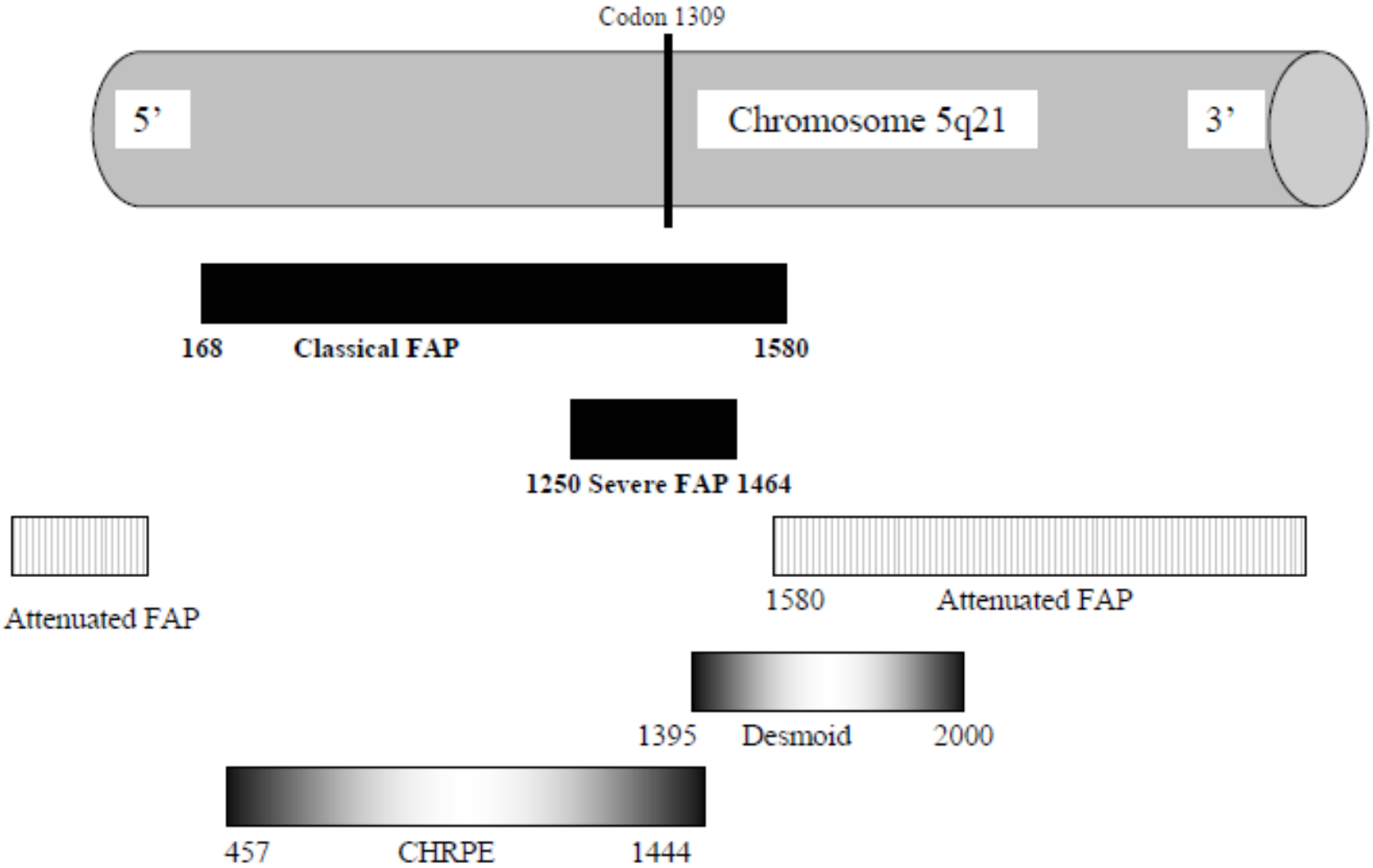
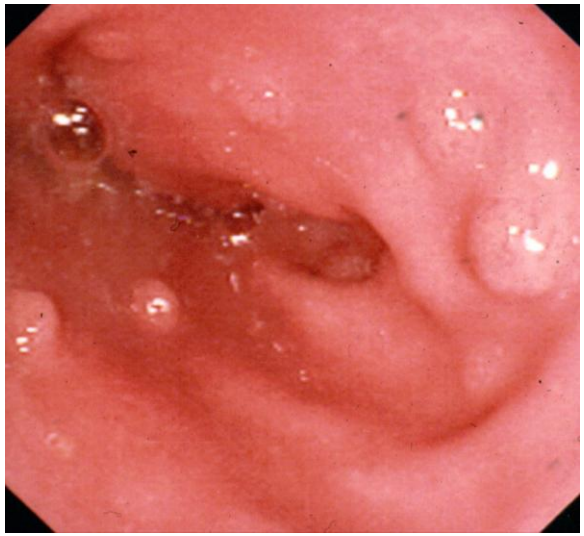
Polyposis in children, and the CHIP study

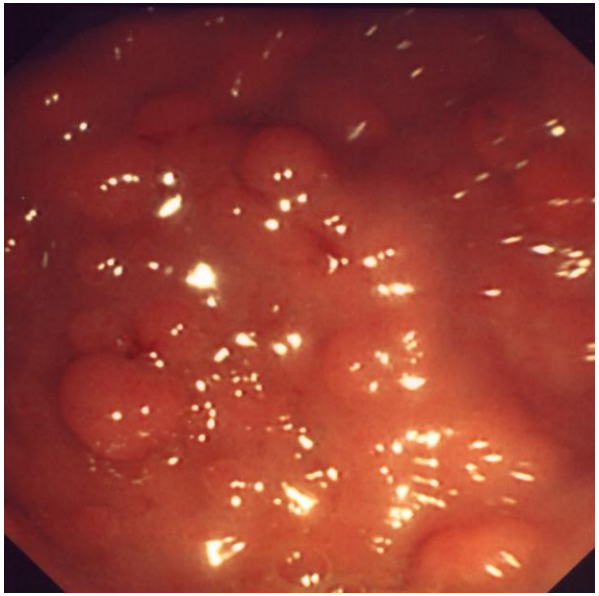
Dr Warren Hyer
Consultant Paediatric Gastroenterologist
Northwick Park and St Mark's Hospital


Codon 1309
5'
Chromosome 5q21
3'
168
Classical FAP
1580
1250 Severe FAP 1464
Attenuated FAP
1580
Attenuated FAP
1395
Desmoid
2000
457
CHRPE
1444

