New Zealand
Familial GI
Cancer Service

NZFGCS 2019 annual update

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Medical advisor

Improving Outcomes for New Zealand Families

Year ending 30th June 2019

- Referrals increased by 4.2% in the last year
- 35% increase over 5 years
- Waiting list times:
  - Triage 2: 62% seen (21% on time)
  - Triage 3: 53% seen (11% on time)
  - Follow up: 89% seen (53% on time)
- Enrolled on surveillance programme – net increase of 218 individuals

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Projection for year 2020

- Register of 3,600 patients
- 2,100 new referrals
- “Multiple polyp” cases make up 23% of total new referrals

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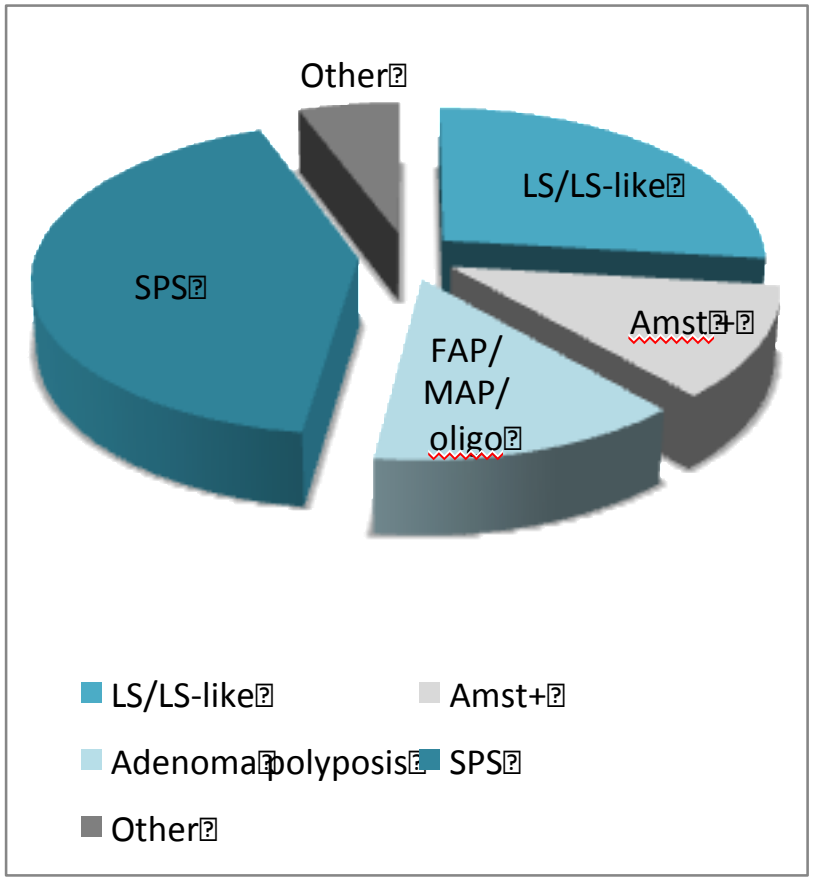
Register family numbers

- Lynch/Presumed 684
- Amsterdam positive/FCCTX 297
- FAP/MAP/Oligoadeno polyposis 347
- SPS 1072
- Other syndromes 147



