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Assessing barriers to a rational chemoprevention trial design in young patients with familial adenomatous polyposis

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Abstract

Familial adenomatous polyposis coli (FAP) is an autosomal dominant condition caused by a germline mutation in the adenomatous polyposis coli gene. Colonic adenomas form and almost all patients will develop colorectal cancer if they are not managed at an early stage. The safest preventive strategy is surgical resection of the colon most commonly performed in late teenage years. There is a paucity of trials investigating the use of primary chemoprevention to delay polyp formation in paediatric FAP. There are extensive preclinical and early clinical data demonstrating that curcumin may be a safe and effective chemotherapeutic agent in reducing the polyp burden in this disease. We ultimately proposed to design and conduct a clinical study to assess whether curcumin treatment delays the need for surgery and/or prevents cancer in young patients with FAP. Research into clinical trial protocols has demonstrated that assessing patients' perceptions at the initial stage leads to better outcomes. We therefore conducted a questionnaire study of patients and parents of children affected by FAP to gain information to aid the protocol design. Results demonstrated that there are some FAP patients for whom this study is relevant and desirable. Those with a personal history of curcumin use reported that it was well tolerated. However, the response rate was poor (25%), indicating that there are potential difficulties ensuring adequate recruitment to the proposed trial. This report draws on lessons learnt from prior trials and the findings from the questionnaire to outline the challenges faced in designing such a study.

Keywords

chemoprevention; curcumin; familial adenomatous polyposis

Background

Familial adenomatous polyposis (FAP) is an autosomal dominant condition occurring in ~ one in 10 000 births (Bisgaard *et al.*, 1994). Affected individuals usually inherit a germline

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Conflicts of interest

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mutation in the adenomatous polyposis coli (*APC*) gene; however, up to 15–20% of cases arise ‘de novo’ without clinical or genetic evidence of FAP in the parents (Aretz *et al.*, 2004). Patients with FAP are predisposed to developing colorectal adenomas and eventual adenocarcinomas in the lower gastrointestinal tract and, less frequently, the upper gastrointestinal tract. Two childhood cancers – medulloblastoma and hepatoblastoma – and other neoplasms including desmoid tumours and pancreatic and papillary thyroid cancers also occur with increased frequency in individuals with this condition (Belchetz *et al.*, 1996; Vasen *et al.*, 1997).

Colon polyps typically develop during the mid-teenage years and almost all patients will eventually develop colorectal cancer (CRC) if they are not identified and managed at an early stage (Cruz-Correa and Giardiello, 2003). Given the predictable development of CRC, the safest preventive strategy is currently surgical resection of the colon. Such surgery aims to minimize CRC risk while providing a good functional and socially acceptable outcome. The two main prophylactic operations that are performed are colectomy with ileorectal anastomosis and restorative proctocolectomy with the formation of an ileoanal pouch. Restorative proctocolectomy is more extensive and often reserved for the more severely affected patients. Unfortunately there are complications associated with surgery that vary depending on the procedure performed. These complications include the following: increased bowel frequency; faecal urgency; incontinence; the need for a temporary ileostomy; reduced fertility; and sexual dysfunction. These complications have been reported to affect up to half of the patients (Aziz *et al.*, 2006; Tudyka and Clark, 2012). Ongoing surveillance is still required following surgery as adenomas and carcinomas may occur in the retained rectum or the ileoanal pouch. Surveillance policies and prophylactic colectomy have resulted in a reduction in the number of FAP patients who die from CRC; nowadays, a greater proportion of deaths are attributable to extracolonic manifestations of this disease (Vasen *et al.*, 2008; Tudyka and Clark, 2012).

Chemoprevention in FAP

Several randomized, placebo-controlled clinical trials in adults (usually after colectomy) have demonstrated that chemopreventive agents including sulindac, celecoxib, rofecoxib and eicosapentaenoic acid may reduce polyp burden in the colon, duodenum or the retained rectal stump following surgery (Labayle *et al.*, 1991; Nugent *et al.*, 1993; Vasen *et al.*, 1997; Steinbach *et al.*, 2000; Phillips *et al.*, 2002; Higuchi *et al.*, 2003; West *et al.*, 2010).

On the contrary, the use of primary chemopreventive agents in paediatric FAP has not been widely studied, with only three trials being published to date, just two of which were randomized controlled trials (summarized in Table 1). The paucity of chemoprevention studies in this group is perhaps surprising as one could argue that treatment to delay polyp and subsequent CRC formation, thus postponing the need for prophylactic colectomy with its potential complications, would be an improvement to the current standard of care.