Natural history of paediatric FAP

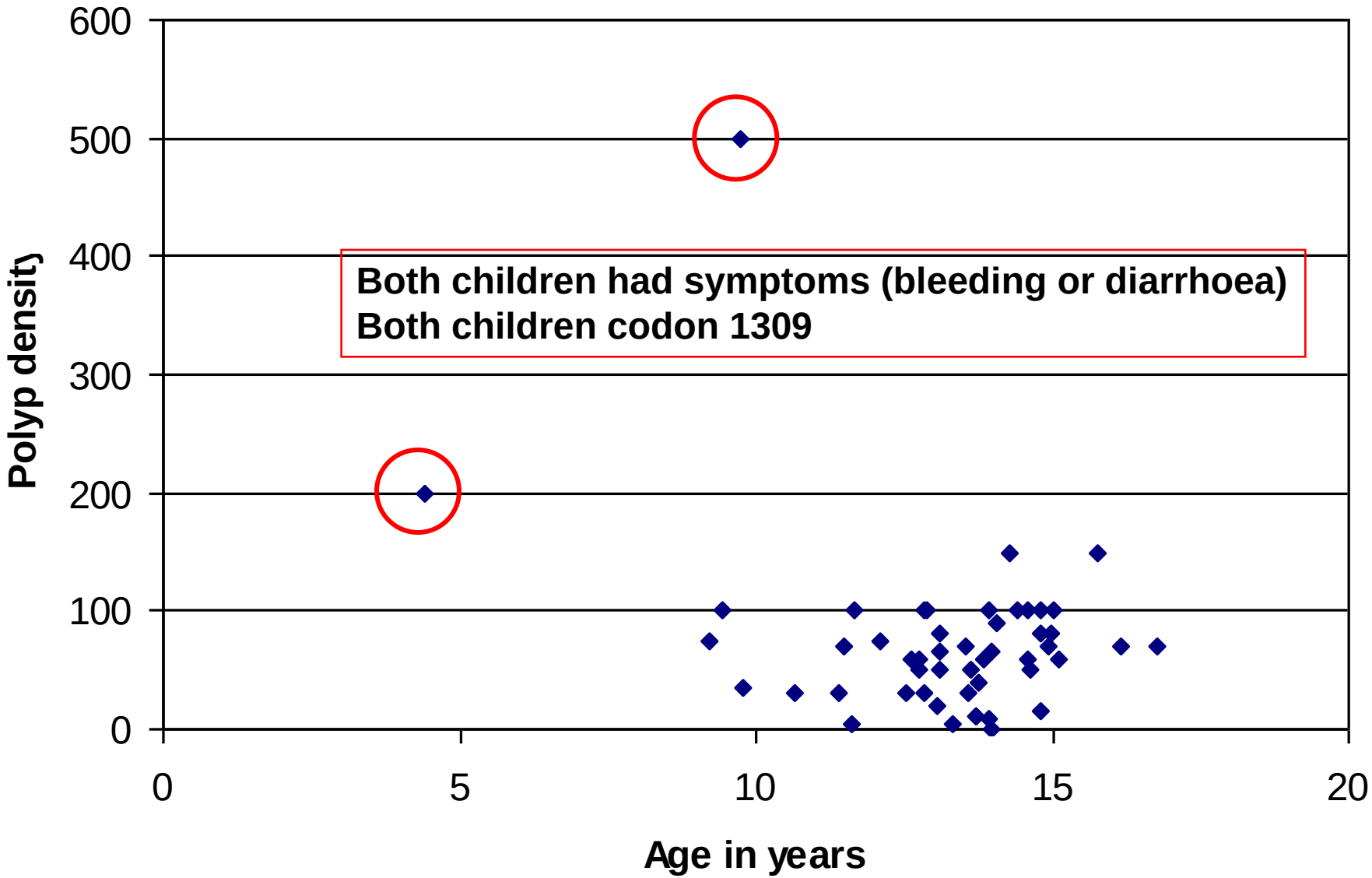


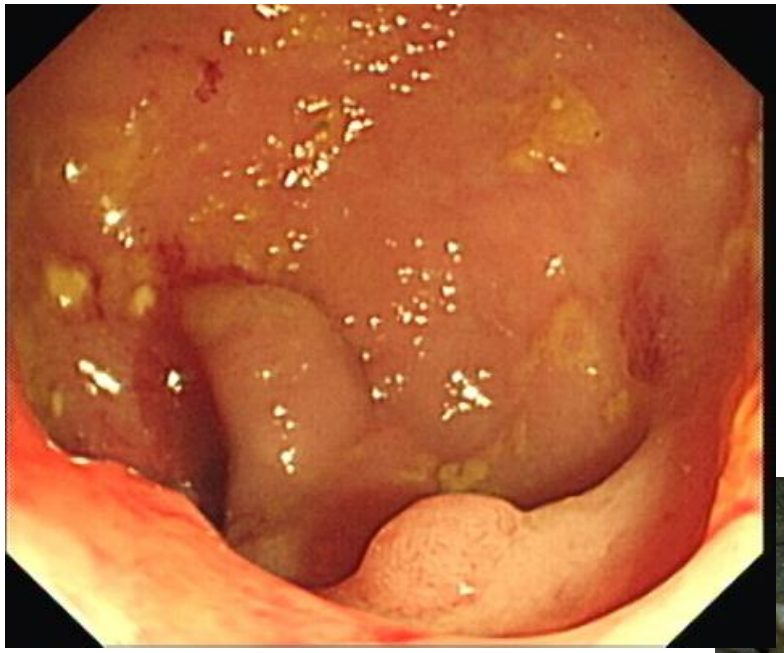
? Too early

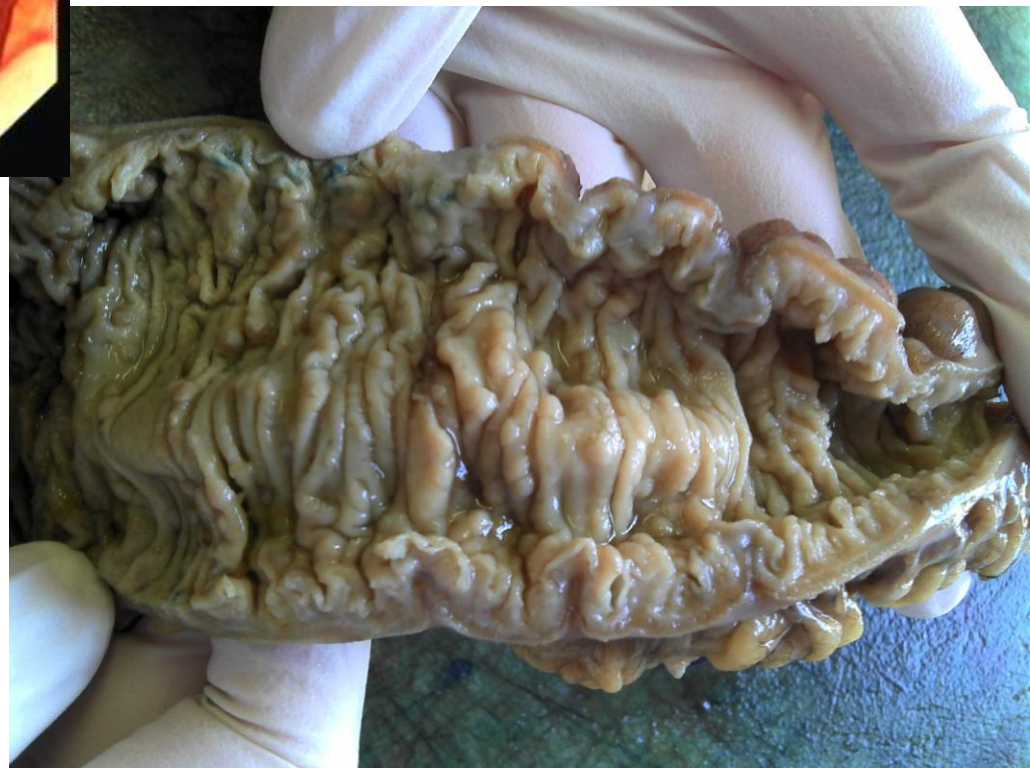


Too late?

Which children had high polyp density?







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But when will a patient develop a cancer?

Table 3 Proportion of FAP patients with CRC diagnosed at $\leqslant$20 years of age*

Polyposis registry	Total number of CRCs	Number of CRCs (%) diagnosed		
		0–10 years	11–15 years	16–20 years
The Netherlands	106	0	1	1
Denmark	190	0	0	3
Germany	524	0	1	7
St Mark's	96	0	0	3
Finland	157	0	0	1
Total	1073	0	2 (0.2%)	15 (1.3%)

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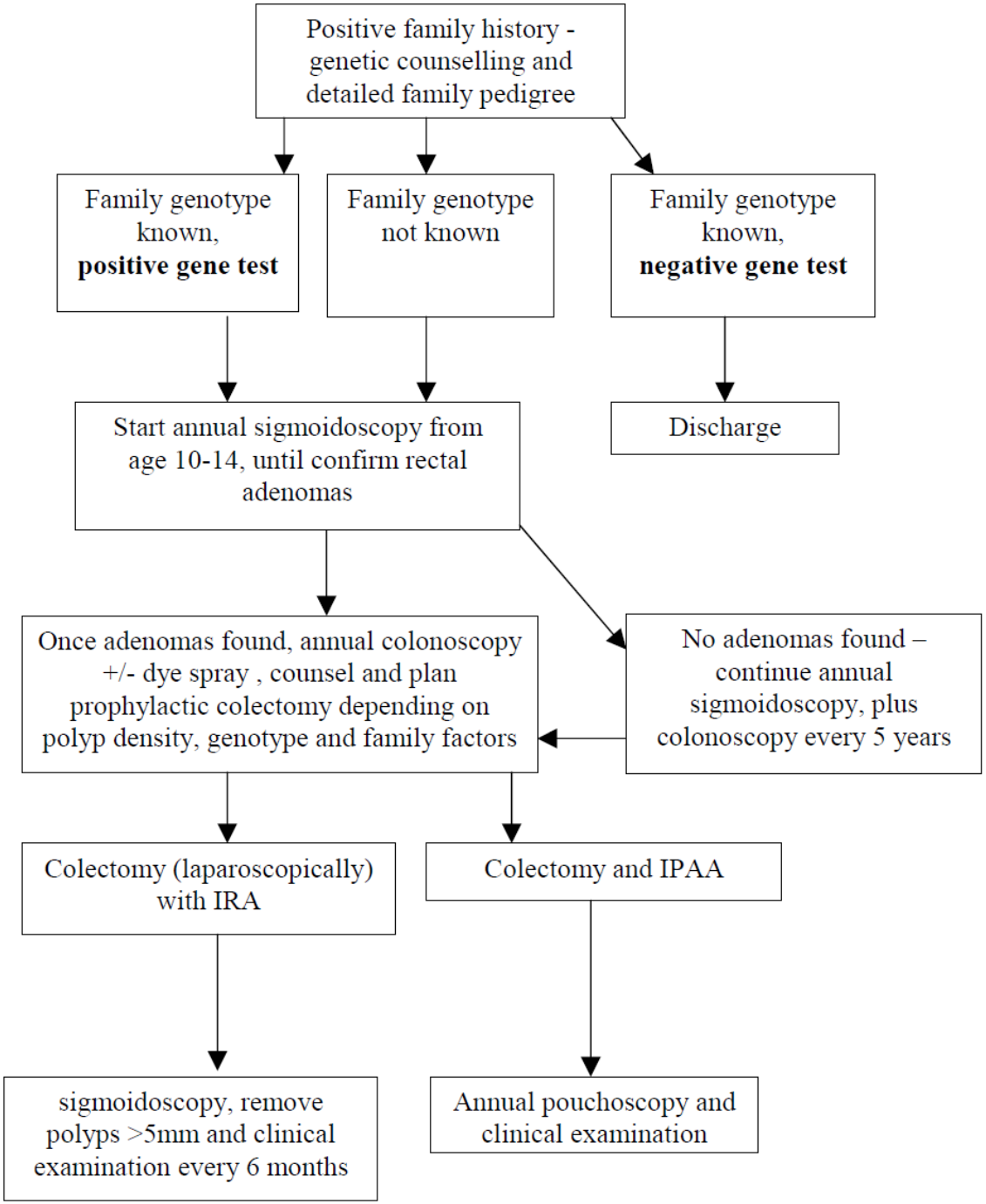
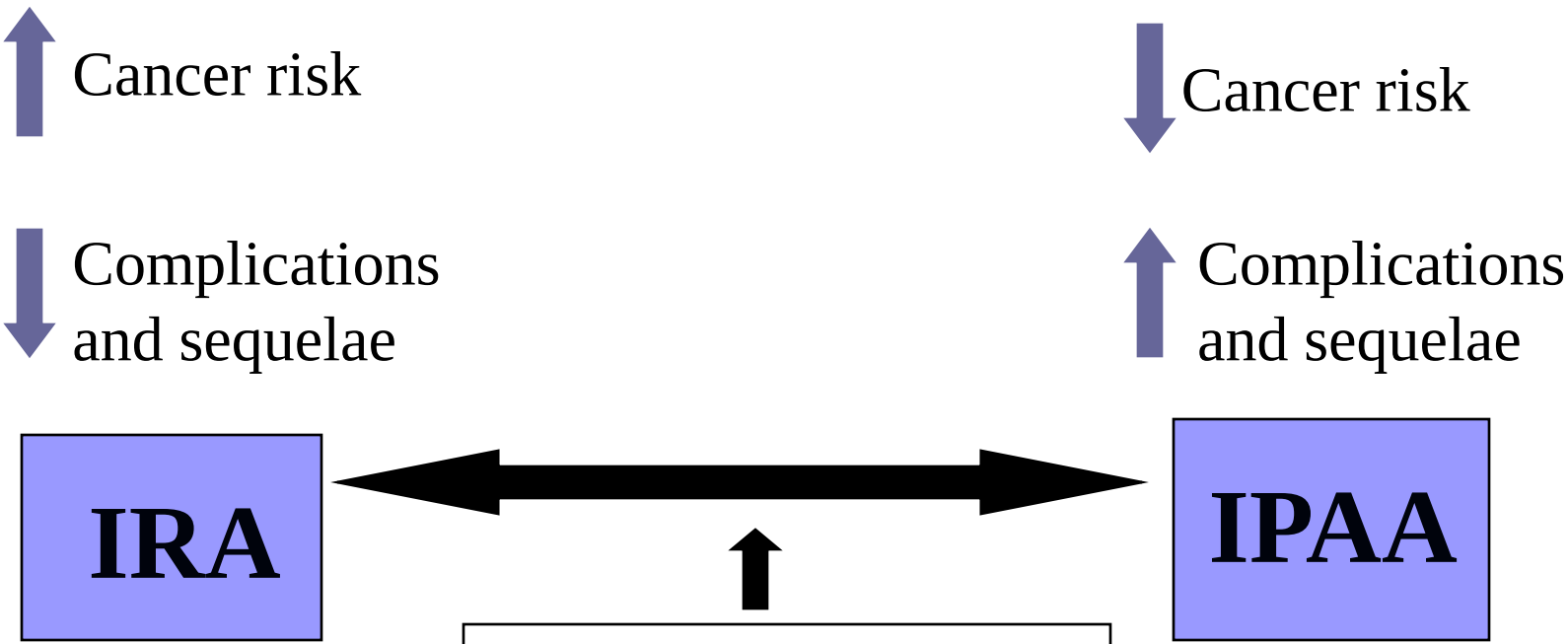
Guidelines for the clinical management of familial adenomatous polyposis (FAP)

