Management of Familial Adenomatous Polyposis in Children and Adolescents: Position Paper From the ESPGHAN Polyposis Working Group

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ABSTRACT

Familial adenomatous polyposis (FAP) is a well-described inherited syndrome, characterized by the development of hundreds to thousands of adenomas in the colorectum, with implications in children and adolescents. Almost all adult patients will develop colorectal cancer if they are not identified and treated early enough. Identifying and screening for FAP commences in adolescence. The syndrome is inherited as an autosomal dominant trait and caused by mutations in the adenomatous polyposis (*APC*) gene. This European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) position paper provides a guide for diagnosis, assessment, and management of FAP in children and adolescents. This is the first position paper regarding FAP published by ESPGHAN. Literature from PubMed, Medline, and Embase was reviewed and in the absence of evidence, recommendations reflect the opinion of paediatric and adult experts involved in the care of polyposis syndromes. Because many of the studies that form the basis for the recommendations were descriptive and/or retrospective in nature, these of the recommendations are supported on expert opinion. This position paper will instruct on the appropriate management and timing of procedures in children and adolescents with FAP.

Key Words: adolescent, child, colonoscopy, colorectal cancer, familial adenomatous polyposis, polyposis

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What Is Known

- There are published guidelines for the management of familial adenomatous polyposis in adults. In paediatric practice, timing of diagnosis, screening colonoscopies, and colectomy varies across institutions and between paediatric and adult clinicians, and between different countries.
- There are no prior published evidence-based guidelines specifically for children and adolescents at risk, or affected by familial adenomatous polyposis.

What Is New

- We provide clear recommendations regarding the diagnosis, assessment, screening, and treatment of familial adenomatous polyposis in children and adolescents.
- This position paper represents a useful practical guide to assist paediatric gastroenterologist involved in the care of paediatric polyposis syndromes.

The aim of this evidence-based and consensus-based position statement, commissioned by the European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) is to provide a comprehensive review of the diagnosis and management of familial adenomatous polyposis (FAP) in paediatric patients. This position statement will address the issue of diagnosis, time to screen at risk children, role and timing of colonoscopy, and colectomy and risk of cancer. This is not designed to be a comprehensive overview of FAP and its complications.

This undertaking is the first position paper published on FAP in the paediatric age group. Our aspiration is that the guideline may lead to a degree of standardization in the approach and management of FAP thereby contributing to excellence and correct timing of diagnosis and treatment. This article represents the basis for further data collection and research to develop a more robust paediatric evidence base to guide future decisions regarding managing this polyposis syndrome, with a view to updating this advice in 3 years.

METHODS

ESPGHAN commissioned position papers on polyposis syndromes in 2016. Three task force leaders (W.H. for FAP, S.C. for juvenile polyposis syndrome and A.L. for Peutz-Jeghers syndrome) invited the listed authors to participate in the project. The key questions for important management issues were identified by the core team and working group in face to face meetings in 2016 and 2017 and then approved by the other members. Each task force performed a systematic literature search to prepare evidence-based and well-balanced statements on their assigned key questions.

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Searches were performed in PubMed and EMBASE and Medline and Cochrane (publication year from 2000 to 2017) or before if needed, including as a minimum the key words " paediatric," or "adolescent" or "teenage" and "familial adenomatous polyposis." Case reports and articles in languages other than English were excluded. When insufficient information or publications were available in specific paediatric or adolescent papers then the search was broadened to include publications regarding adult patients. References in these documents were also searched to ensure acquisition of relevant source data. In the absence of evidence we relied on the expert of opinion and personal practice of the authors. The working group comprised paediatricians involved in the care of paediatric polyposis patients, experts from the field of adult polyposis disease and contributions by surgeons.

All articles studying FAP in the age range were selected by title or abstract. The abstracts and then the full publications were reviewed. Although FAP is a rare condition, most articles were not amenable for grading by the level of evidence and strength of recommendation according to the GRADE system (Grading of Recommendations Assessment, Development and Evaluation). Many articles were case series, with its attendant report bias. International guidelines were reviewed, and their evidence and referenced papers were also assessed. Each task force proposed statements on their assigned key questions, which were discussed by email exchange or face-to-face meetings and voted on during the subsequent year. In April 2018, a draft prepared by W.H. was sent to all group members and then subsequently modified. In ESPGHAN 2018, all members of the faculty discussed and reworded the final manuscript, and voted on the statements included in this article.

The manuscript was then submitted to the *Journal of Paediatric Gastroenterology and Nutrition* for publication in full length.

FAMILIAL ADENOMATOUS POLYPOSIS INTRODUCTION

In children, gastrointestinal (GI) colonic adenomas are almost always associated with hereditary adenomatous polyposis syndromes. FAP is characterized by the development of up to hundreds or thousands of adenomas in the colon and rectum and several extracolonic manifestations. Polyps begin to appear in childhood or adolescence and increase in number with age. The standard clinical diagnosis of typical/classical FAP is based on the identification of >100 colorectal adenomatous polyps. By the fifth decade, colorectal cancer (CRC) is almost inevitable if colectomy is not performed. Attenuated FAP (AFAP) is a milder form of the disease which is observed in 8% of cases. It is characterized by fewer adenomas and later presentation. Such cases are less likely to present in childhood. There are many extraintestinal manifestations which are apparent in childhood (Table 1).

FAP is an autosomal dominant inherited condition caused by a mutation in the adenomatous polyposis gene (*APC*) gene occurring in 1 to 3:10,000 births, with almost 100% penetrance. In 20% to 30% of cases the condition is caused by a spontaneous mutation with no clinical or genetic evidence of FAP in the parents or family.

The gene responsible for FAP, *APC* (adenomatous polyposis coli), is located on chromosome 5q21 and appears to be a tumour suppressor gene, that is part of the WNT signalling pathway. Most mutations are small deletions or insertions which result in the production of a truncated *APC* protein. In FAP, a germline mutation inactivates 1 of the 2 *APC* alleles. Many mutations have been identified on this large gene and there is a correlation between the genetic site and severity of clinical manifestation (Fig. 1). There are some common mutational hotspots forming mutation cluster regions. Mutations between codons 1250 and 1464, and especially those with a mutation at codon 1309, are associated with a more severe colonic phenotype of FAP. Mutations localized at the extreme ends of the gene and in the alternatively spliced part of exon 9 are associated with an AFAP, and an intermediate expression of disease is found in patients with mutations in the remaining parts of the gene. Other phenotype-genotype correlations have been observed. Each child of an affected individual carries a 50% chance of inheriting the mutated gene.

TABLE 1. Extracolonic manifestation of familial adenomatous polyposis

Site	Examples
Bone	Osteomas, mandibular, and maxillary (50%–90%)
	Exostosis
	Sclerosis
Dental abnormalities	Impacted or supernumerary teeth
	Unerupted teeth (11%–27%)
Connective tissue	Desmoid tumours (10%–30%)
	Excessive intra abdominal adhesions
	Fibroma
	Subcutaneous cysts
Eyes	Congenital hypertrophy of the retinal pigment epithelium
CNS	Glioblastomas, eg, Turcot syndrome
Adenomas	Stomach
	Duodenum
	Small intestine
	Adrenal cortex (7%–13%)
	Thyroid gland
Carcinomas	Thyroid gland (2%–3%)
	Adrenal gland
Liver	Hepatoblastoma (<1%)

CNS = central nervous system.

MYH-associated polyposis is characterized by the presence of adenomatous polyposis of the colorectum. Patients more commonly present in adulthood with a variable number of polyps but no apparent extraintestinal features. It may mimic FAP and lead to diagnostic confusion. This is an autosomal recessive condition and has no paediatric implications, so will not be discussed in this article.

Recommendation 1:

At what age should predictive genetic testing be offered in children at risk of inheriting FAP?