The first of these studies to be reported was a randomized, double-blind, placebo-controlled study. Recruitment occurred over almost 8 years at the Johns Hopkins Polyposis Registry. The subjects received either 75 or 150 mg of sulindac orally twice a day or identical-appearing placebo tablets for 48 months. The number and size of new adenomas and side

effects of therapy were evaluated every 4 months for 4 years. Although the average rate of compliance exceeded 76% in the sulindac group, this was a negative study. Eleven patients were withdrawn from the study in total (seven because of an increasing number of polyps, one because of persistent neutropaenia, and three because they were unable to make scheduled visits) (Giardiello *et al.*, 2002).

The second study was a phase I dose escalation trial in which children were treated with celecoxib (4–16 mg/kg a day) for 3 months. Colonoscopy was performed at baseline and at 3 months. Follow-up was conducted at 2-week intervals during drug administration. During the 22 months that this study was open to recruitment, 22 patients were evaluated for eligibility of whom two were excluded, having been found to be genotypically unaffected, and another patient was excluded because of excessive polyp burden. One otherwise eligible patient declined participation because of the parents' desire for surgery. All of the patients were at least 75% compliant with the study agent (Lynch *et al.*, 2010).

The final study was the largest ever to be undertaken in FAP patients. All polyposis registries and clinics in Europe were invited to participate in this randomized, placebo-controlled trial of aspirin (600 mg/day) and/or dietary resistant starch (30 g/day). Recruitment occurred over 8 years. Initially 227 patients were recruited into the study and 206 of them started the intervention. Only 59% of those recruited had a baseline and at least one other endoscopy and were therefore eligible for data analyses.

The most common reasons for patients withdrawing were the following: loss to follow-up ($n = 32$); no known reason ($n = 16$); referred for early surgery ($n = 8$); family/personal reasons ($n = 5$); could not tolerate treatment ($n = 3$); refused endoscopy ($n = 3$); and complied with only one of the study medications ($n = 3$).

One of the over-riding issues with all three of these trials was that of ensuring that a sufficient sample size was recruited and maintained. The recruitment and withdrawal numbers detailed above may have limited the power to detect a significant difference in the treatment groups. It is also noteworthy that the most recent chemoprevention study in this patient group, the 'Trial In Pediatric Patients With FAP' (CHIP) study, which compared celecoxib with placebo, was terminated early because of the low number of participants (Pfizer, 2014).

Differences between these studies raise questions about the optimal trial design in this patient group. At what age is it appropriate to start recruiting patients? Clearly there may be ethical issues raised about treating very young children and bringing the genetic testing forward, which is usually performed around the age of 12 (Tudyka and Clark, 2012). The youngest included so far was 8 (Giardiello *et al.*, 2002). Traditionally, chemopreventive agents are targeted at diseases affecting the adult population (e.g. tamoxifen for breast cancer (Cuzick *et al.*, 2003). Instinctively however, one may hypothesize that earlier initiation of the chemopreventive agent, before polyps have started to form, would be more efficacious. It is possible that commencing the treatment earlier may have led to more positive findings in the above studies. Cancer prevention commencing in childhood is now established and accepted in routine clinical practice with the introduction of the human

papillomavirus vaccine to protect against cervical cancer. An example where chemoprevention has safely and effectively been administered from a very young age is provided by fluoride supplementation in toothpaste and water supplies, which reduces tooth decay (Featherstone, 1999), and this could perhaps set a precedent for chemoprevention in the young.

The duration of intervention in the above FAP studies varied from 3 months to 12 years. Again, one would postulate that, the longer the exposure to the agent, the greater the likelihood of detecting and maintaining efficiency. However, it has been estimated that the compliance rate of long-term medication therapies is between 40 and 50%, whereas short-term therapy compliance rates are much higher at between 70 and 80% (DiMatteo, 1995). Thus, a challenge to trial design is that longer treatment exposure must not be at the expense of poor compliance and high dropout rates compromising the quality of the data. Low compliance is known to especially be a problem in children and adolescents with chronic diseases (Kyngas, 1999)

The studies also varied in the frequency and duration of follow-up. Burn *et al.* (2011) used an eligibility cut-off of 21 years based on concerns that continuation beyond this age might risk delaying preventive surgery. Indeed, there is a reluctance among FAP specialists to consider treatments that may delay colectomy, as in the vast majority of patients the decision to operate is not made on the biology of the disease but instead is dictated by a combination of social and educational factors, the aim being to impact as little as possible on the individual's personal development. Generally this involves performing surgery somewhere between the ages of 16 and 20 years, often during a long summer holiday to minimize interference with educational or work activities (Tudyka and Clark, 2012).