H F A Vasen,[1] G Möslein,[2] A Alonso,[3] S Aretz,[4] I Bernstein,[5] L Bertario,[6] I Blanco,[7] S Bülow,[8] J Burn,[9] G Capella,[10] C Colas,[11] C Engel,[12] I Frayling,[13] W Friedl,[4] F J Hes,[14]



Colectomy in adolescents- IRA or IPAA? St Mark's approach



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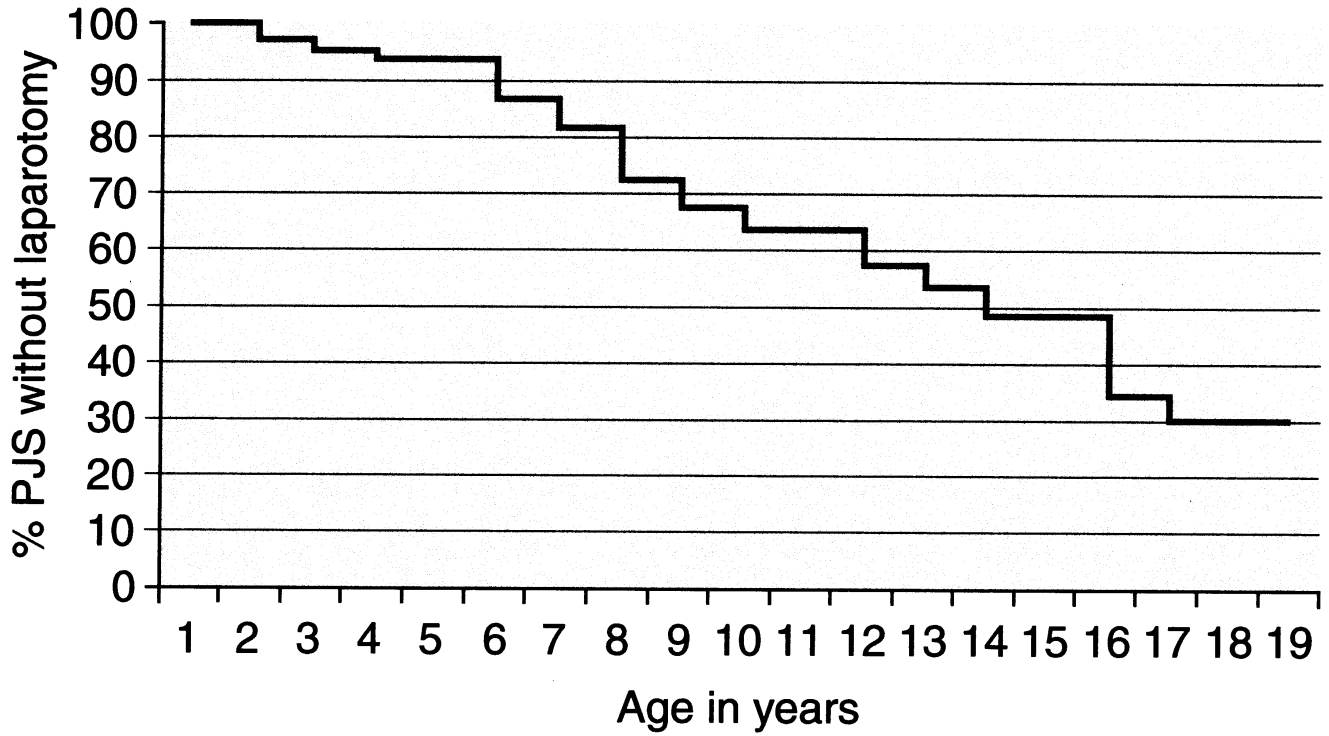
Complications of Childhood Peutz-Jeghers Syndrome: Implications for Pediatric Screening

*R. Hinds, †C. Philp, †W. Hyer, and *J. M. Fell

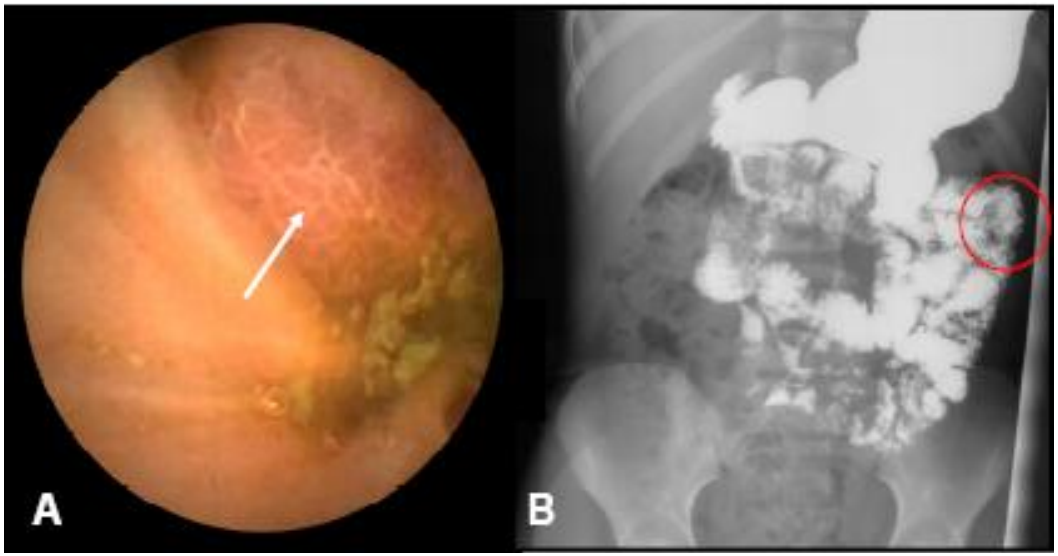
*Department of Paediatric Gastroenterology, Chelsea and Westminster Hospital, London; and the †The Polyposis Registry, St. Mark's Hospital, London, England



The end of the barium in PJS…..VCE is not perfect enough….

ABSTRACT

Video Capsule Endoscopy in the management of children with Peutz-Jeghers Syndrome: a blinded comparison with Barium Enterography for the detection of small bowel polyps.