Recommendation 1:
Predictive genetic testing should be offered to at risk children at age 12 to 14 years. Families should receive genetic counselling before and at the time of testing. Children who are symptomatic with rectal bleeding should undergo earlier testing (weak recommendation, low-quality evidence, consensus agreement 100%).

Although the earliest colonic manifestation of FAP is mostly in the early teenage years, and CRC are exceptionally rare before the age of 20 years in FAP, current practice is to offer predictive genetic testing for FAP to children at risk from age 12 to 14 years onwards. Although adenomas may first appear age 8 to 12 years, these are largely not clinically significant. Some patients may, however,

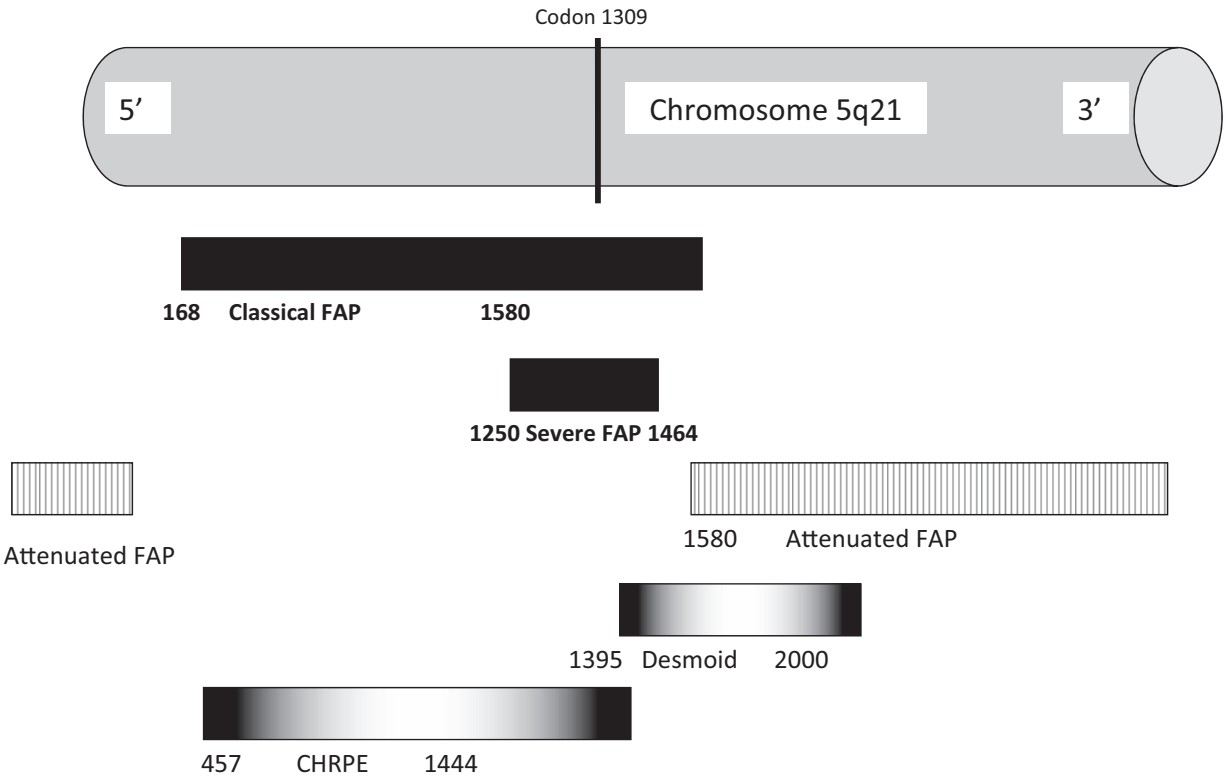

FIGURE 1. Genotype phenotype correlations of the *APC* gene. FAP = familial adenomatous polyposis.

develop symptoms earlier if they have an unfavourable phenotype. There is consensus amongst genetic authorities that predictive genetic testing should be performed at an age corresponding to the earliest onset of the disease. Presymptomatic and predictive testing can be postponed or prearranged either until a child is able to give his or her own consent, or there is a clinical requirement to know the result to inform on whether to embark on colonoscopic surveillance. (1,2). Age 12 to 14 years would meet the criteria suggested above, but there may be some children with maturity and understanding in whom consent can be obtained at the age of 10 to 12 years.

Despite this recommendation, some parents will request predictive genetic testing for FAP at a much earlier age citing that if the result is negative this will provide reassurance both for themselves and for the child. The main arguments against genetic testing at a younger age are respect for the child's autonomy and largely theoretical potential psychosocial harm. Other considerations regarding the age of genetic testing relate to whether the family may be lost to later contact if the testing is delayed to teenage years, or there is a risk to the professional working relationship with the family, especially since the counsellor or doctor will need to negotiate consent, procedures, or colectomy in the challenging adolescent age group. Genetic counsellors should advise on why deferring genetic predictive testing until the age 12 to 14 years is in the interest of the child, plus leaving the decision with the family, after a period of reflection (3). It is not unusual for parents to request earlier testing so that siblings may all be tested at the same time, or the parents want relief from their own uncertainty about the child's carrier status. In reported case series, there is no evidence of adverse consequences of genetic testing in children younger than 10 years, nor impact on parent-child relationship (4). Nor do children show significant distress over the first year following predictive testing for FAP (5). All genetic testing should be preceded by counselling regarding the implication of the result by clinicians experienced in the management of the disease or by genetic counsellors (6), with 1 study advocating ongoing contact with genetics long after testing (7). This would ensure onward care to experts in polyposis and access to polyposis registries.

Clinical circumstances exist when testing at a younger age (<10 years) may be necessary. In particular the presence of rectal bleeding, especially when the family mutation is associated with a more aggressive phenotype (eg, codon 1309) would be an indication for earlier genetic testing and colonoscopy (8).

Recommendation 2:

How should the genetic testing be interpreted in FAP?

Recommendation 2a:
In relation to predictive testing, if the child is found to have the familial *APC* variant, they have a diagnosis of FAP. If the familial *APC* variant is absent in the child, then they have not inherited FAP.

Recommendation 2b:
In a patient with colonic adenomas who undergoes genetic testing for FAP (diagnostic testing), the finding of a pathogenic variant will confirm the diagnosis of FAP. If no pathogenic variant is identified, this does not exclude FAP.

(strong recommendation, moderate-quality evidence, consensus agreement 100%)

Predictive Testing

In a child from a family pedigree known to be affected with FAP, to define which screening protocol is appropriate for a given family, the first step is to determine, where possible, which *APC* mutation is present in the FAP affected index member in the family. For the 90% to 95% in which a mutation is detected, at-risk relatives can be offered predictive genetic testing. Identifying the family gene mutation test confirms the diagnosis of FAP and the child/adolescent should undergo colonoscopic assessment. A negative test is considered accurate in excluding FAP and the patient should be considered to hold an average population risk for the subsequent development of adenomas and cancer and can be discharged from follow-up. Those patients in whom the familial mutation has not been successfully sequenced and identified as a pathogenic mutation (5%–10% of families), then FAP has not been excluded in this individual, they should not be discharged and they should undergo endoscopic surveillance (Fig. 2).

In children from families in which the mutation is not known or cannot be identified, the genetic testing is noninformative and it will not be possible to offer predictive testing to asymptomatic at-risk children. Protocols vary but current approach is to perform colonoscopy on all first-degree relatives from the age of 12 to 14 years every 3 to 5 years until adenomas are found. If by the age of 20 years, no adenomas have been identified despite the use of chromoendoscopy, colonoscopy should be performed at 5 yearly intervals.