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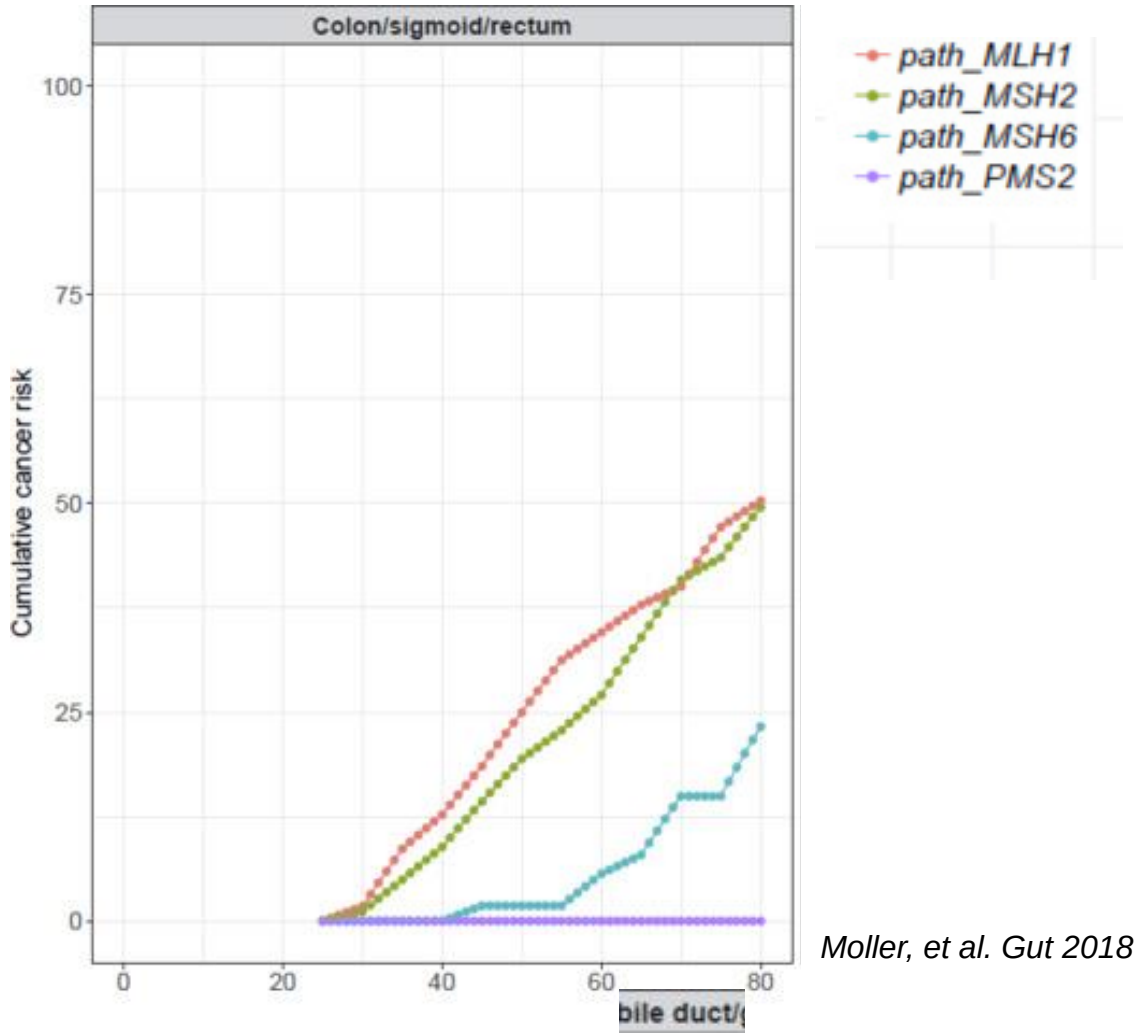
Lynch syndrome

- Autosomal dominant mutation affecting mismatch repair genes
- MLH1, MSH2, MSH6, PMS2
  - MLH1: 26%
  - MSH2: 42%
  - MSH6: 27%
  - PMS2: 5%