Postgate A, Hyer W, Phillips R, Brown G, Schofield G, Burling D, Gupta A, Marshall M, Bartram C, Taylor S, Latchford A, Bassett P, Fitzpatrick A, **Fraser C**

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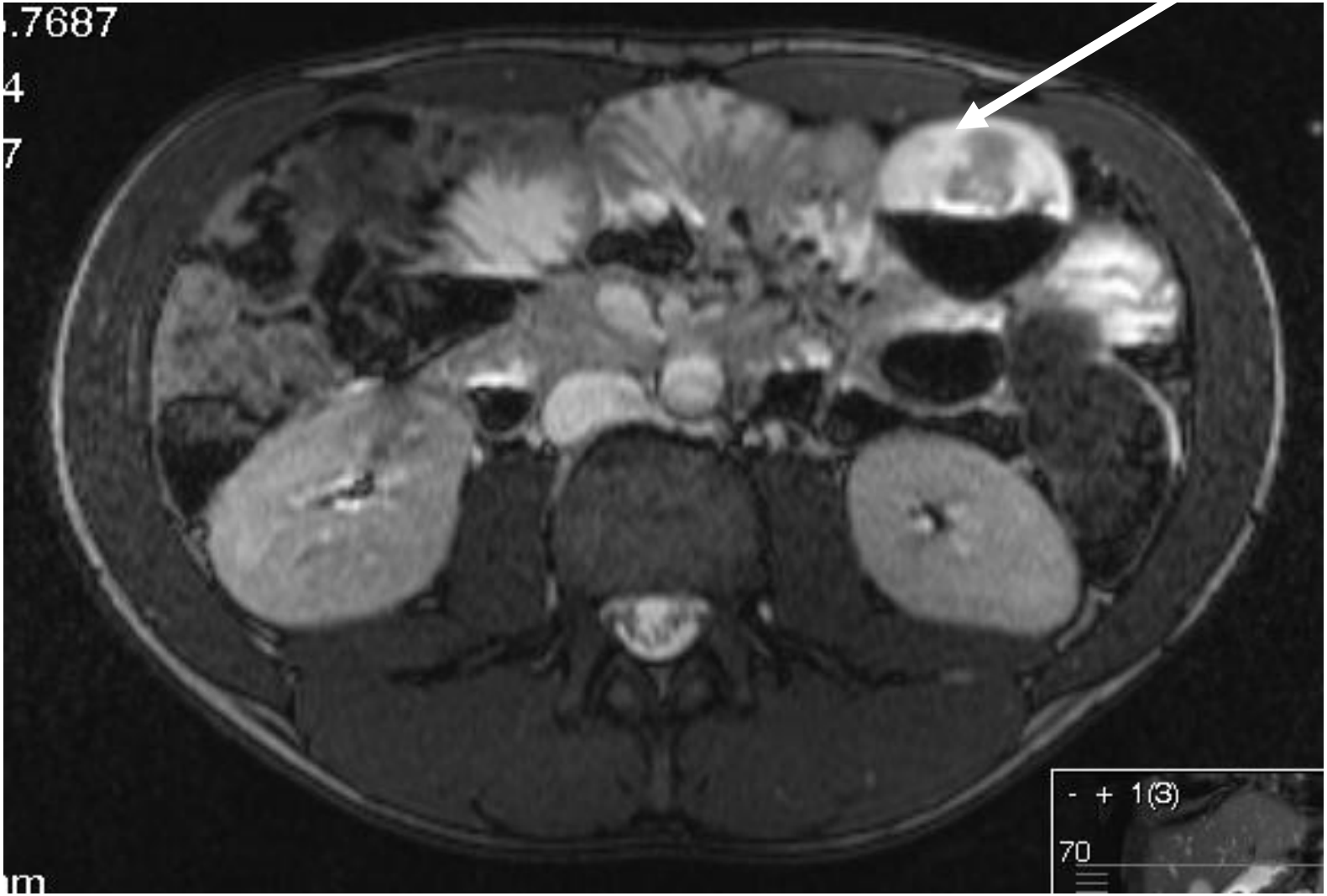
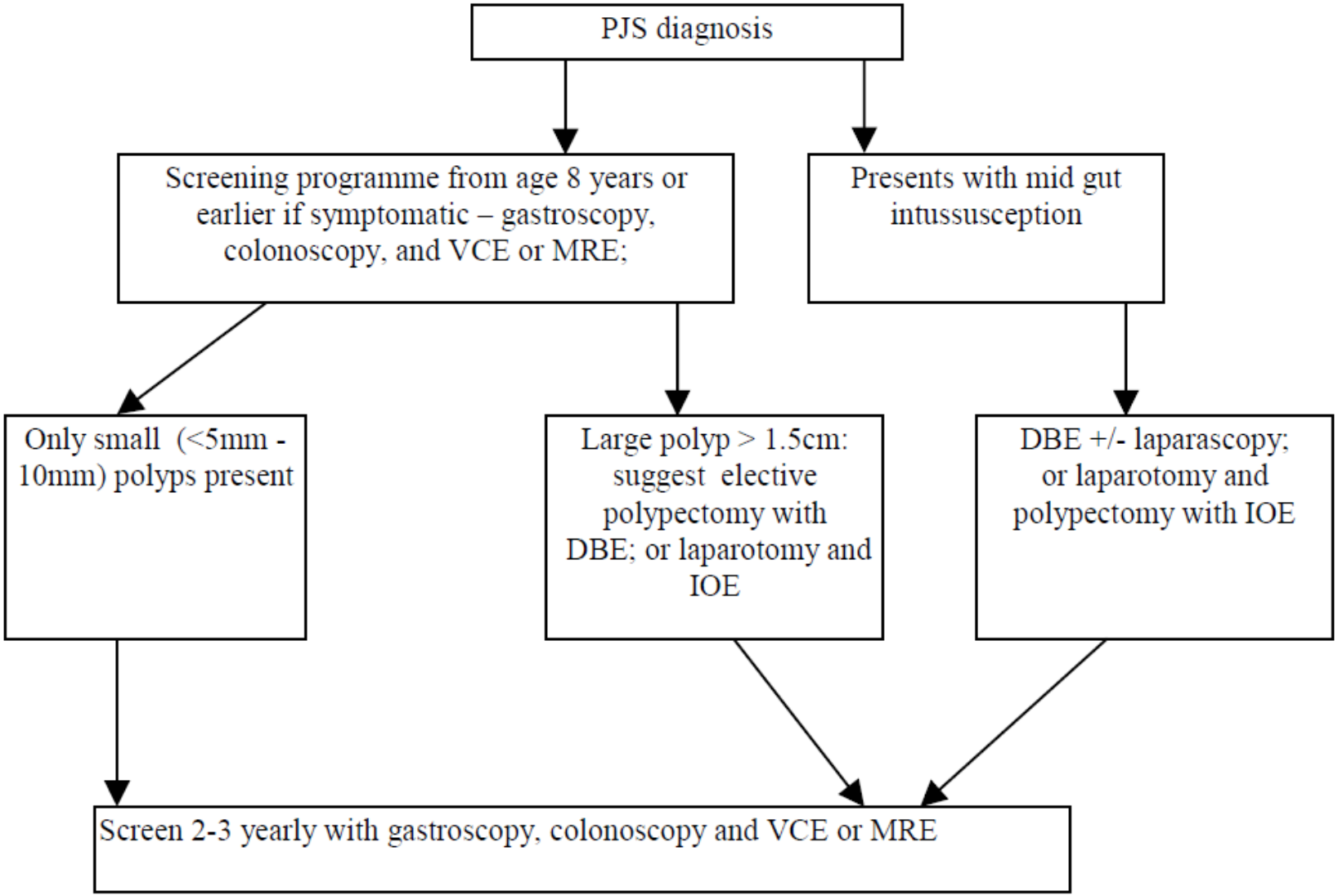


Close correlation between MRI and capsule endoscopy in adults (and children) with PJS. Gut 2009 Postgate A et al (n=9)



DBE= double balloon enteroscopy
IOE = intra-operative enteroscopy
MRE = magnetic resonance enterography

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Double balloon enteroscopy in children

Adult case series/reports:

Small-Intestinal Peutz-Jeghers Polyps Resected by Endoscopic Polypectomy with Double-Balloon Enteroscopy and Removal Confirmed by Ultrasonography