Diagnostic Testing

De novo genetic mutations account for 15% to 20% of cases of FAP. When colonic adenomas have been identified in a child at colonoscopy, for example, for rectal bleeding, they should be examined for extracolonic features of FAP, for example, skin, dental, or bone manifestations (Table 1), and the family referred to a specialist or a geneticist for counselling for diagnostic genetic testing, and a detailed family history. At genetic testing, if a pathogenic mutation is identified, then the diagnosis of FAP will have been confirmed and other first-degree relatives should be offered predictive testing (Fig. 3). If no pathogenic mutation is identified, then other family relatives cannot be offered diagnostic testing, and they should be referred for colonoscopy. If a variant of unknown significance is identified, then the advice of a geneticist should be obtained but until more work has been performed, as such variant of unknown significance cannot be used for predictive testing.

Recommendation 3:

At what age should colonic surveillance commence in children predicted to be affected by FAP?

Recommendation 3:
In those confirmed to have FAP on predictive genetic testing, and those considered at risk where genetic testing is not possible, colonic surveillance should commence age 12 to 14 years. Once adenomas have been identified, intervals between surveillance colonoscopy should be individualized depending on colonic phenotype every 1 to 3 years. Rectal bleeding or mucous discharge should lead to a colonoscopy at any age.

(weak recommendation, low-quality evidence, consensus agreement 100%)

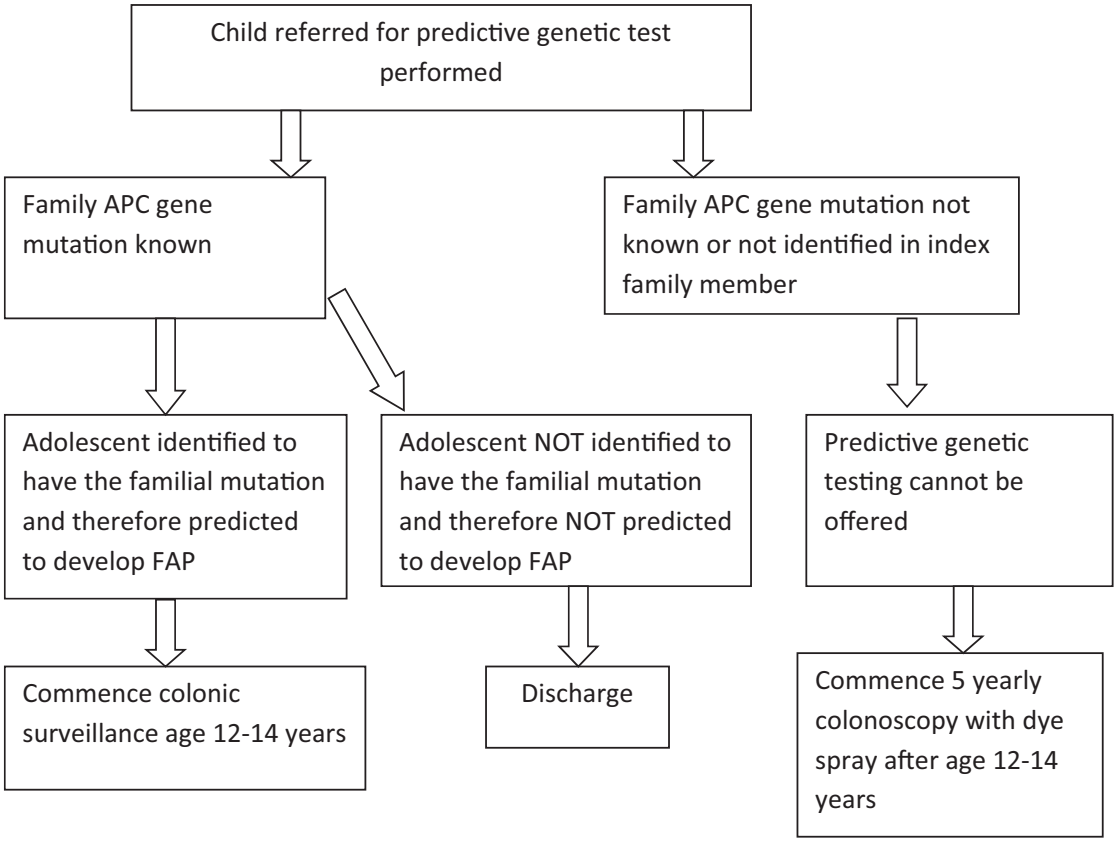

FIGURE 2. Interpreting genetic testing in FAP—predictive testing. FAP = familial adenomatous polyposis.

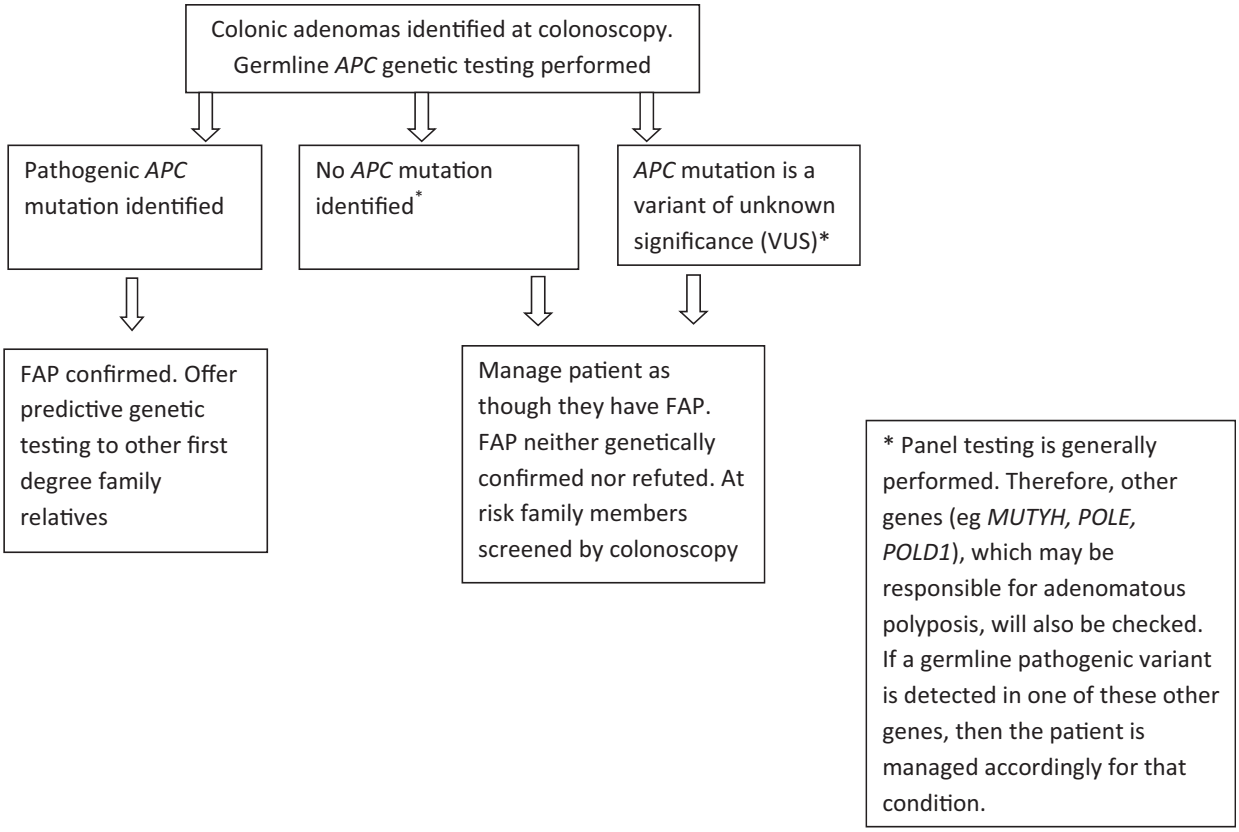

FIGURE 3. Interpreting genetic testing in FAP—diagnostic testing. FAP = familial adenomatous polyposis.