- *Current recommendation:*
  - Yearly colonoscopy from age 25y

Lynch syndrome – lifetime CRC risk Prospective LS Database



Moller, et al. Gut 2018

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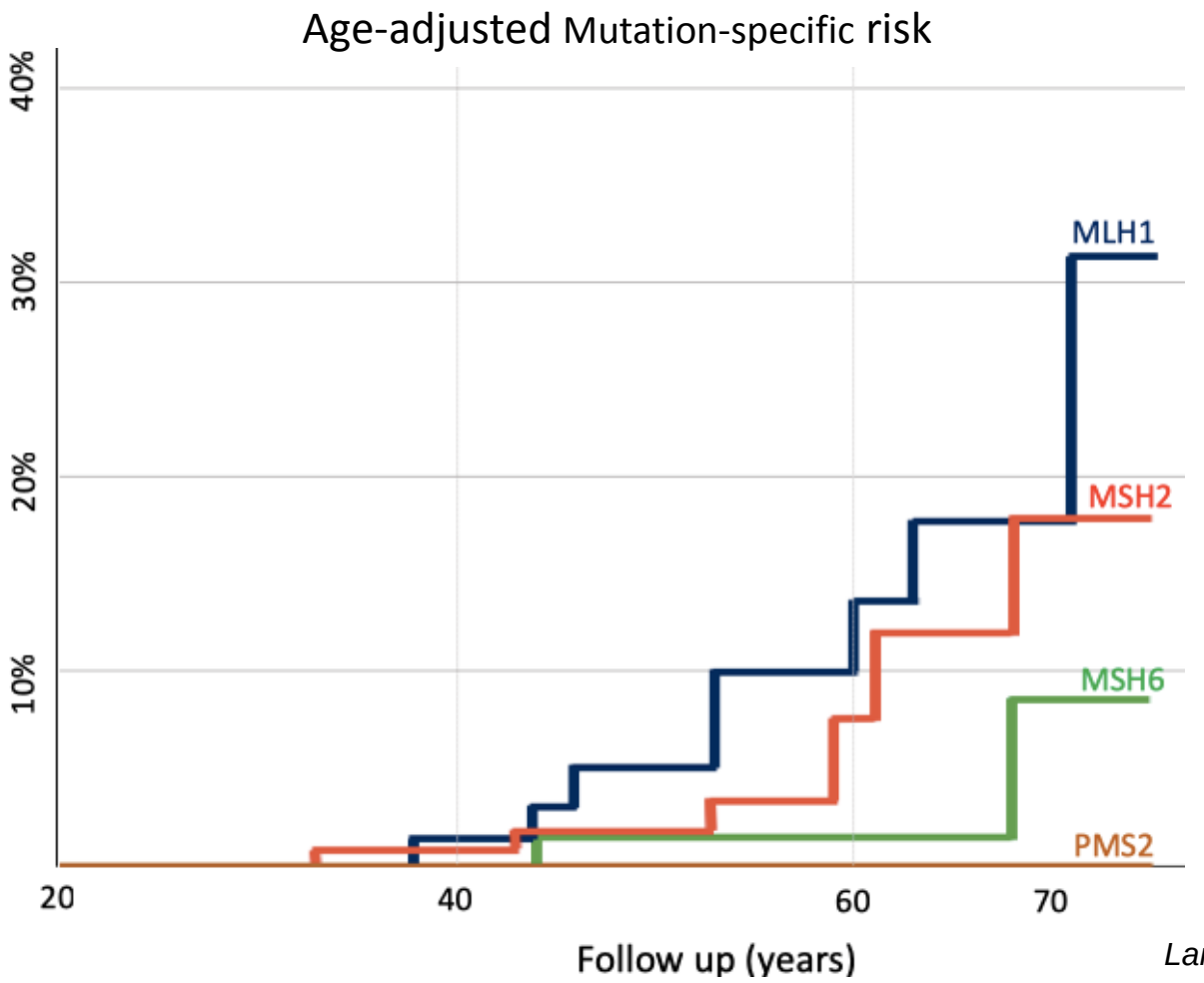
Lynch syndrome – interval CRC risk in NZ



Lamba, et al. Abstract

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Lynch syndrome

- *Proposed change:*
  - MSH6 and PMS2 mutation carriers to have 2-yearly colonoscopy from age 35y
  - MLH1 and MSH2 mutation carriers will continue to have yearly colonoscopy from age 25y

Lynch syndrome – gastric cancer

- Increased gastric cancer risk, but still low i.e. not a very common LS-associated cancer
- Lower risk in MSH6 and PMS2
- Efficacy of gastroscopy surveillance is unproven

- *Current recommendation:*
  - MLH1 and MSH2 mutation carriers have a one-off gastroscopy at age 35y
  - MSH6 and PMS2 mutation carriers not routinely recommended unless family history gastric cancer