Y. Matsumoto · N. Manabe · S. Tanaka · A. Fukumoto · T. Yamaguchi · M. Shimamoto · M. Nakao · Y. Mitsuoka · K. Chayama

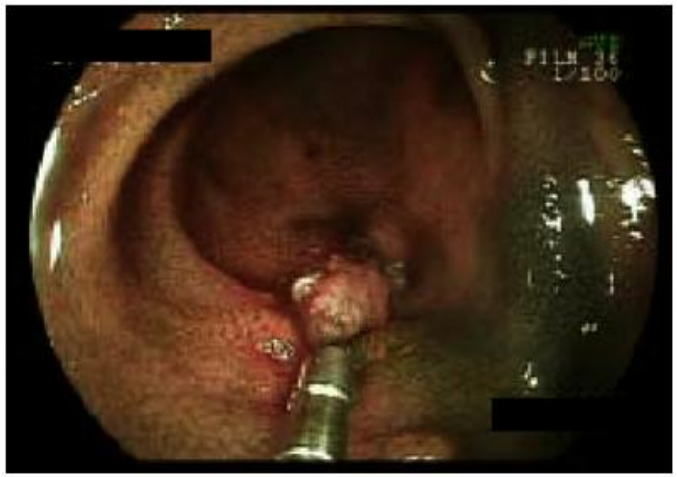
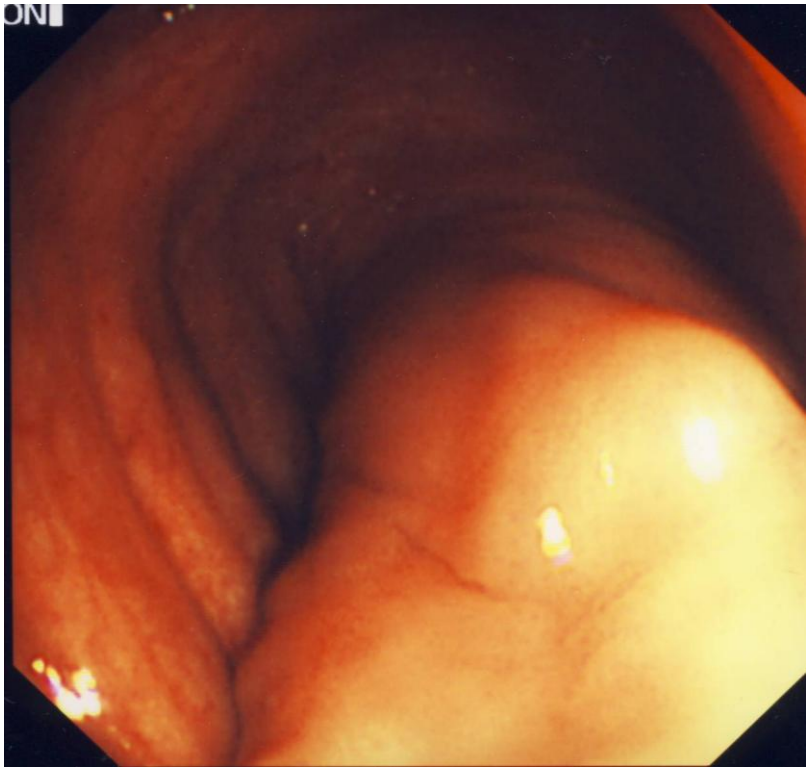
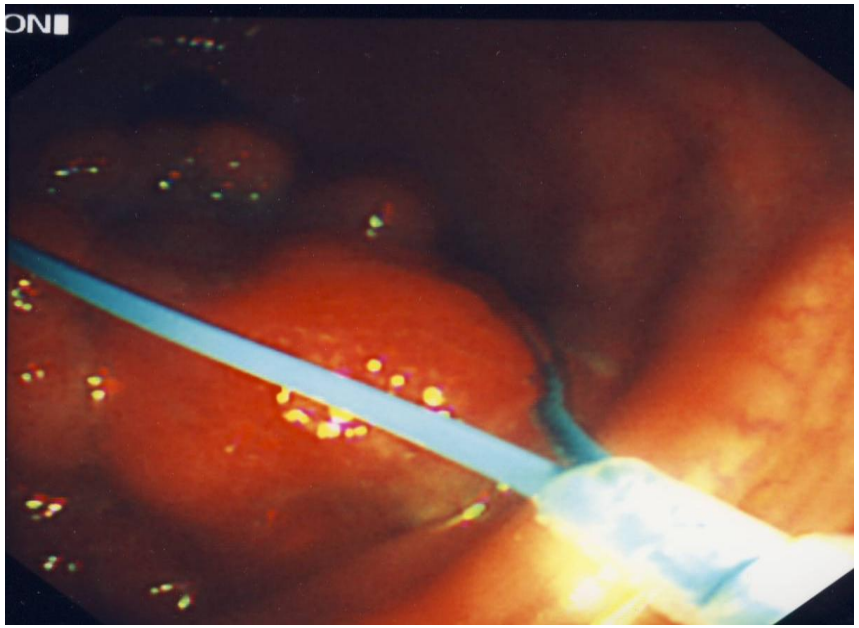


Fig. 5 DBE image showed that the polyp was resected, and the ulcer was clipped

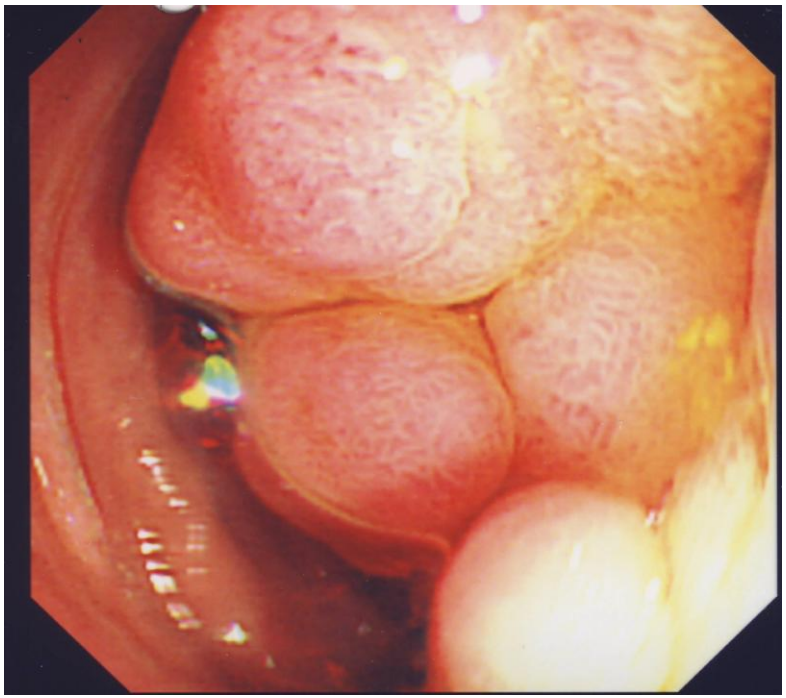
- But how big a polyp can we resect without injury to the submucosa?
- Lacking evidence and experience with DBE, and polypectomy in PJS in children

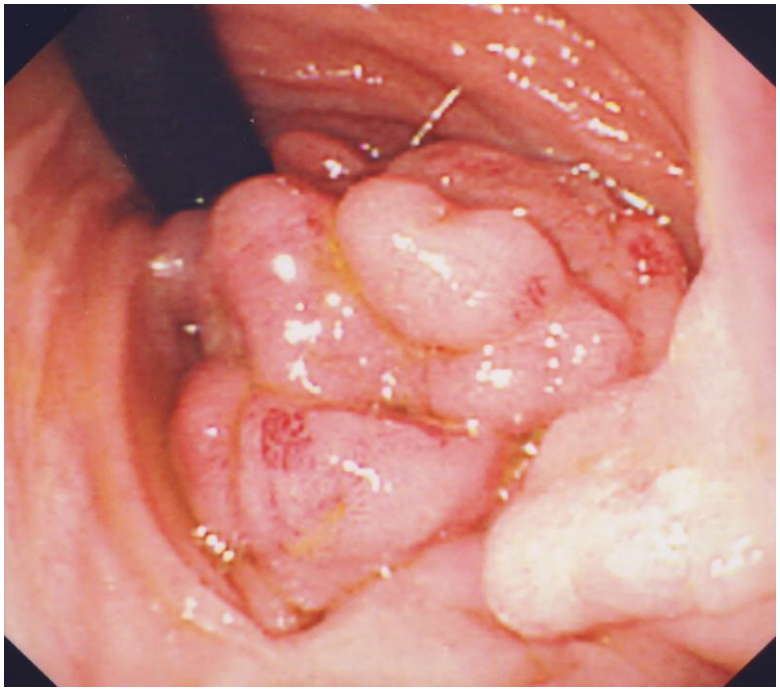
What polyp is too big in a child?