The studies also differed in whether to exclude patients with several polyps already present at baseline. This exclusion is beneficial in that it ensures a homogeneous study population. However, it reduces the potential patient number and may be attributed to the failure of the CHIP study, which stipulated that patients required less than 30 polyps that needed to be removed to render the colon polyp-free before the study drug could be given (Pfizer, 2014).

As illustrated by Burn *et al.* (2011) an adequate sample size for this rare disease can only be achieved by conducting a multinational, multicentre study. This has its own challenges, as different centres may have slightly different practices. Standardizing colonoscopy and polyp scoring procedures in FAP trials is notoriously difficult, and an area of research in its own right (Lynch *et al.*, 2013). Reproducible scoring of adenomas can probably best be achieved through the use of videos in which interobserver and intraobserver variation can be monitored, with scores averaged across a number of repeated measures (Lynch *et al.*, 2010, 2013).

Despite acknowledging that the design of a chemoprevention study in young patients with FAP presents many unique challenges, we considered that use of diet-derived agents with very favourable side effect profiles may offer a more attractive interventional agent for the paediatric setting. In adult cohorts of individuals at high familial risk for cancer, such agents

were perceived as ‘healthier’ than their synthetic counterparts, and thus were more likely to be considered acceptable in long-term prevention regimens (Iwuji *et al.*, 2014).

One such agent considered to have high acceptability within this cohort was the naturally occurring phytochemical curcumin. Curcumin is an extract of turmeric, a commonly used spice in Asia, where populations have a low incidence of CRC. Extensive preclinical data support the use of curcumin as a chemopreventive agent in FAP (Kawamori *et al.*, 1999; Mahmoud *et al.*, 2000), and in a small, uncontrolled study of five adults the combination of curcumin and quercetin was associated with a mean decrease in rectal and ileal polyp number and size (Cruz-Correa *et al.*, 2006). As already emphasized, the paediatric FAP population has proven a difficult cohort to target for such studies, obviating a need for prior engagement with this patient group to aid in study design, which has previously been demonstrated to lead to better uptake outcomes.

To this end, a questionnaire was designed, with the aim of obtaining the views of patients and their families affected by FAP to aid in the design of a chemoprevention study using curcumin as the model test agent.

Methods

Ethical approval for this study was granted by the NRES Committee South Central – Oxford A (REC reference 13/SC/0358). Patients affected by FAP or healthy parents of children with this condition were eligible to take part. There were separate sections for adults and a less extensive one for children to complete. Participants were recruited in one of the following three ways: directly by the clinical team when attending hospital appointments; by post to known FAP patients recorded on the local hospital database; or by e-mail invitation to members of the FAP gene patient support group (FAP Gene Support Group, 2015). Participants were given the option of responding either electronically or by returning a paper copy in a prepaid envelope. All responses were anonymous. χ^2 -Tables were used for comparisons between groups. A copy of the questionnaire can be found in Supplementary Table 1, Supplemental digital content 1, <http://links.lww.com/EJCP/A69>.

Results and discussion

Questionnaires were posted to the 21 FAP families on the local hospital database, e-mailed to 72 members on the mailing list of the FAP gene support group (FAP Gene Support Group, 2015), and 60 were distributed to patients attending clinics at the St Marks polyposis registry during the period of data collection (January 2014 to February 2015).

The characteristics and treatment history of the respondents are summarized in Table 2. The response rate was 25%, with 33 adults and six children completing the survey. Only one of the adults was a healthy parent of a child affected by FAP; the other 32 were diagnosed with FAP themselves. While typically the demographics of a FAP cohort would be equal proportions of men and women with ~ 75% being diagnosed before adulthood, this questionnaire generated more responses from women and the age of diagnosis was older than anticipated. These older patients most likely presented with de novo mutations that generally present symptomatically with either advanced adenomatous polyposis or CRC

(Tudyka and Clark, 2012). They were thus probably more highly motivated to complete the questionnaire as they had developed more severe symptoms than those diagnosed at a younger age with genetic testing.