Children and adolescents predicted to develop FAP should undergo colonoscopic surveillance. Patients should not wait until they are symptomatic before they undergo their first colonoscopy. A study comparing patients with FAP who presented with symptoms compared with relatives of patients referred for screening, observed a much lower incidence of CRC in those screened by colonoscopy (incidence 3%–10%) compared to those patients who presented with symptoms (50%–70%) (9). Of note this article reflected practice in the late 1980s and range of age of diagnosis in those patients being screened was variable, from age 8 to 59 years, yet this publication does add evidence to the value of presymptomatic screening and recall through a polyposis registry.

Although CRC is particularly rare under age of 20 years, we recommend starting colonoscopy before the onset of symptoms, age 12 to 14 years, after diagnostic genetic testing has been performed in at-risk children. This is in agreement with other international guidelines (10).

The role of colonoscopic surveillance is to assess adenoma burden and determine adenoma distribution especially in the rectum as these impact on surgical options for colectomy. Extra time should be spent in the rectum counting adenomas, especially those = or >2 mm. If polyps are small or hard to visualize, chromoendoscopy should be considered to improve visibility of polyps.

The National Comprehensive Cancer Network guidelines (11) for asymptomatic patients with a known *APC* mutation recommend either colonoscopy or sigmoidoscopy every 12 months starting age 10 to 15 years. Although this National Comprehensive Cancer Network guideline advocates annual colonoscopy, there is no evidence for accelerated carcinogenesis and therefore no indication that the colonoscopy should be performed every year. The risk of developing cancer in teenage years is as low as 0.2% (10), so waiting 1 to 3 years between colonoscopy would appear safe, so long as families are not lost to follow-up if endoscopies are as far apart as every 3 years (eg, in those patients with less than a total 50 adenomas under 2 mm at colonoscopy).

It should be acknowledged there is a phenotypic variation in this age group and the interval between colonoscopies needs to reflect this. Intrafamilial variation is well recognized so relying on family history alone is unsafe. The presence of a gene mutation associated with a more aggressive phenotype (eg, codon 1309) should not dictate alone the timing of colonoscopy. The presence of symptoms, in particular rectal bleeding and/or anaemia, suggests a significant polyp burden and requires an earlier colonoscopy (12). In patients with FAP-related symptoms such as rectal bleeding, diarrhoea, or mucous discharge should lead to a colonoscopy at any age (13).

The depth of colonoscopy has not been studied. Although sigmoidoscopy is adequate to detect polyps in those with colonic polyposis, polyps may appear earlier on the right side of the colon. Historical registry data by Bussey (14) demonstrated 170 adult patients with FAP, the rectum is affected in all cases, but this was not a paediatric cohort. Out of 245 colonoscopies in patients younger than 25 years with FAP, proximal colonic polyps were found in 8 children when no polyps were seen in the rectosigmoid. Given these findings, and the fact that most endoscopic procedures are performed under general anaesthesia in children and young teenagers, we feel that colonoscopy gives a more comprehensive

assessment of the patient, without increasing the burden to the child. We concluded that sigmoidoscopy alone should not be recommended as the preferred investigation either for screening or surveillance. In patients who undergo colonoscopy where infrequent or small adenomas are seen, or none are visible at all, dye spraying the rectal mucosa with methylene blue or indigo carmine (chromoendoscopy) will substantially increase the sensitivity of the examination (15).

Clinicians should be aware that colonoscopy cannot be used to judge severity of dysplasia as it is difficult endoscopically to diagnose advanced lesions when numerous or innumerable polyps are present. Polyp features that are more likely to be associated with advanced dysplasia or malignancy include ulceration, surface bleeding or adenoma diameter >10 mm. Polypectomy of adenomas should not be performed routinely to delay the inevitable colectomy, but there is benefit in removing larger polyps >10 mm, or those with concerning appearance to assess the degree of dysplasia and assist in determining timing for colectomy. Biopsy alone of large lesions may still fail to identify a malignancy within the polyp.

First-degree family relatives without an identified APC mutation should be surveyed by colonoscopy every 5 years from the age of 12 to 14 years until adenomas have been identified, then once adenomas have been confirmed, the patient should undergo repeat colonoscopy at a frequency depending on the colonic phenotype (16). It is difficult to know at what age screening can safely cease in those not found to have adenomas. More than 90% of individuals with FAP will have developed polyps by the age of 25 to 30 years, but in view of the variation in phenotype within families and the existence of AFAP, it is reasonable to consider continuing surveillance until the age of 50 years.

Recommendation 4:

At what age should children and adolescents be referred for colectomy and what is the preferred surgical procedure?

Recommendation 4:
Colectomy is necessary to prevent CRC in adulthood. Decision on the timing for colectomy should be determined by polyp burden and characteristics of colonic adenomas in the context of social, personal, and educational factors. Ileorectal anastomosis (IRA) or ileal pouch-anal anastomosis (IPAA) has their merits and disadvantages and many factors affect on the choice of surgery. The choice should be based on patient phenotype (rectal and colonic burden) and genotype, at the discretion of the surgeon.

(weak recommendation, low-quality evidence, consensus agreement 100%)

Removal of the colon for FAP is required to prevent the almost inevitable development of CRC. The age at which prophylactic colectomy is performed is not fixed and is a topic that needs to be discussed in adolescence. There are no guidelines regarding the timing of surgery, nor evidence to dictate the point at which colectomy should be performed based on polyp burden (number or size). The adenoma-carcinoma sequence is not accelerated in FAP, so it may take more than 10 years before a cancer develops in a colon with adenomas.

There is no clear evidence to dictate at what polyp size or colonic burden should lead to colectomy and any recommendations remain arbitrary. Current practice is arbitrary recommending colectomy when there are many adenomas >10 mm, > 500 of polyps >2 mm, or carpeting of the colon of polyps. Many teenagers and young adults will undergo colectomy before this point, fitting the procedure around gaps in their education or working careers or their domestic or social circumstances.

If high-grade dysplasia is identified in colonoscopic biopsies, then this would be an indication for colectomy sooner. Waiting for serial biopsies to change from low-grade to high-grade dysplasia is unsafe and will put patients at risk of developing CRC especially as it is not clear which polyps should be biopsied at colonoscopy for histological assessment (17). Colonoscopy can overlook high-grade dysplasia because it is difficult to endoscopically diagnose advanced lesions that are progressing to malignancy, when numerous or innumerable polyps are present. Given this, there is no justification for routine biopsies or polypectomy to assess dysplasia. Polypectomy or biopsy should be targeted to polyps that have a suspicious/advanced appearance (ulceration, surface or contact bleeding, and diameter >10 mm). If there is sufficient concern about polyp size, polyp density, and the presence of feature suggestive of advanced changes, the patient should be referred for colectomy. There are rare occasions in which colectomy may wish to be delayed (eg, a personal or family history of desmoid disease). The decision making around such cases may be complex. It would be prudent for such cases to be referred to a specialist centre, where a full multidisciplinary team can evaluate the case to ensure the management is tailored appropriately to the individual and where polypectomy can be performed by individuals who are experienced in the endoscopic management of FAP.

The 2 main surgical options are colectomy with IRA and proctocolectomy with IPAA. Both surgical choices have their merits and weaknesses. The IRA is a relatively straightforward operation that can be readily performed laparoscopically, reducing hospital length of stay and recovery with preservation of bowel function and continence, and small surgical scars with cosmetic advantage (18). The IPAA requires more extensive surgery with pelvic dissection with its attendant risks of haemorrhage, damage to pelvic nerves, and possible reduction in fertility.

Current adult practice, based on large cases series and expert consensus published in FAP international guidelines (10) recommends IPAA in those with a significant rectal burden of adenomas and this advice should be extended into paediatric practice. Those children or adolescents with an adenoma burden of >20 rectal polyps, or a total colonic burden of >500 adenomas should preferably be referred for a primary IPAA (19). Conversely, those patients with a few rectal adenomas (<20) or infrequent colonic polyps can be referred for an IRA.