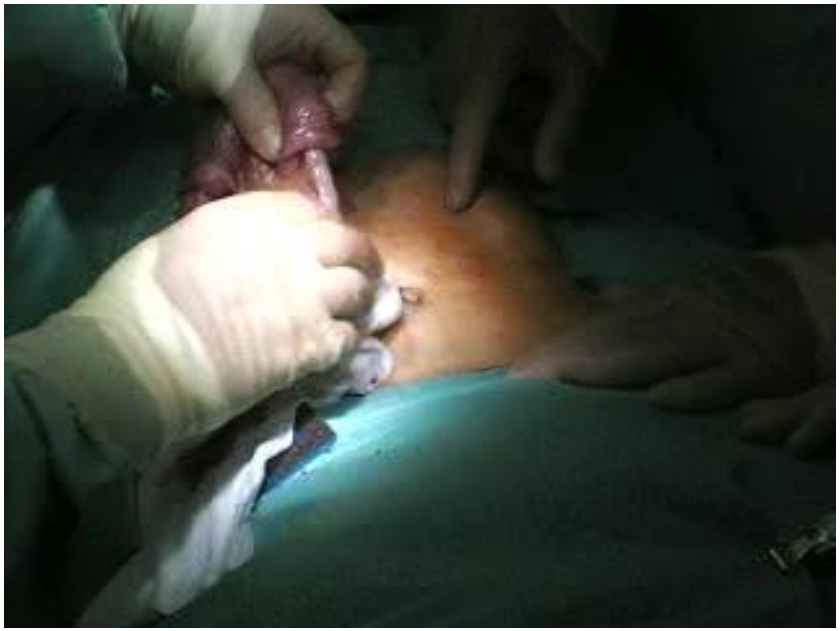


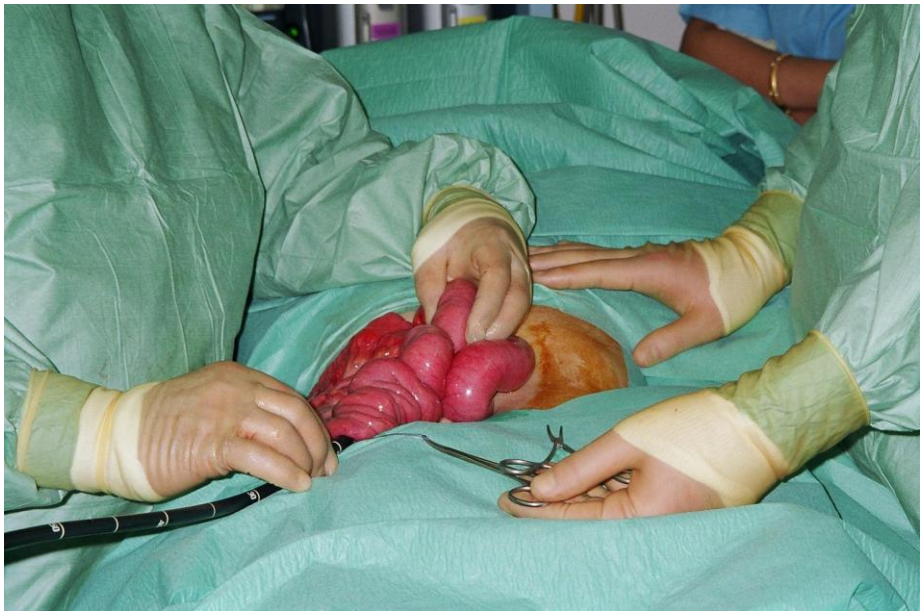
Closer prediction about surgical/endoscopic choices



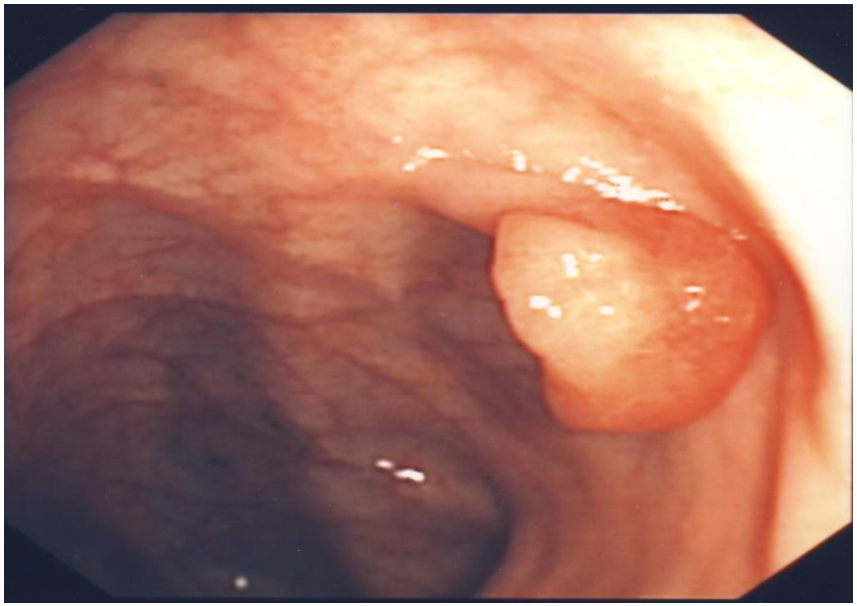


Surgery in PJS





Juvenile polyposis



Unwinding the Heterogeneous Nature of Hamartomatous Polyposis Syndromes

John M. Carethers, MD

IN ANY CLASSIC "WHODUNIT" MYSTERY, THE GOAL OF THE investigator is to find and expose the guilty party. At the onset, there may be many suspects, some of whom may appear guilty. However, the shrewd investigator picks through those distractors to clearly eliminate them and focuses on specific details to finally identify the true culprit. The same approach holds for the recognition of the hamartomatous polyposis syndromes, many of which demonstrate phenotypic features that overlap with each other.

See also p 2465.

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Corresponding Author: John M. Carethers, MD, GI Section, 111D, Veterans Administration San Diego Healthcare System, 3350 La Jolla Village Dr, San Diego, CA 92161 (jcarethers@ucsd.edu).

Issues for the severe infantile juvenile polyposis /Bannayan- Riley-Ruvalcaba

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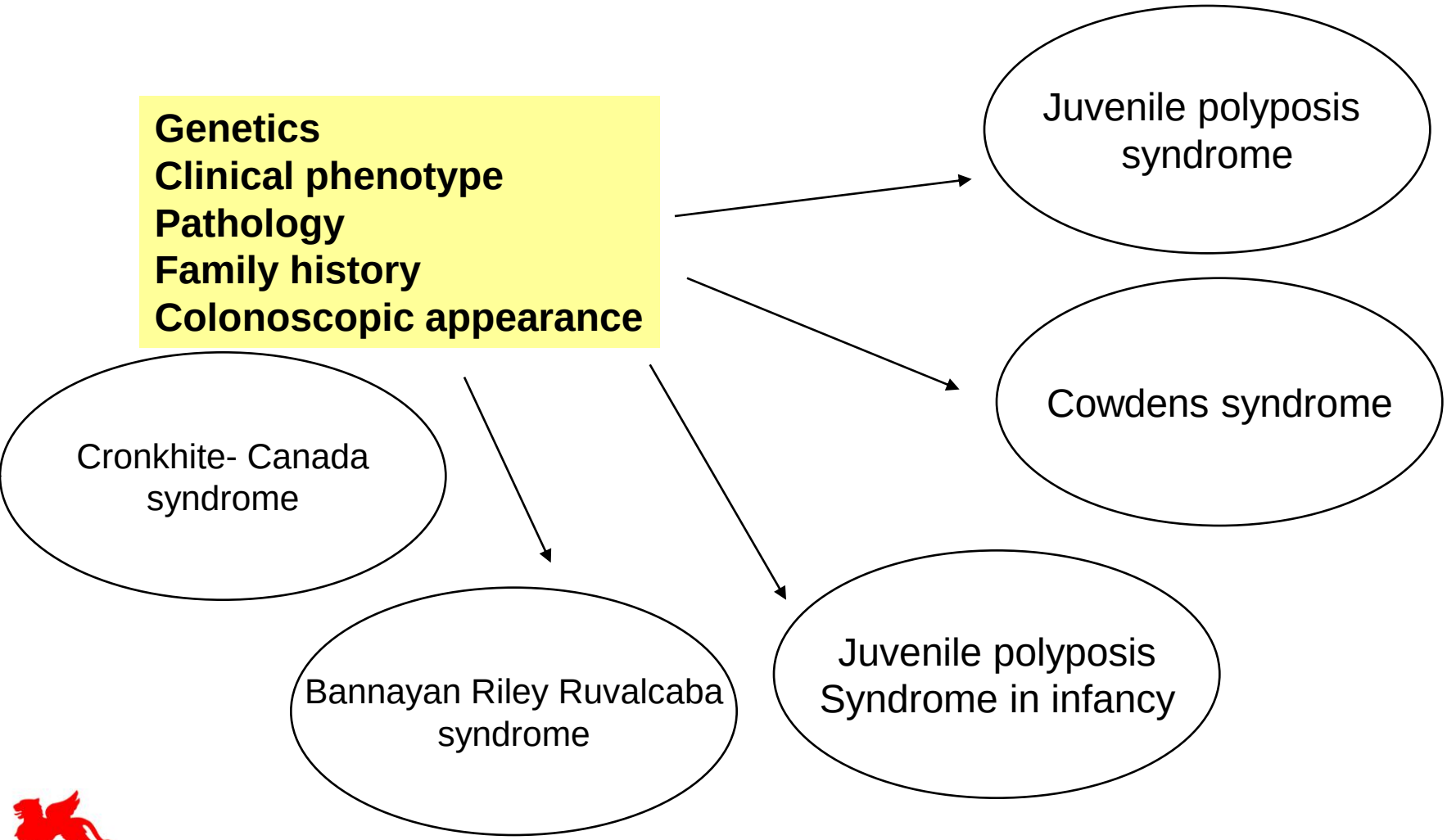
Unpicking the hamartomous syndromes – 21st century style