- *Proposed change:*
  - No surveillance gastroscopy in LS patients unless family history of gastric cancer
  - *H. pylori* testing and eradicate if positive

Lynch syndrome – CAPP2 study

- Lynch mutation carriers
- Aspirin 600mg/day or placebo

	Aspirin (n=427)	Aspirin placebo (n=434)	Total (n=861)
Time in CAPP2 intervention study (months)	25·0 (12·5; 0·8–60·6)	25·4 (14·2; 1·1–74·4)	25·2 (13·4; 0·8–74·4)
Time since study entry (months)	56·6 (30·9; 0·8–125·4)	54·8 (31·8; 1·6–128·0)	55·7 (31·4; 0·8–128·0)

Burn, et al. Lancet 2011

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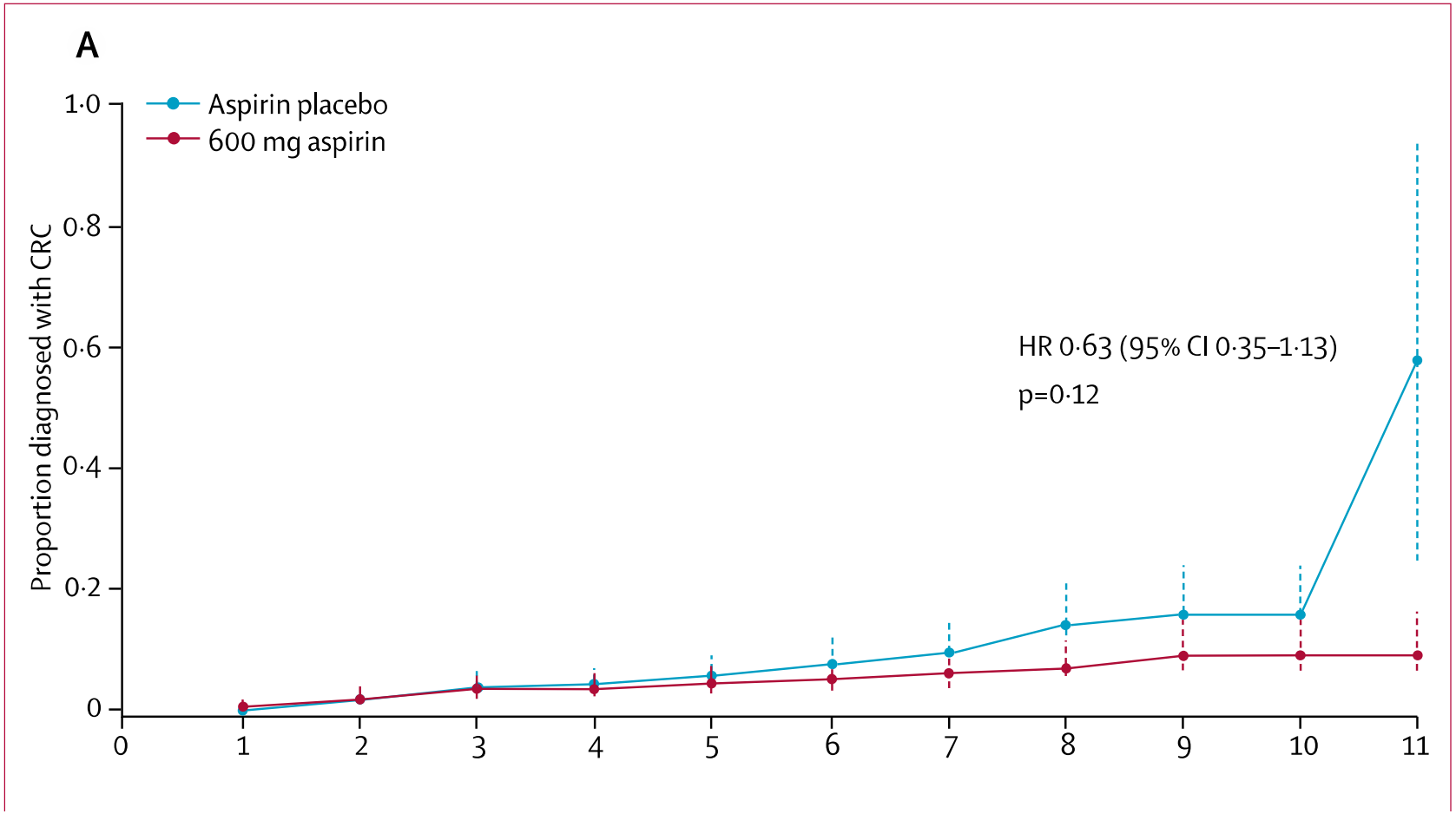
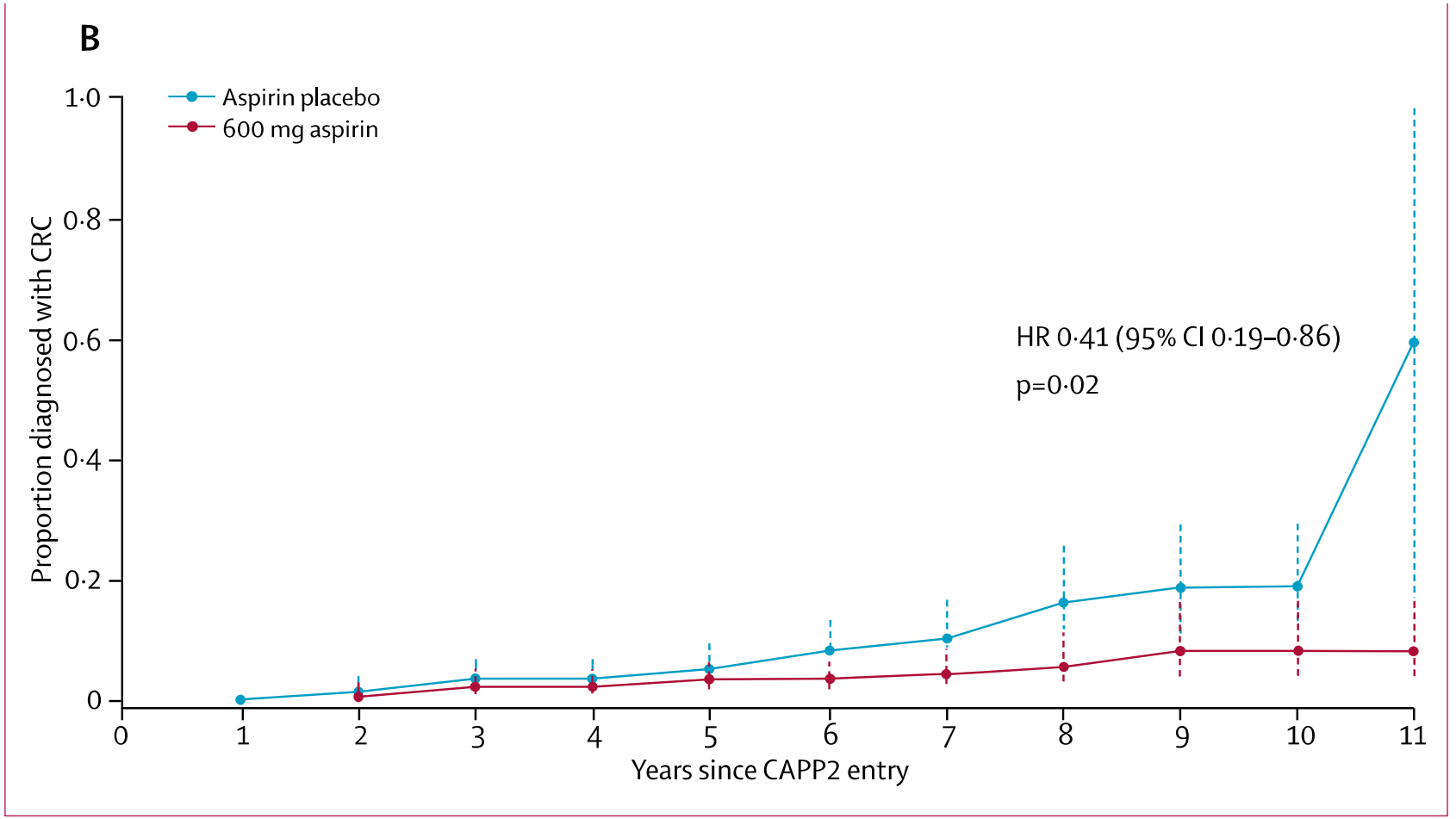