Other considerations regarding surgical choice include genotype (20–22), the impact on fertility (23) and the risk of desmoid disease. Despite these data, the phenotype of the colon and rectum should principally guide surgical choice (Table 2). The decision regarding surgical choices should rest with the surgeon, who can counsel the patient and parents further regarding the pros and cons

TABLE 2. Clinical factors influencing the surgical choice of either ileorectal anastomosis or ileal pouch-anal anastomosis

Rectal and colonic adenoma burden
Site of mutation
Risk of desmoid, or presence of desmoid tumours
Risk of impact on fertility in females
Long term function

of both surgical options and the rationale behind the surgical decision-making process. The choice should not be determined by the paediatric gastroenterologist. Current opinion recommends IPAA should be performed in expert centres by surgeons who have experience in performing numerous IPAA operations per annum. A colonoscopy should be performed before the colectomy to assist the surgical choice, assessing rectal and colonic polyp burden.

Postcolectomy, the rectal remnant after an IRA and the pouch after IPAA must be endoscopically surveyed. Post IRA, guidelines suggest 6 monthly—annual examination of the rectum (10). There are no data to support optimal frequency of surveillance and it would be reasonable for this to be tailored according to an individual's phenotype. Post IPAA, the gastroenterologist needs to be aware that there will be retained rectal mucosa. It is this that dictates the surveillance interval post-IPAA, rather than the risk of pouch body adenomas. The pouch should be endoscopically examined for adenomas in the residual rectal mucosa of the cuff, and the pouch body, preferably annually. Cuff adenomas can be technically difficult to treat endoscopically, so detecting them early, when small, is likely to improve the chance that they are successfully treated endoscopically. Pouch body adenoma risk appears to increase with the age of the pouch. They can be subtle but appear to run an indolent course and endoscopic resection of larger lesions is reasonable. Endoscopic assessment of pouches post IPAA, and assessment and therapy for pouch adenomas should be performed by clinicians with appropriate expertise.

Recommendation 5:

At what age should upper gastrointestinal surveillance commence in children affected with FAP?

Recommendation 5:
Despite the presence of gastric polyps in children, and the later risk of duodenal polyposis and ampullary cancer in adult practice, there is no justification to commence routine upper GI (UGI) surveillance until age 25 years.

(weak recommendation, low-quality evidence, consensus agreement 90%)

After prophylactic subtotal colectomy, the risk of subsequent UGI cancer is greater than the risk from the retained rectal segment post-IRA. Lifetime risk of duodenal polyposis approaches 100% (24). The absolute lifetime risk of developing duodenal cancer is estimated to be 3% to 5%. Although the diagnosis of duodenal cancer before the age of 30 years is rare, there are isolated reported cases of duodenal malignancy before 20 years of age. Over a 10-year period, 368 patients with FAP were assessed, with their first gastroscopy performed at mean age 20 years. The median age of diagnosis of duodenal adenomas was 38 years (range 20–81). The median age of diagnosis in duodenal cancer in this cohort was 52 years (range 26–58) (25). The recommendation from this series was to start duodenal surveillance age 30 years.

Although duodenal adenomas and dysplasia have been identified in children younger than 12 years, the youngest UGI cancer reported was in a 17-year old (26). Periampullary duodenal adenomatous nodules and polyps are common in adolescents with FAP (reported in 11/49 gastroscopies in 1 series), but again no reported cancers in this age group (27). Symptoms do not predict pre malignant changes.

Subsequent published recommendations based on case series suggest first surveillance gastroscopy procedure should be performed in the patient's mid 20s (or 5 years earlier than the youngest case of advanced duodenal adenomatosis in those with a significant family history) (28). Others advocate earlier gastroscopy whilst more than half of the cohort (59% of n = 96) had developed UGI polyposis with a mean onset at age 17 years, but there were no invasive cancers in this group (29). The reviewers in this position statement understand the concern of clinicians about missing a possible UGI cancer, because it is so easy to perform a gastroscopy within the same anaesthetic procedure. However, despite the fact that in current paediatric endoscopy practice many perform a ''routine'' gastroscopy at the same procedure as a colonoscopy under general anesthesia, there is little to be gained by identifying or documenting UGI manifestations of FAP with such a low probability of identifying malignancy. The working group considered that the incidental finding of polyps in the duodenum should not influence when or whether a gastroscopy needs to be performed in patient with FAP and the criteria should be based on clinical need (eg, unexplained anaemia).

Endoscopic surveillance of the ampulla and duodenum is best performed with a side viewing duodenoscope (±forward viewing scope). Duodenal disease is classified according to the Spigelman staging system, which facilitates determining the interval for duodenal surveillance and treatment options (30). Were there to be an indication for gastroscopy prior to age 25 years, for example, dyspepsia, then any duodenal lesions incidentally identified should be discussed with an adult gastroenterologist with expertise in assessing the duodenum in adults with FAP.

Gastric lesions are also common in adult patients with FAP. Fundic gland polyps (FGPs) are the most common seen in 40% to 75% of FAP patients, followed by gastric foveolar-type gastric adenomas. FGPs are usually small, <5 mm, sessile and multiple, asymptomatic, and limited to the stomach (31). Gastric adenomas in childhood are uncommon in FAP (32). Although there is a current debate regarding the malignant risk of FGPs, given that no gastric cancers have been identified in patients younger than 25 years, routine gastroscopy can be delayed until 25 years.

High-grade dysplasia is rarely seen on baseline upper GI endoscopy (33). No causal link has been found between *Helicobacter pylori* and FAP-associated FGPs. Other uncommon lesions include pyloric gland adenomas, gastric hyperplastic polyps, and intestinal-type gastric adenoma.

UGI endoscopy may be indicated for nonspecific abdominal symptoms (eg, dyspepsia, epigastric pain) in patients with FAP to detect and treat GI disease unrelated to FAP.

Recommendation 6a:

Should infants and children from families affected by FAP be screened for hepatoblastoma and should children with hepatoblastoma undergo testing for FAP?

Recommendation 6a:
Routine screening for hepatoblastoma (HPB) in patients with FAP is not recommended. In children found to have HPB, there is no evidence that routine genetic testing or endoscopic screening for FAP is required.

(weak recommendation, low-quality evidence, consensus agreement 90%)

Should infants from affected families be screened for hepatoblastoma?

The risk of HPB is 750 to 7500 times higher in children from FAP families than in the general population (34), with an absolute risk reported as 2% of FAP-affected children. The majority of the cases occur before 3 years of age (relative risk of HPB in patients with FAP suggested to be relative risk = 847) (35). The prognosis to some degree correlates with tumour size, and authors have inferred that some patients would have a better prognosis if the diagnosis was made earlier. The outcomes for HPB are excellent with current treatment using partial hepatectomy and chemotherapy (survival >90% in patients with stage I and II disease), it has been suggested that earlier tumour detection may improve cure rates and also may limit the chemotherapy needed to produce that cure, but this has not been substantiated (36). Surveillance has thus been proposed in children who have a diagnosis of FAP or have a parent with FAP, often starting with alpha-feto protein laboratory testing and 3 monthly ultrasound scans of the liver from birth (37). Thus, some authors suggest that children with an *APC* mutation diagnosing FAP, or who have a parent with known *APC* mutation (even if no genetic testing has been performed in the infant) should be offered surveillance consisting of alpha-feto protein measurement and abdominal ultrasound every 3 to 4 months from birth to 5 years of age. This would be an onerous undertaking and conflicts with recommendation 1 (recommending delaying genetic screening until after age 12–14 years). When this regime was applied to a small (and therefore not statistically significant cohort) of 20 patients at risk of FAP who underwent HPB screening, none developed liver tumours (38). No studies have identified the benefit of screening for HPB in FAP.

There is insufficient evidence to suggest screening for HPB confers any advantage and therefore the recommendation currently is not to offer screening investigations for HPBs in at-risk infants and children. Parents should be counselled regarding the increased relative risk of HPB in patients with FAP, but very low absolute risk, and explaining there is no evidence that screening is effective and improves patient outcome. We anticipate that such counselling would be sufficient to avoid HPB screening.