Over 95% of respondents reported side effects following a colectomy (Fig. 1). This high percentage, rather than being a true representation of the complication rate itself, most likely represents the fact that those who have experienced difficulties were more motivated to complete the questionnaire.

Table 3 summarizes the respondents' experiences and ideas about chemoprevention and study design. However, because of the low response rate and non-representative patient demographics as detailed above it is questionable how generalizable these findings are to the FAP community as a whole. Over 80% stated that a tablet treatment that could delay polyp formation and thus postpone the need for surgery in children with FAP would be beneficial. There was no concordance about how long delaying a colectomy would be perceived as being beneficial, with responses ranging from just months to greater than 10 years.

Of interest, over half of the respondents reported a history of current or previous chemopreventive agent use. This suggests that there is some interest within the FAP community towards the concept of chemoprevention in an attempt to delay polyp formation, and some patients have been proactive in seeking it outside the setting of a clinical trial. Although this in itself is encouraging, the downsides include the potential to confound clinical trial findings. It could also be detrimental to recruitment if patients were not prepared to stop current agents to go on study. Many of the respondents did not have children with FAP. Thus, there was limited response to questions regarding trial design in this age group. However, of eight adult respondents five felt that it would be appropriate to stop current chemoprevention to go on study. Two of the three children taking curcumin stated they would stop it to go on trial instead, and one did not know.

Responses varied greatly with the perceived acceptable frequency of endoscopic investigations, with responses ranging from once every 6 months to once every 2 years.

An important consideration is the issue of acceptability of placebo to trial participants. Ten of 16 adults (63%) stated that they would still be happy if their child were to take part in a primary chemoprevention study with the possibility of being allocated to the placebo group, whereas 25% said no and 12% did not know. In contrast, the use of a placebo was of more importance to the six young patient respondents. Only 50% would partake if there was a placebo, with 33% replying no and 17% stating they did not know, whereas 83% would partake if they were guaranteed to receive curcumin at a specified dose.

Finally patients' previous experiences using curcumin were surveyed. Table 4 summarizes these findings. Responses demonstrated that it has generally been well tolerated and 80% of current or previous curcumin users would recommend its use to young FAP patients. Defining the dose and schedule in this paediatric population is a major factor in trial design. Doses taken ranged from 500 mg to 8 g daily in adult participants. No information was obtained on the children's doses in this questionnaire but a previous study on children with IBD demonstrated that doses up to 2 g twice daily were well tolerated (Suskind *et al.*, 2013).

Conclusion

Primary chemoprevention studies in young patients with FAP are lacking. The trials performed previously have experienced difficulties, particularly with poor recruitment and high dropout rates. How these issues are to be addressed requires considerable thought that should be centred around engagement with this particular group. Involving patient cohorts with trial design can lead to the development of clinical protocols that exhibit enhanced recruitment rates and study compliance, and so should be considered for paediatric FAP patients. A questionnaire was thus undertaken to assess whether a primary chemoprevention study of curcumin in FAP patients would be feasible.

Feedback demonstrated that there are some FAP patients for whom this study is relevant and desirable. Those with a personal history of curcumin use reported that it was tolerable and would recommend it to others. However, the poor response rate to the questionnaire, in particular the few responses from families at whom this trial would be directed, indicates that inadequate recruitment [such as that observed in the CHIP study (Pfizer, 2014)] is likely. One could speculate that the low response rate indicates that many are satisfied with the current standard of care. With modern laparoscopic surgical techniques a colectomy is not as major an undertaking as it has been previously.

A major challenge is to identify clinically relevant and measurable endpoints in FAP studies. The relevance of polyp number or size is unclear as the main research question is really whether these agents prevent colon cancer, which clearly would be an unethical endpoint. As a significant proportion of FAP deaths now occur because of extracolonic manifestations of the disease, such as duodenal cancers (Vasen *et al.*, 2008; Tudyka and Clark, 2012), these may be preferable endpoints. Other areas or unmet clinical need could be targeted towards preventing desmoids or cancers in the retained rectal stump following surgery. Curcumin studies in adult FAP patients are currently recruiting (US National Institutes of Health, 2015) and perhaps the results of these will provide more impetus to investigate the potential for use of such agents in the paediatric setting.

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Fig. 1.

The toxicities experienced by adult familial adenomatous polyposis respondents following a colectomy.