Figure 2: **Time to first colorectal cancer in participants randomly assigned to aspirin compared with those assigned to aspirin placebo**

(A) Kaplan-Meier analysis, adjusted for sex. (B) Kaplan-Meier analysis restricted to participants who had taken the intervention for 2 years or more, adjusted for sex. Each point on the plots shows the estimated cumulative incidence by years of follow-up; error bars show 95% CIs. HR=hazard ratio. CRC=colorectal cancer.

Burn, et al. Lancet 2011



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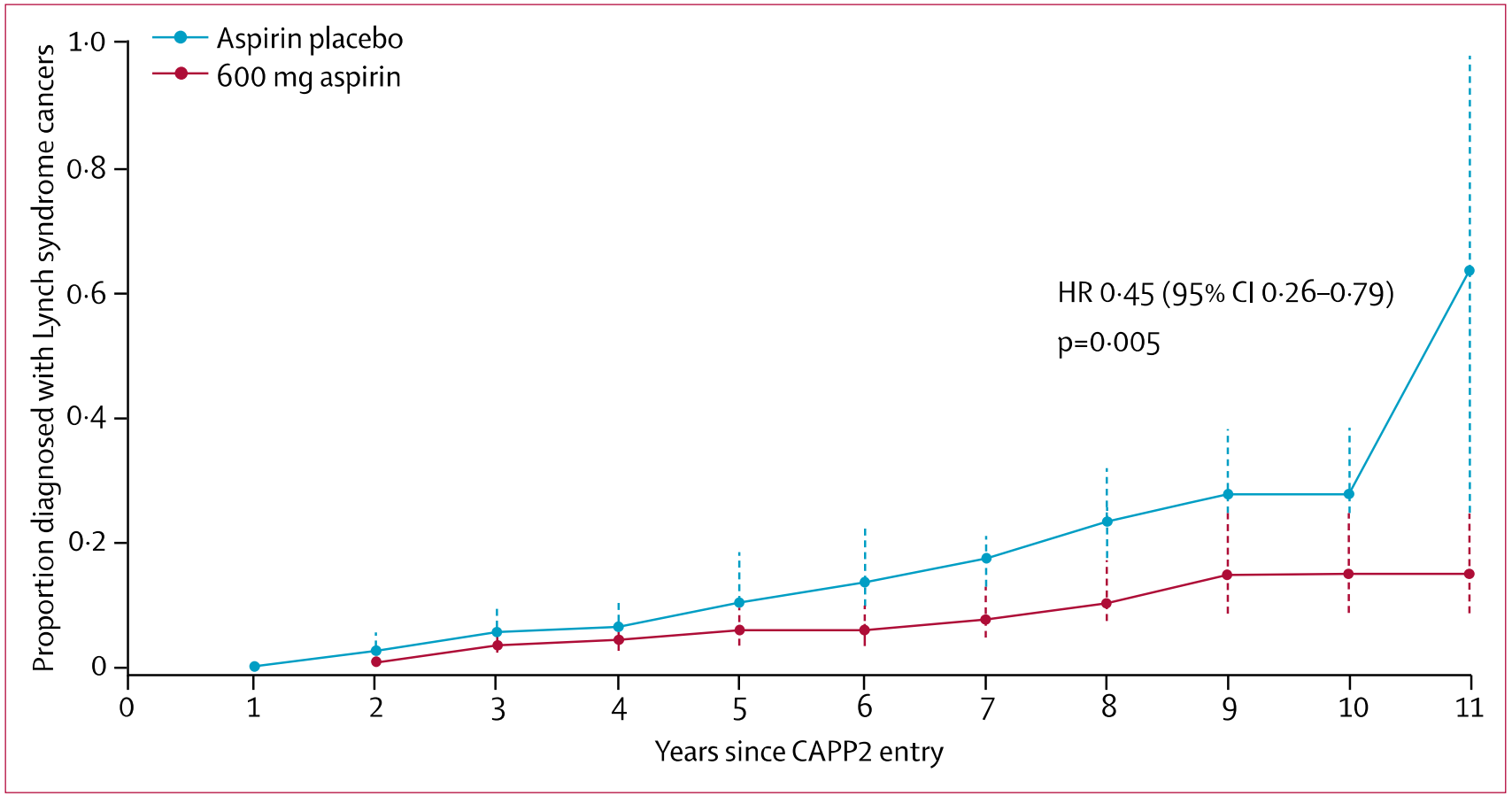