Should children diagnosed with an HPB be screened for FAP?

HPB is the most common primary liver tumour in children. Published series have suggested that approximately 10% of children with a diagnosis of HPB may have a germline *APC* mutation (39) and thus children with HPBs should be referred for screening for FAP even in the absence of family history. Others have found no *APC* mutations in 29 cases of apparently sporadic HPB (40).

Based on these data, FAP should be considered in a child with an HPB by seeking a suggestive family history of early onset CRC and polyps, or extraintestinal manifestations. If there is a clinical suspicion of FAP, the family should be referred for screening. In the absence of these factors, there is insufficient evidence to suggest routine screening in adolescence for children with HPB. If a child or teenager develops GI symptoms, they should be investigated accordingly. Clinicians should be aware of the association of HPB and FAP. The risk of FAP in patients who had HPB in childhood needs to be discussed with the family (39), and the decision to screen, or not to screen for FAP should be shared with the parents and adolescent.

Recommendation 6b:

Should children with congenital hypertrophy retinal pigmentation epithelium (CHRPE) be investigated for FAP?

Recommendation 6b:
Children with bilateral and multiple CHRPE lesions should undergo colonoscopy at age 12 to 14 years. If CHRPE lesions are single or unilateral in the absence of relevant family history, further evaluation should not be required.

(weak recommendation, low-quality evidence, consensus agreement 100%)

Up to two thirds of patients with FAP have CHRPE identified at ophthalmoscopy, and this should be verified by an ophthalmologist knowledgeable about the condition (41). Idiopathic solitary CHRPE is described in the general population with a prevalence of 1% to 4% (42). CHRPE lesions associated with FAP are most often multiple, bilateral (bilateral in 86% of cases) and in an oval or pisciform shape (43). Multiple retinal lesions appear to have a 40% to 70% sensitivity and close to 100% specificity as a phenotypic marker for FAP (44). Four bilateral and large size lesions are highly predictive of FAP. Children and adolescents with CHRPE in the pattern suggestive of FAP, should be referred for genetic counselling and evaluation by a paediatric gastroenterologist. If there is a known family history of FAP with an identified *APC* mutation in an index family member, targeted genetic testing should be offered. Otherwise, with a specificity approximating to 100%, those with multiple bilateral lesions should be investigated for FAP; we suggest that colonoscopy and subsequent genetic testing can be deferred until age 12 to 14 years, unless the patient is symptomatic.

If an experienced ophthalmologist considers the CHRPE lesions to be single and unilateral, then referral to a paediatric gastroenterologist is not required. If there are additional concerns identified from the family history or clinical examination, then further evaluation by a geneticist is recommended.

Recommendation 6c:

Should infants and children found to have a desmoid tumour be investigated for FAP?

Recommendation 6c:
The vast majority of desmoids tumours are sporadic; children identified to have a desmoid tumour (DT) have approximately 10% risk of FAP. If the kindred is known to have FAP and the child has a desmoid, it should be presumed the child has FAP.

In a child presenting with a DT, testing the DT for a *β-catenin/CTNNB1* mutation is recommended. If a *β-catenin/CTNNB1* mutation is found, this indicates sporadic desmoid and further investigations for FAP are not required. If *β-catenin/CTNNB1* mutation is not found, the patient should be investigated for FAP.

(weak recommendation, low quality evidence, consensus agreement 100%)

DTs develop in 10% to 30% of patients with FAP, the majority are intra-abdominal. Although they are nonmetastasising, they can be locally invasive. DTs are consistently cited as the second leading cause of mortality in FAP patients with the overall lifetime mortality in patients with FAP attributable to desmoids over 11% (45). FAP-associated DTs made up 7.5% of all DTs, and the relative risk of an FAP patient developing a DT was more than 800-fold higher than the general population (46). Approximately 7% to 15% of all DTs are found in people diagnosed with FAP (47). In a single-centre retrospective series, 10% of 93 patients younger than 21 years with a DT were identified to have FAP (48). Desmoids associated with FAP are often found at a young age (second or third decade), and are most commonly seen 3 to 5 years after prophylactic colectomy and the risk is increased if there is a family history of desmoid disease (49). There is genotype-phenotype correlation with desmoid disease in FAP correlating to mutation 3' to codon 1399 associated with an OR of 4 for the development of DT in FAP (Fig. 1).

Children with DTs are clearly at a substantially greater risk of having FAP. If the child with a DT is from a kindred known to be affected with FAP, then it is safe to assume that the affected child has inherited FAP and targeted genetic testing can be performed to seek the mutation known to that family.

DTs in patients with FAP carry biallelic *APC* mutations. This is in contrast to desmoids which arise sporadically which manifest *β-catenin* /*CTNNB1* mutations (50). To assess for a *β-catenin* / *CTNNB1* mutation, DNA extraction from biopsy of the DT should be performed. *CTNNB1* mutations are highly prevalent in sporadic DTs (51). Thus if the mutation is identified in the desmoid sample, then this is predictive of sporadic desmoid unrelated to FAP.

On the contrary, the absence of CTNNB1 mutations in the desmoid should suggest the possibility of FAP. If β-catenin/ CTNNB1 mutations cannot be isolated in the desmoid, then clinicians cannot be confident that this is a sporadic desmoid and thus genetic testing and colonoscopy should be offered to the affected child ages 12 to 14 years (even in the absence of a family history as the APC mutation could be de novo).

If DNA extraction of the DT is not feasible and if there are no clinical clues in the child or family suggestive of FAP, the child with DT should undergo colonoscopy with chromoendoscopy in teenage years.

The management of desmoid disease in FAP is complex and lacking good data. Options include surgery resection, surgery for complications, for example, small bowel obstruction, or adopting a conservative surgery sparing approach. Various pharmacological agents have been used, including NSAIDs (sulindac and celecoxib) and hormonal medications (tamoxifen, toremifene, LHRH-agonists, and anastrozole) and chemotherapy (doxorubicin) (52) but randomized controlled data are lacking and therefore given the variable natural history of desmoids, it is difficult to establish and qualify the benefit of these medical therapies.

Recommendation 7:

Under what circumstances should children and adolescents be offered chemoprevention with NSAID medication?

Recommendation 7:
There is no role for the use of chemoprevention agents in children with FAP.

Evidence (strong recommendation; moderate-quality evidence, 100% consensus)

NSAIDs have been the most commonly employed chemopreventive agents in patients with FAP to delay the development of adenomas and to prevent recurrence of adenomas in the retained rectum of patients after prophylactic surgery with colectomy and IRA. Sulindac and selective cyclooxygenase-2 (COX-2) inhibitor celecoxib have been the most extensively studied.

The efficacy of NSAIDs has been demonstrated in clinical trials and animal studies. NSAIDs inhibit COX, a key enzyme in the conversion of arachidonic acid to prostaglandins and other eicosanoids. Prostaglandins appear to play a key role in the adenoma-carcinoma sequence by altering cell adhesion, inhibiting apoptosis, and promoting angiogenesis.

The ultimate goal of chemoprevention in FAP is to prevent the inevitable development of CRC among these patients. Despite evidence that sulindac may regress adenomas in the rectum after colectomy with IRA, no evidence exists that the drug delays or prevents the development of malignancy in these rectal segments. In fact, there are several case reports of patients developing malignancy despite chemopreventive regimens (53,54). If used, chemopreventive regimens should be accompanied with a strict endoscopic surveillance regimen. Use of NSAIDs should not replace standard surveillance and treatment.