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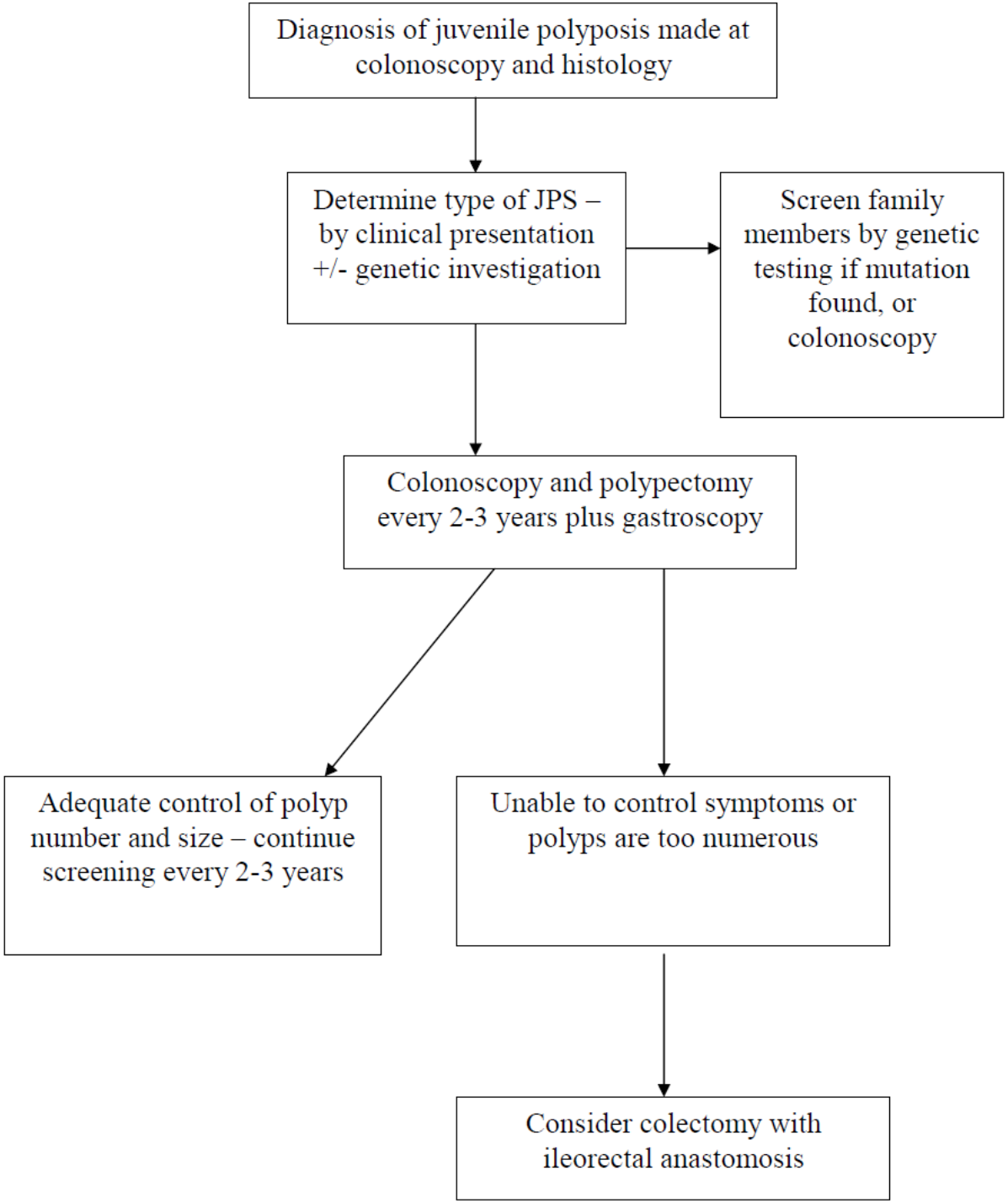
What genetics?

- LKB1
  - PJS
- PTEN
  - 85% of Cowden
  - 65% of Bannayan Riley Ruvalcaba syndrome
  - JPS
- SMAD 4
  - 20-50% JPS
- BMPR1A
  - 20-40% of JPS
- ENG
  - JPS, HHT



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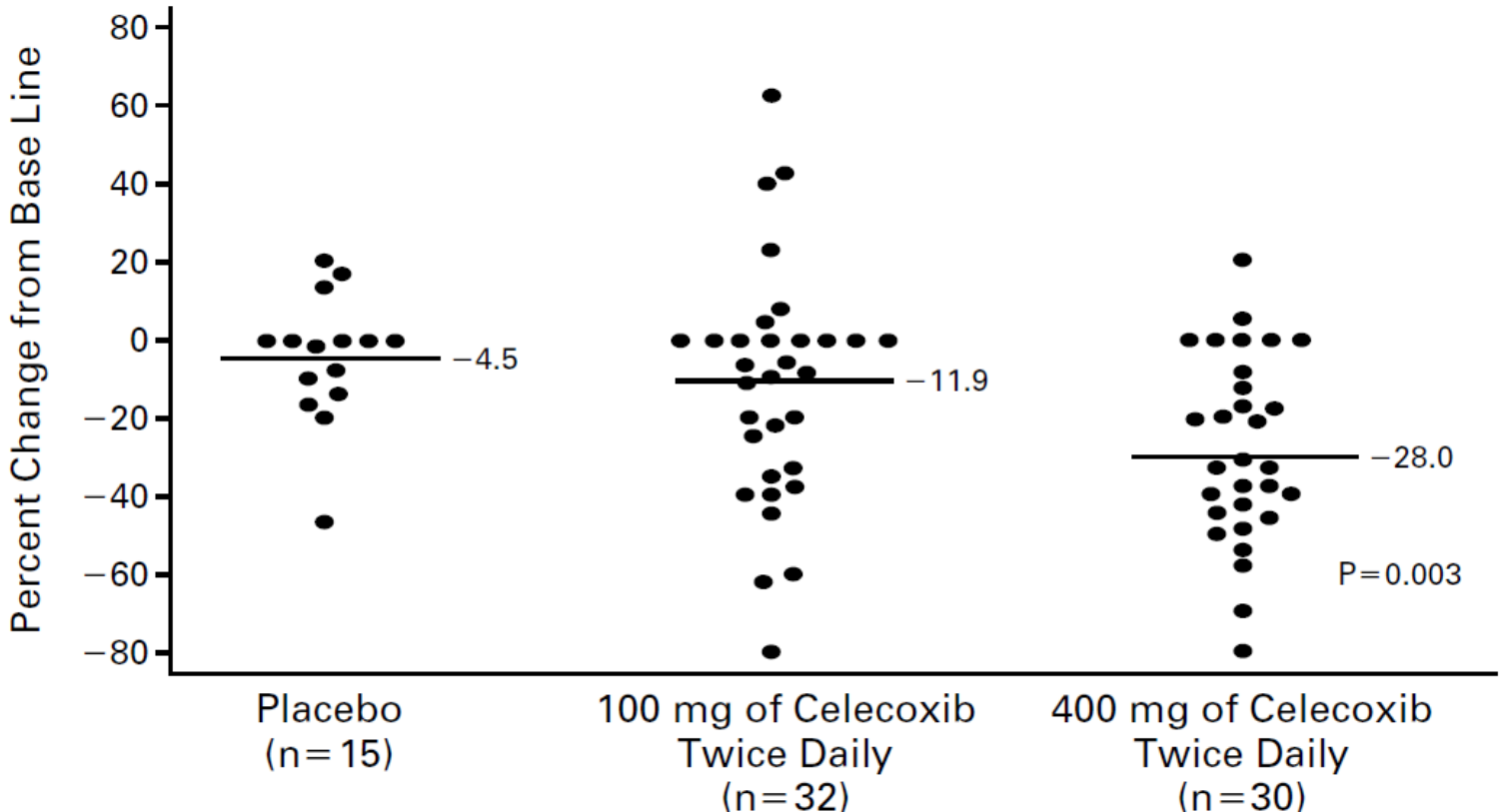
Now the chance for adenoma prevention?

The New England Journal of Medicine

THE EFFECT OF CELECOXIB, A CYCLOOXYGENASE-2 INHIBITOR, IN FAMILIAL ADENOMATOUS POLYPOSIS

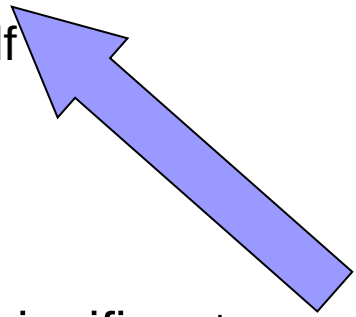
GIDEON STEINBACH, M.D., PH.D., PATRICK M. LYNCH, M.D., J.D., ROBIN K.S. PHILLIPS, M.B., B.S., MARINA H. WALLACE, M.B., B.S., ERNEST HAWK, M.D., M.P.H., GARY B. GORDON, M.D., PH.D., NAOKI WAKABAYASHI, M.D., PH.D., BRIAN SAUNDERS, M.D., YU SHEN, PH.D., TAKASHI FUJIMURA, M.D., LI-KUO SU, PH.D., AND BERNARD LEVIN, M.D.



How might Coxibs cause increased MI risk

- Depression of I_2 prostaglandin formation
- Elevate blood pressure
- Accelerate atherogenesis
- Thus exaggerated thrombotic response

"The higher a **patient's intrinsic risk of cardiovascular disease**
The more likely it would be that such a hazard would manifest itself
Rapidly in the form of a clinical event"



insignificant
in an adolescent

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Celecoxib for the Prevention of Colorectal Adenomatous Polyps

Nadir Arber, M.D., Craig J. Eagle, M.D., Julius Spicak, M.D., István Rácz, M.D.,

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 31, 2006 VOL. 355 NO. 9

Celecoxib for the Prevention of Sporadic Colorectal Adenomas

Monica M. Bertagnolli, M.D., Craig J. Eagle, M.D., Ann G. Zauber, Ph.D., Mark Redston, M.D.,