Figure 3: **Time to first Lynch syndrome cancer in participants randomly assigned to aspirin compared with those assigned to aspirin placebo**

Kaplan-Meier analysis restricted to participants who had taken the intervention for 2 years or more, adjusted for sex. Each point on the plot shows the estimated cumulative incidence by years of follow-up; error bars show 95% CIs. HR=hazard ratio.

Burn, et al. Lancet 2011

Lynch syndrome – CAPP3 study

- Not completed yet
- Double-blinded, dose non-inferiority study
- Randomised to enteric coated 100mg, 300mg, or 600mg/day aspirin for 2 years then open label 100mg/day

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Lynch syndrome - aspirin

- *Current recommendation:*
  - Advises mutation carriers to consider aspirin after discussion with GP

- *Proposed change:*
  - Aspirin <u>at least</u> 100mg/day EC under GP supervision

Oligoadenopolyposis

- No universal definition
- Multiple colorectal adenomas
- Consideration for germline testing, although this is often uninformative

- NZFGCS criteria
  - Under 70y with 10 or more adenomas in one examination; or
  - 70y or above with 10 or more adenomas in one examination with at least one advanced adenoma (villous/10mm or greater in size/high grade); or
  - 20 cumulative adenomas

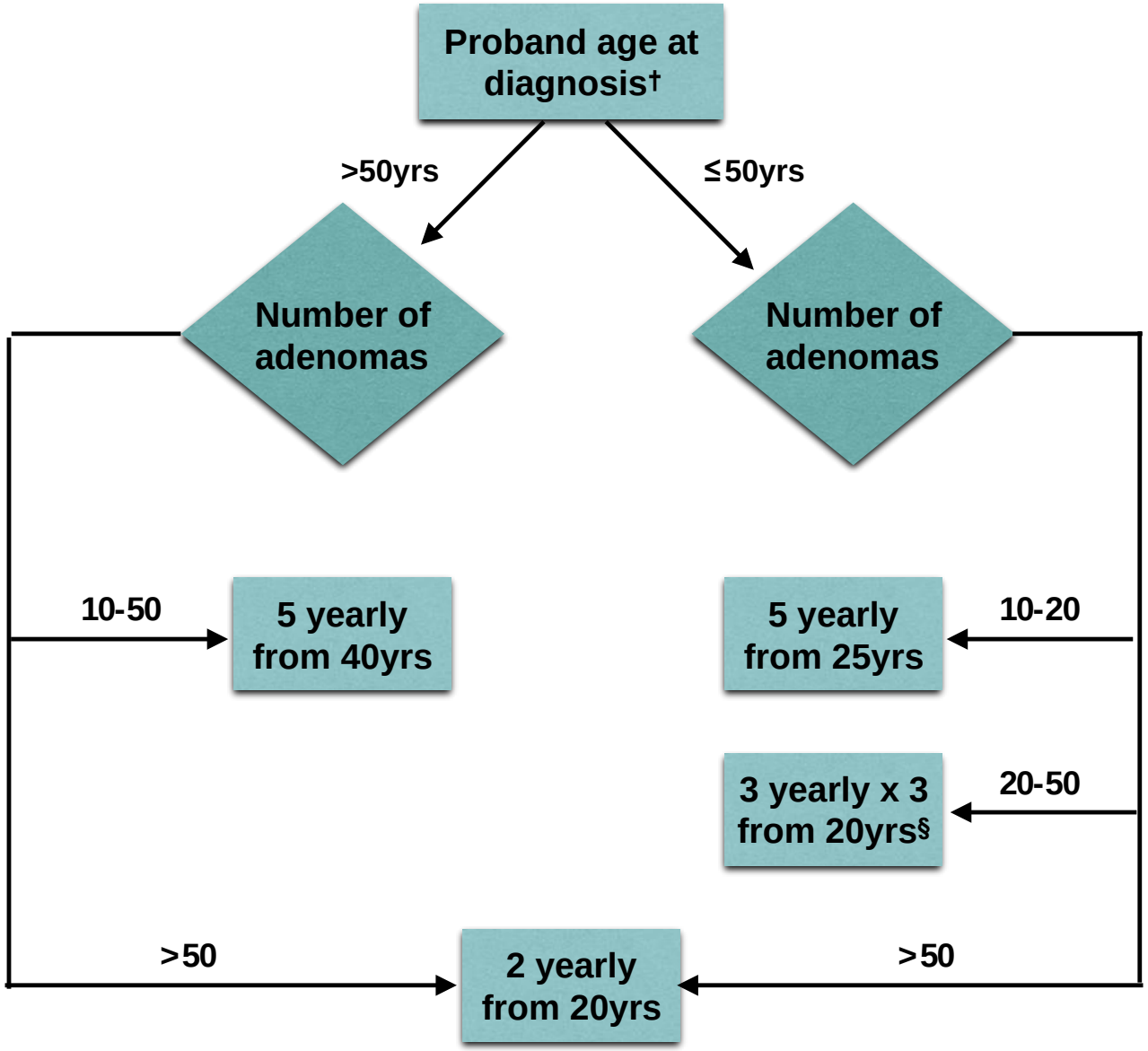
Oligoadenopolyposis

- For the proband
  - Referral to NZFGCS
  - One-off gastroscopy to look for gastroduodenal polyps
  - Refer for genetic testing
  - For those who test negative: 1-2 yearly colonoscopy