Sulindac

A significant decrease in the mean number and size of polyps in patients treated with sulindac compared with placebo has been reported in FAP patients in short term (55,56); however, this does not prevent progression of polyps towards malignancy. In a trial involving FAP patients who have undergone colectomy with IRA, sulindac for an average of 63 months significantly reduced rectal polyp number in all 12 patients. Higher-grade adenoma recurrence was also significantly reduced. The most common side effect was rectal mucosal erosions. Of concern, 1 patient developed a rectal carcinoma. The occurrence of cancer in the rectal remnant of patients with FAP during sulindac therapy has been described in other patients (54).

The use of sulindac as a primary chemopreventive agent in paediatric FAP patients has been studied by Giardello et al (57). Standard doses of sulindac, compared with placebo, did not prevent the development of adenomas in 41 young subjects (age range, 8–25 years) who were predicted to be affected with FAP but not yet developed adenomas. Currently, sulindac is not recommended as a primary chemopreventive agent.

Celecoxib

Interest in COX-2 inhibitors as chemopreventive agents in FAP was prompted by the GI toxicity noted with a long-term use of nonselective NSAIDs. In adult patients randomized to celecoxib or placebo, those receiving 400 mg twice a day had a 28% reduction in the mean number of colorectal polyps over a 6-month period (58). The safety and efficacy of celecoxib as chemopreventive agent in paediatric population was first studied by Lynch et al (59). They studied a cohort of 18 children of ages 10 to 14 years with *APC* gene mutations and/or adenomas with a family history of FAP. Celecoxib at a dose of $16\,mg \cdot kg^{-1} \cdot day^{-1}$, corresponding to an adult dose of 400 mg twice per day, was well tolerated and significantly reduced the number of colorectal polyps by 44.2% at 3 months ($P = 0.01$), but the cohort was small ($n = 18$). Although this study showed a short-term safety of daily use of celecoxib in children with FAP, cardiovascular toxicity has been shown in several COX-2 inhibitor trials of adults with nonfamilial adenomas (60). The largest randomized placebo controlled chemopreventive study in children using celecoxib ($n = 106$) suggested the drug was well tolerated

and there was a nonsignificant trend to slower progression of colorectal adenomas in the therapeutic arm compared to placebo (61). One randomized clinical trial in adults identified a marginal reduction in duodenal polyposis but the significance of this in paediatrics is unclear (62). Studies combining celecoxib and difluoromethylornithine have suggested a marginal additive effect of combining chemopreventive therapies (63).

An effective chemopreventive agent with favourable toxicity may be of substantial benefit to paediatric FAP patients if found in the long term to prevent cancer. Although it is not feasible to accurately assess polyp density or burden in an intact colon, and the difficulties in undertaking trials in children who require deep sedation for colonoscopy, plus complexity confirming drug adherence, and aiming for useful end points such as delay in colectomy or prevention of CRC, the design of study with meaningful end points will pose significant challenges. It may not be possible to perform an adequate clinical trial to prove the value of NSAID medication as chemoprevention in children or adolescents, with end points that are valuable and clinically relevant, and reproducible (64).

Recommendation 8:

What should the clinician advice regarding the cancer risk in children and young adults with FAP

Recommendation 8:
CRC is very rare in children and teenagers younger than 20 years. The risk of developing CRC before age 20 is as low as 0.2%. Duodenal cancer has not been reported in teenagers. Extracolonic malignancies are very rare, for example, HPB, brain, and thyroid cancers, reported in 1% to 2% of FAP-affected young adults. Patients can be reassured that they have a very low cancer risk in childhood and teenage years.

(strong recommendation, good quality evidence, consensus agreement 100%)

Virtually all patients with FAP will develop adenocarcinoma of the colon or rectum if left untreated by the ages 40 to 50 years. Although rare, CRC can, however, develop in adolescence. CRC in FAP patients younger than 20 years usually is associated with a severe polyposis phenotype. Church et al (8) surveyed polyposis registries around the world to assess risk of colorectal carcinoma in children and teenagers with FAP. Among the 16 registries that responded, 14 patients younger than 20 years were identified with CRC. The youngest was 9 years old. In 3 cases, the cancer was identified at surgery. Nine of the 14 young patients with CRC had severe polyposis (defined as >1000 colonic polyps). The authors calculated an estimated incidence of 1 case of CRC per 471 affected FAP patients younger than 20 years. A subsequent review published within the FAP guidelines 2008 lists data from multiple European FAP registries, there were 1073 CRC's; none of them in children younger than 10 years, 2 were present in those ages 11 to 15 years, and 15 in children age 16 to 20 years (10). It must be emphasized that this cancer risk is ascertained in a cohort of patients who would have undergone prophylactic colectomy in adolescence, and these data cannot influence the timing of surgery in teenagers in whom the polyp burden necessitates colectomy.

One of the largest single institution reviews of paediatric FAP reported a total of 6 patients with CRC among a total of 163 patients younger than 20 years over a 24-year study period (29). Cancer was found in 1 colonoscopy biopsy (age 18 years) and 5 colectomy specimens (ages: 1 at 19 years, 2 at 18 years, and 2 at 17 years of age). Papillary thyroid cancer was diagnosed in 5 patients and presented at a mean age of 20.8 years. Two patients were found to have brain tumours (1 craniopharyngioma at age 29 years and 1 glioblastoma at age 8 years). An 18-year-old who presented with advanced rectal cancer died at age 22 due to progression of metastatic disease. More than half of patients (59%) developed UGI polyposis, with mean onset at age 17 years but none had progressed to invasive cancer of the UGI tract under 20 years old.

Cohen et al (65) published a series of 33 children with FAP <18 years. On their first colonoscopy, 31 children (94%) had colonic adenomas with low-grade dysplasia and 2 patients (6%) had a normal first colonoscopy. Among these normal first colonoscopy patients, 1 child was later diagnosed with colonic adenocarcinoma at the age of 12.5 years. A prospective clinical trial using celecoxib involving 106 children, age range 10 to 17 years, followed patients 2 to 5 years and none developed CRC during that timeframe (61).

After CRC, the second most common malignancy in patients with FAP over their lifetime is duodenal cancer. Because of a slow progression, only a small fraction of affected subjects will develop duodenal cancer in adulthood (3% to 5%). There is a paucity of data describing UGI neoplasms in paediatric FAP patients. As a result, there is little evidence to support the initiation of UGI surveillance in childhood or adolescence in subjects with FAP (recommendation 5) (66).

The central nervous system (CNS) tumours associated with FAP include medulloblastoma, astrocytomas, and less frequently ependymoma, pinealoblastoma, and ganglioglioma. Given the relatively low risk (<1% overall risk), screening for CNS tumours is currently based on physical examination. In patients with FAP and identifiable *APC* gene mutation, CNS tumours, especially medulloblastoma, are more common in girls, younger than 20 years and with FAP and *APC* gene mutation in codons 686–1217 (67). Further studies are necessary to determine whether this observation has implications for genetic counselling for individuals with FAP and potentially affecting the risk-benefit assessment for surveillance for brain tumours within this subpopulation.

The risk of developing thyroid cancer in FAP is greatest during the second and third decade of life (<30 years old in 90% of cases; range 15–62 years) and is higher in girls (female-to-male ratio, 17:1) (68). Patients should be informed at transition to adult care regarding the young age on onset of thyroid cancers and the role of thyroid examinations. Of note however, there are no data to demonstrate benefit of routine thyroid surveillance in FAP.

Although relatively uncommon, paediatric patients with FAP may present in the first decade of life with HPB (37). The implications of this are discussed above. Adrenal adenocarcinoma has also been reported in a teenager with FAP (69).

Recommendation 9:

Should children and families with familial adenomatous polyposis be managed within a polyposis registry?

