndrome) with hyperplastic polyposis and BRAF mutations with multiple synchronous cancers or advanced adenomas at initial diagnosis should be considered following surgery to continuing with more frequent surveillance than would otherwise be recommended. 	Practice Point	No change	N/A
<p>Intervals for surveillance colonoscopy following resection for CRC Colonoscopy should be performed one year after the resection of a sporadic cancer, unless complete post operative colonoscopy has been performed. If this colonoscopy reveals an advanced adenoma, then the next colonoscopy should be three years. If the colonoscopy performed at one year is normal or identifies one or two non advanced adenomas, then the interval before the next colonoscopy should be five years.</p>	Grade B: Strongly recommend Grade C: Recommend Grade C: Recommend	No change	N/A
<p>Patients undergoing either local excision or or ultra-low anterior resection of rectal cancer or advanced adenomas should be considered for six monthly endoscopies and digital examinations, independently of the colonoscopies as above.</p>	Practice Point: Recommend	No change	N/A

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