Table 1
Summary of primary chemoprevention studies in children and young patients with FAP

Study description	Number of participants	Age of participants	Inclusion criteria	Exclusion criteria ^a	Treatment/follow-up duration	Outcome	Toxicities	References
Randomized, double-blind, placebo-controlled study of sulindac	41	8–25	Mutation of the <i>APC</i> gene No endoscopically detectable colorectal adenomatous polyps No history of colonic surgery	NSAID or aspirin use for more than 1 week in the 3 months preceding the study Unwillingness to discontinue taking NSAIDs Body weight of less than 20 kg Specified blood parameters Refusal to use appropriate birth control	4 years	No effect	No significant differences in AEs by treatment assignment	Giardiello <i>et al.</i> (2002)
Phase I, dose escalation trial of celecoxib	18	10–14	Known colorectal adenomas (diagnosed by previous colonoscopy or flexible sigmoidoscopy), and/or an <i>APC</i> mutation	NSAID use (>3 doses/week in the preceding 3 months) Adenomas with severe dysplasia > 10 Adenomas that were >9 mm in size >100 Adenomas of any size	3 months	Reduction in the number of polyps over a 3-month period	No significant differences in AEs by treatment assignment	Lynch <i>et al.</i> (2010)
Randomized, double-blind, placebo-controlled study of aspirin +/- resistant starch	206	10–21	<i>APC</i> mutation or Linked DNA markers or the presence of Multiple colonic polyps, and/or multiple areas of congenital Hypertrophy of retinal pigment epithelium in the Context of a known FAP family history	Nonclassical FAP Current NSAID therapy Major intercurrent illness Pregnancy Advanced FAP was not a reason for exclusion unless surgery was planned within the next 12 months	1–12 years	No reduction in polyp count but there was a significant decrease in polyp size if treated for >1 year	One participant in the aspirin/RS arm withdrew because of persistent nose bleeds	Burn <i>et al.</i> (2011)

AEs, adverse events; *APC*, adenomatous polyposis coli; FAP, familial adenomatous polyposis; RS, resistant starch.

^a Agent specific exclusion criteria for example, history of peptic ulcer disease are not included on this table.

Table 2
Patient characteristics and treatment history of the questionnaire respondents

	Adult FAP patients [n (%)]	Information on child FAP patients provided by parents	Child FAP patient responses
Number of patients	32	5	6
Age			
Mean	42.1	13	11
Range	18–67	9–16	4–17
Sex			
Male	10 (31)	0	2
Female	20 (62)	0	3
Not recorded	2 (7)	5	1
Age at diagnosis			
Mean	30	9	Not assessed
Range	12–63	4–15	
Previous colectomy			
Yes	25 (78)	0	Not assessed
No	5 (16)	5	
Not recorded	2 (6)	0	
If yes, surgery performed			
IRA	10 (40)		
RPA	6 (24)		
TPCI	5 (20)		
Not recorded	4 (16)		
Age at colectomy			
Mean	29.15	NA	Not assessed
Range	13–56		

FAP, familial adenomatous polyposis; IRA, colectomy with ileorectal anastomosis; NA, not applicable; RPA, restorative proctocolectomy with the formation of an ileoanal pouch; TPCI, total proctocolectomy and ileostomy.

Table 3
Patients' experience and ideas about chemoprevention and clinical study design

	<i>n</i> (%)		
	Adult respondents ^a	Information on child FAP patients provided by parents	Children respondents
Currently using chemopreventive medicine ^b			
None	19 (59)	4 (80)	Not assessed
Curcumin	7 (22)	1 (20)	
Fish oil	5 (16)	1 (20)	
Sulindac	2 (6)	0	
Vitamin C	3 (9)	0	
Vitamin E	1 (3)	0	
Calcium carbonate	1 (3)	0	
Raloxifene	2 (6)	0	
Primrose	1 (3)	0	
Previously used chemopreventive medicine ^b			
None	17 (53)	4 (80)	Not assessed
Curcumin	5 (16)	0	
Fish oil	6 (19)	1 (20)	
Sulindac	3 (9)	0	
Vitamin C	2 (6)	0	
Vitamin E	2 (6)	0	
Raloxifene	1 (3)	0	
Aspirin	1 (3)	0	
Who recommended agent?			
Clinical trial	1 (7)	0	Not assessed
Specialist (not as part of a trial)	3 (21)	0	
Another patient	2 (14)	0	
Another family member	2 (14)	0	
Personal research	6 (43)	1 (50)	
Unknown	0	1 (50)	
Reason for stopping agent			
Side effects	3 (33)	0	Not assessed
Personal choice	1 (11)	0	
Expense	2 (22)	0	
Ulcers	1 (11)	0	
Informed it was ineffective	1 (11)	1 (100)	
Trial protocol	1 (11)	0	
Believe that a chemoprevention study in young patients would be beneficial ^b			
Yes	27 (82)	NA	5 (83)
No	1 (3)		0