Recommendation 9:
Where feasible, children and adolescents should be enrolled into their regional or national polyposis registry (depending on local and national provision) to coordinate their care. Polyposis registries improve outcome for FAP patients by improving the rate of diagnosis of FAP and reduce the incidence of CRC.
(weak recommendation, moderate-quality evidence, consensus agreement 100%)

TABLE 3. Role and benefit of managing familial adenomatous polyposis within a polyposis registry

Role of a polyposis registry	Proven benefit from a polyposis registry
Registration of polyposis patients and family members	Increasing the rate of diagnosis of FAP and enabling earlier diagnosis
Counselling and genetic testing	Improve outcomes and reducing the incidence of CRC
Access to the multi disciplinary team including psychology.	Improved survival of patients from presymptomatic screening
Initiation and coordination of screening of family members at risk of a polyposis syndrome	More complete recall of patients for screening and surveillance
Distribution of information and scientific knowledge and initiating research	
Recalling patients for screening endoscopies and maintaining postsurgical follow-up, eg, after IRA for FAP	

CRC = colorectal cancer; FAP = familial adenomatous polyposis; IRA = ileorectal anastomosis.

Polyposis registries are now established across the world. The aims and benefits of a polyposis registry are listed in Table 3. Many registries will take responsibility for co-ordinating care, whereas others offer advice and guidelines for local clinicians responsible for occasional patients with a polyposis condition. The improved survival of patients registered is almost certainly attributable to the improvement in organization and coordination of patient screening (70). Patients identified to be at risk of FAP and called for screening had a lower risk of CRC. There are no studies comparing the outcome of children or adolescent patients affected by FAP, who undergo screening and surveillance in a polyposis registry, compared to those who are carefully recalled for screening in a local or regional paediatric gastroenterology service.

After screening and colectomy, surveillance will still be required for the rectum/pouch; furthermore, patients are at long-term risk from extracolonic manifestations especially desmoid disease and duodenal cancer. Maintaining enrolment and contact through a registry will encourage patients to participate in lifetime surveillance (71), and ensure that paediatric patients attend for their surveillance and have structured and staged transition into adult care. The published improvement in survival of FAP patients who are enrolled in a surveillance programme should encourage paediatricians to register their patients with their regional polyposis registry, if accessible and amenable to the patients and their families.

Enrolment will ensure access to paediatric and adult gastroenterologists skilled in colonoscopic surveillance in patients with polyposis, and a multidisciplinary team who have experience in looking after such families, facilitating compliance, and transitional care. Adolescents can access psychological support offered within the multidisciplinary team, and this is made more pertinent in young patients compared to adults while, younger patients tend to worry more about the risk of cancer (72). Mental healthrelated quality of life scores are reported to be significantly lower among FAP-affected patients younger than 18 years compared to adults. It is therefore imperative for paediatric gastroenterologists and geneticists to develop trust and empathy with patients and their families addressing individual social, psychological, and medical conditions, establishing compliance to screening investigations, and individually tailored planning of the timing of colectomy. Psychological support for patients is needed most around the time of colectomy, and this can be accessed by the wider polyposis registry team of nurses and psychologists, or provided locally by a motivated paediatric gastroenterology team (73).

In addition, supervision and enrolment into a polyposis registry offers added benefits including support groups, meeting other affected families for advice and support, access to experienced expert care, and timely advice regarding pregnancy and preimplantation genetic diagnosis. The latter choice can be offered to older teenagers before starting a family enabling them to make planned and careful decisions regarding future pregnancies. Evolving resources within social media offer new and exciting possibilities in the context and patient and physician and patient support structures (Table 4).

TABLE 4. Areas requiring research in the field of familial adenomatous polyposis in children and adolescents

What is the natural history and polyp progression is children with FAP?
Does a gene mutation located at or adjacent to codon 1309 confer an increased risk of cancer in adolescents necessitating earlier genetic testing and colonoscopy?
What is the future role for a colon specific video capsule for colonic surveillance in reducing the burden of colonoscopic surveillance?

FAP = familial adenomatous polyposis.

SUMMARY OF RECOMMENDATIONS

Recommendation 1:

Predictive genetic testing should be offered to at-risk children at the age of 12 to 14 years. Families should receive genetic counselling before and at the time of testing. Children who are symptomatic with rectal bleeding should undergo earlier testing.

(weak recommendation, low-quality evidence, consensus agreement 100%)

Recommendation 2a:

In relation to predictive testing, if the child is found to have the familial *APC* variant, they have a diagnosis of FAP. If the familial *APC* variant is absent in the child, then they have not inherited FAP.

Recommendation 2b:

In a patient with colonic adenomas who undergoes genetic testing for FAP (diagnostic testing), the finding of a pathogenic variant will confirm the diagnosis of FAP. If no pathogenic variant is identified, this does not exclude FAP.

(strong recommendation, moderate-quality evidence, consensus agreement 100%)

Recommendation 3:

In those confirmed to have FAP on predictive genetic testing, and those considered at risk where genetic testing is not possible, colonic surveillance should commence age 12 to 14 years. Once adenomas have been identified, intervals between surveillance

colonoscopy should be individualized depending on colonic phenotype every 1 to 3 years. Rectal bleeding or mucous discharge should lead to a colonoscopy at any age.

(weak recommendation, low-quality evidence, consensus agreement 100%)

Recommendation 4:

Colectomy is necessary to prevent CRC in adulthood. Decision on the timing for colectomy should be determined by polyp burden and characteristics of colonic adenomas in the context of social, personal, and educational factors. IRA or IPAA have their merits and disadvantages and many factors impact on the choice of surgery. The choice should be based on patient phenotype (rectal and colonic burden) and genotype, at the discretion of the surgeon.

(weak recommendation, low-quality evidence, consensus agreement 100%)

Recommendation 5:

Despite the presence of gastric polyps in children, and the later risk of duodenal polyposis and ampullary cancer in adult practice, there is no justification to commence routine UGI surveillance until the age of 25 years.

(weak recommendation, low-quality evidence, consensus agreement 90%)

Recommendation 6a:

Routine screening for HPB in patients with FAP is not recommended. In children found to have HPB, there is no evidence that routine genetic testing or endoscopic screening for FAP is required.

(weak recommendation, low-quality evidence, consensus agreement 100%)

Recommendation 6b:

Children with bilateral and multiple CHRPE lesions should undergo colonoscopy at age 12 to 14 years. If CHRPE lesions are single or unilateral in the absence of relevant family history, further evaluation should not be required.

(weak recommendation, low-quality evidence, consensus agreement 100%)

Recommendation 6c:

The vast majority of desmoids tumours are sporadic; children identified to have a DT have approximately 10% risk of FAP. If the kindred is known to have FAP and the child has a desmoid, it should be presumed the child has FAP.

In a child presenting with a DT, testing the DT for a *β-catenin /CTNNB1* mutation is recommended. If a *β-catenin /CTNNB1* mutation is found, this indicates sporadic desmoid and further investigations for FAP are not required. If *β-catenin /CTNNB1* mutation is not found, the patient should be investigated for FAP.

(weak recommendation, low-quality evidence, consensus agreement 100%)

Recommendation 7:

There is no role for the use of chemoprevention agents in children with FAP.

(strong recommendation; moderate-quality evidence, 100% consensus)

Recommendation 8:

CRC is rare in children and teenagers younger than 20 years. The risk of developing CRC before age 20 is as low as 0.2%. Duodenal cancer has not been reported in teenagers. Extracolonic malignancies are very rare, for example, HPB, brain, and thyroid cancers, reported in 1% to 2% of FAP-affected young adults. Patients can be reassured that they have a very low cancer risk in childhood and teenage years.

(strong recommendation, good-quality evidence, consensus agreement 100%)

Recommendation 9:

Where feasible, children and adolescents should be enrolled into their regional or national polyposis registry (depending on local and national provision), to coordinate their care. Polyposis registries improve outcome for FAP patients by improving the rate of diagnosis of FAP and reduce the incidence of CRC.

(weak recommendation, moderate-quality evidence, consensus agreement 100%)

DISCLAIMER

ESPGHAN is not responsible for the practices of physicians and provides guidelines and position papers as indicators of best practice only. Diagnosis and treatment is at the discretion of physicians.

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