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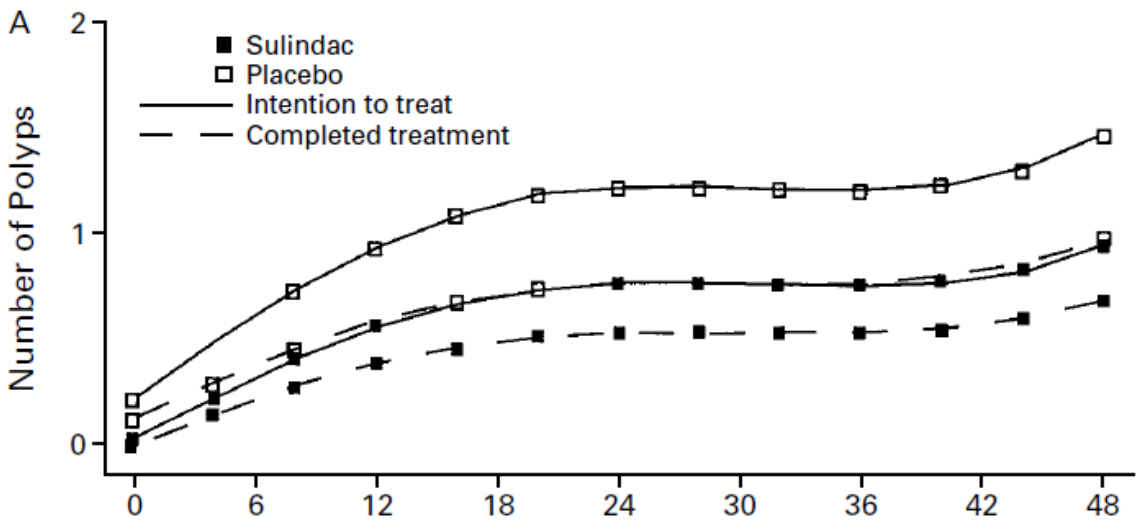
Adenoma prevention with sulindac

The New England Journal of Medicine

PRIMARY CHEMOPREVENTION OF FAMILIAL ADENOMATOUS POLYPOSIS WITH SULINDAC

FRANCIS M. GIARDIELLO, M.D., VINCENT W. YANG, M.D., PH.D., LINDA M. HYLIND, B.S., R.N., ANNE J. KRUSH, M.S., GLORIA M. PETERSEN, PH.D., JILL D. TRIMBATH, M.S., STEVEN PIANTADOSI, M.D., PH.D., ELIZABETH GARRETT, PH.D., DEBORAH E. GEIMAN, M.S., WALTER HUBBARD, PH.D., G. JOHAN A. OFFERHAUS, M.D., M.P.H., PH.D., AND STANLEY R. HAMILTON, M.D.

Sulindac did not slow the development of adenomas



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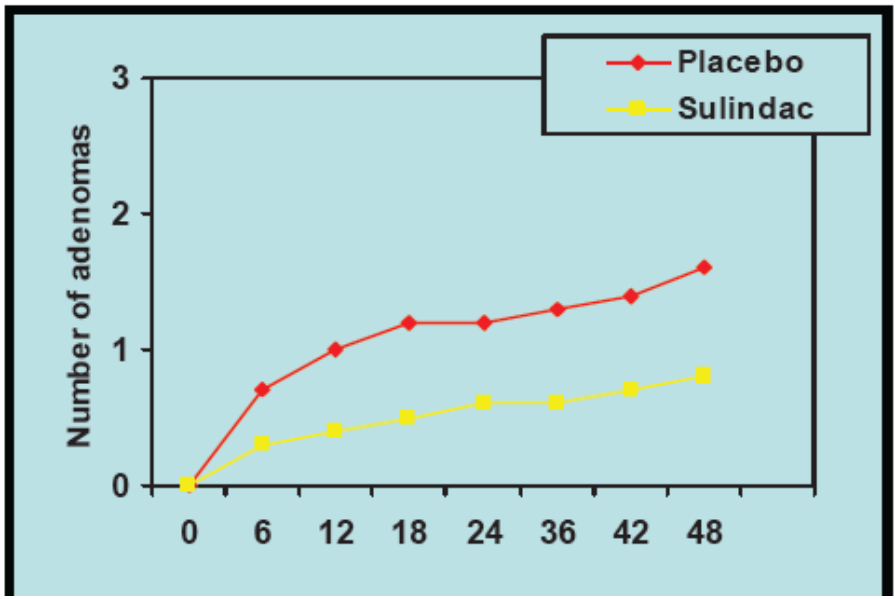
Effect of Sulindac on Rectal Polyps in Pediatric APC Carriers

N = 41
Age = 8-25 yrs
Placebo, sulindac 75 mg or 150 mg BID
Flexible sigmoidoscopy q 4 months

End of study Effect on Adenomas	Sulindac N=21 (%)	Placebo N =20 (%)
0	12 (57)	9 (45)
1-10	3 (14)	6 (30)
Adenoma ≥ 2.5 mm	4 (19)	7 (35)
Tubular Adenoma	9 (43)	11 (55)



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The Safety and Efficacy of Celecoxib in Children With Familial Adenomatous Polyposis

Patrick M. Lynch, MD, JD[1], Gregory D. Ayers, MS[2], Ernie Hawk, MD, MPH[3], Ellen Richmond, RN, MSN[3], Craig Eagle, MD[4], Mabel Woloj, PhD[4], James Church, MD[5], Hennie Hasson, RN[6], Sherri Patterson, RN[7], Elizabeth Half, MD[8] and Carol A. Burke, MD[8]

Table 1. Celecoxib dose assignments by body weight and cohort

	Cohort 1, *n*=6 (2:1 drug: placebo)	Cohort 2, *n*=6 (2:1 drug: placebo)	Cohort 3, *n*=6 (2:1 drug: placebo)
Body weight	Celecoxib dose 4 mg/kg	Celecoxib dose 8 mg/kg	Celecoxib dose 16 mg/kg
25.0–37.5 kg	50 mg BID	100 mg BID	200 mg BID
37.6–50.0 kg	100 mg BID	150 mg BID	300 mg BID
>50.0 kg	100 mg BID	200 mg BID	400 mg BID

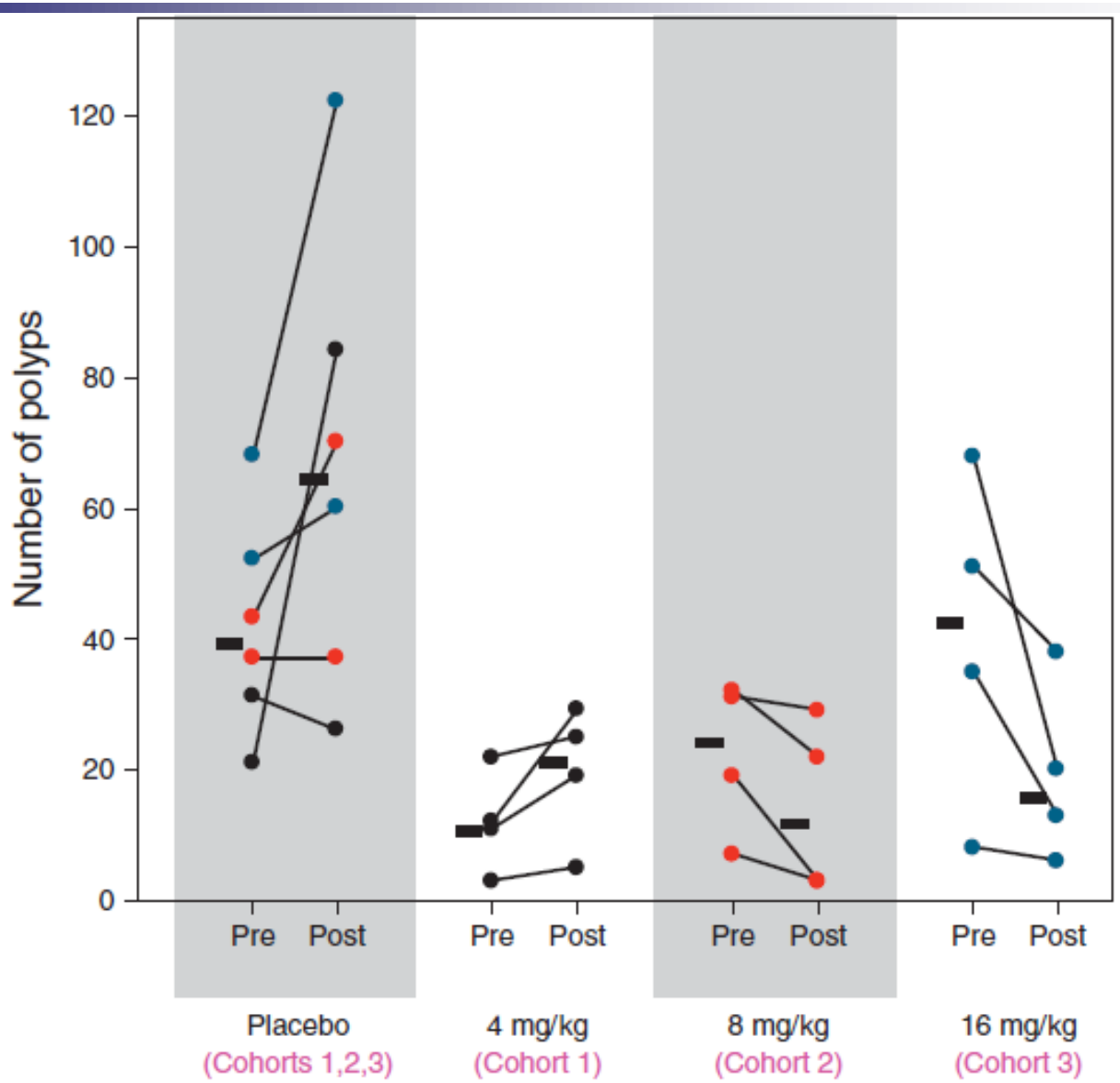

Figure 2. Celecoxib dose–response relationship among pediatric patients with familial adenomatous polyposis. The number of polyps at baseline

- Sue Clark & Professor Phillips
- Warren Hyer, Jo Rawlings, Chris Fraser
- Polyposis Registry, St Mark's Hospital