	<i>n</i> (%)		
	Adult respondents ^a	Information on child FAP patients provided by parents	Children respondents
Don't know	3 (9)		1 (17)
Unreported	2 (6)		0
What is the minimum time that is worthwhile to delay surgery by using chemoprevention ^b ?			
< 1 year	6 (18)	NA	0
1–2 years	1 (3)		2 (33)
2–5 years	7 (21)		0
5–10 years	4 (12)		1 (17)
> 10 years	4 (12)		1 (17)
Don't know	5 (15)		1 (17)
Not reported	6 (18)		1 (17)
The youngest age believed appropriate to treat a child with FAP with curcumin in a clinical study			
<8	4 (12)	NA	1 (17)
8–10	3 (9)		2 (33)
10–12	8 (24)		2 (33)
12–14	7 (21)		1 (17)
14–16	1 (3)		0
>16	2 (6)		0
Do not know	5 (15)		0
Not reported	3 (9)		0
What is the longest time that you feel it would be acceptable for a child/young person with FAP to take curcumin as part of a clinical trial?			
< 6 months	2 (6)	NA	0
6–12 months	3 (9)		0
12–24 months	1 (3)		1 (17)
> 10 years	2 (6)		1 (17)
Until there is a significant increase in polyp number and size	13 (39)		3 (50)
Until colectomy	6 (18)		1 (17)
Not reported	6 (18)		0
What is the maximum number of doses appropriate for a young person to take as part of a clinical study?			
0	1 (3)	NA	0
1	1 (3)		0
2	10 (30)		1 (17)
3	2 (6)		2 (33)
4	5 (16)		1 (17)
> 4	1 (32)		0
Don't know	11 (35)		2 (33)
What are the maximum number of tablets appropriate for a young person to take as part of a clinical study?			

	<i>n</i> (%)		
	Adult respondents ^a	Information on child FAP patients provided by parents	Children respondents
1–2	3 (10)	NA	1 (17)
3–4	11 (37)		0
5–6	3 (10)		0
7–8	3 (10)		1 (17)
9–10	1 (3)		0
11–12	0		1 (17)
>12	1 (3)		0
Don't know	8 (27)		3 (50)
Would it be appropriate for young person with FAP to have an endoscopy purely for research purposes?			
Research purposes	5 (15)	NA	3 (50)
Clinical follow-up only	21 (63)		2 (33)
Don't know	4 (12)		1 (17)
Not reported	3 (9)		
What is the maximum frequency of endoscopies that would be acceptable for a child/young person with FAP to have?			
Only when clinically indicated	9 (27)	NA	1 (17)
Once every 6 months	6 (18)		2 (33)
Once every year	12 (36)		0
Once every 2 years	3 (9)		1 (17)
< every 2 years	0		1 (17)
Don't know	1 (3)		1 (17)
Not reported	2 (6)		0
Are clinic or telephone consultations preferable to assess how a young person with FAP is tolerating the study medication?			
Clinic	6 (18)	NA	2 (33)
Telephone	5 (15)		1 (17)
Either	15 (45)		3 (50)
Don't know	2 (6)		0
Not reported	5 (15)		0

FAP, familial adenomatous polyposis; NA, not applicable.

^a *n* = 32 plus responses from one unaffected parent included when relevant.

^b Some respondents were using multiple agents.

Table 4
Experiences of curcumin reported

	Adult FAP patients	Information on child FAP patients provided by parents	Child FAP patients responses
Ever taken curcumin			
Yes	7	1	3
No/not reported	25	4	3
Experienced side effects			
Yes	1	0	1
No	5	0	2
Don't know	1	1	0
If yes, what			
Loose stools	1	NA	0
Abdominal pain	1		1
Would patients recommend curcumin to young FAP patients?			
Yes	6	NA	2
No	1		1

FAP, familial adenomatous polyposis; NA, not applicable.