Oligoadenopolyposis

- For the first-degree relatives
  - No consensus on surveillance recommendations
  - Depending on age and number of polyps discovered in the proband:
    - Decision on starting age and interval for relatives
    - Starting age as early as 20y
    - Interval from 2-yearly to 5-yearly

Colonoscopy Surveillance Recommendations for FDRs of Oligopolyposis Patients with Uninformative Genetic Testing



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Serrated polyposis syndrome

- WHO criteria:
  - At least 5 serrated/hyperplastic polyps proximal to the sigmoid, of which two are 10mm or greater; or
  - Any serrated polyps proximal to the sigmoid in someone who has a first-degree relative with SPS; or
  - 20 or more serrated/hyperplastic polyps in the colon
- New WHO criteria to be formally released soon…

Serrated polyposis syndrome

ORIGINAL ARTICLE

Personalised surveillance for serrated polyposis syndrome: results from a prospective 5-year international cohort study

Arne GC Bleijenberg,[1] Joep EG IJspeert,[1] Yasmijn J van Herwaarden,[2] Sabela Carballal,[3,4] María Pellisé,[3,4] Gerhard Jung,[3,4] Tanya M Bisseling,[2] Iris D Nagetaal,[5] Monique E van Leerdam,[6] Niels van Lelyveld,[7] Xavier Bessa,[8] Francisco Rodríguez-Moranta,[9] Barbara Bastiaansen,[1] Willemijn de Klaver,[1] Liseth Rivero,[3,4] Manon CW Spaander,[10] Jan Jacob Koornstra,[11] Luis Bujanda,[12] Francesc Balaguer,[3,4] Evelien Dekker[1]

Bleijenberg, et al. Gut 2019

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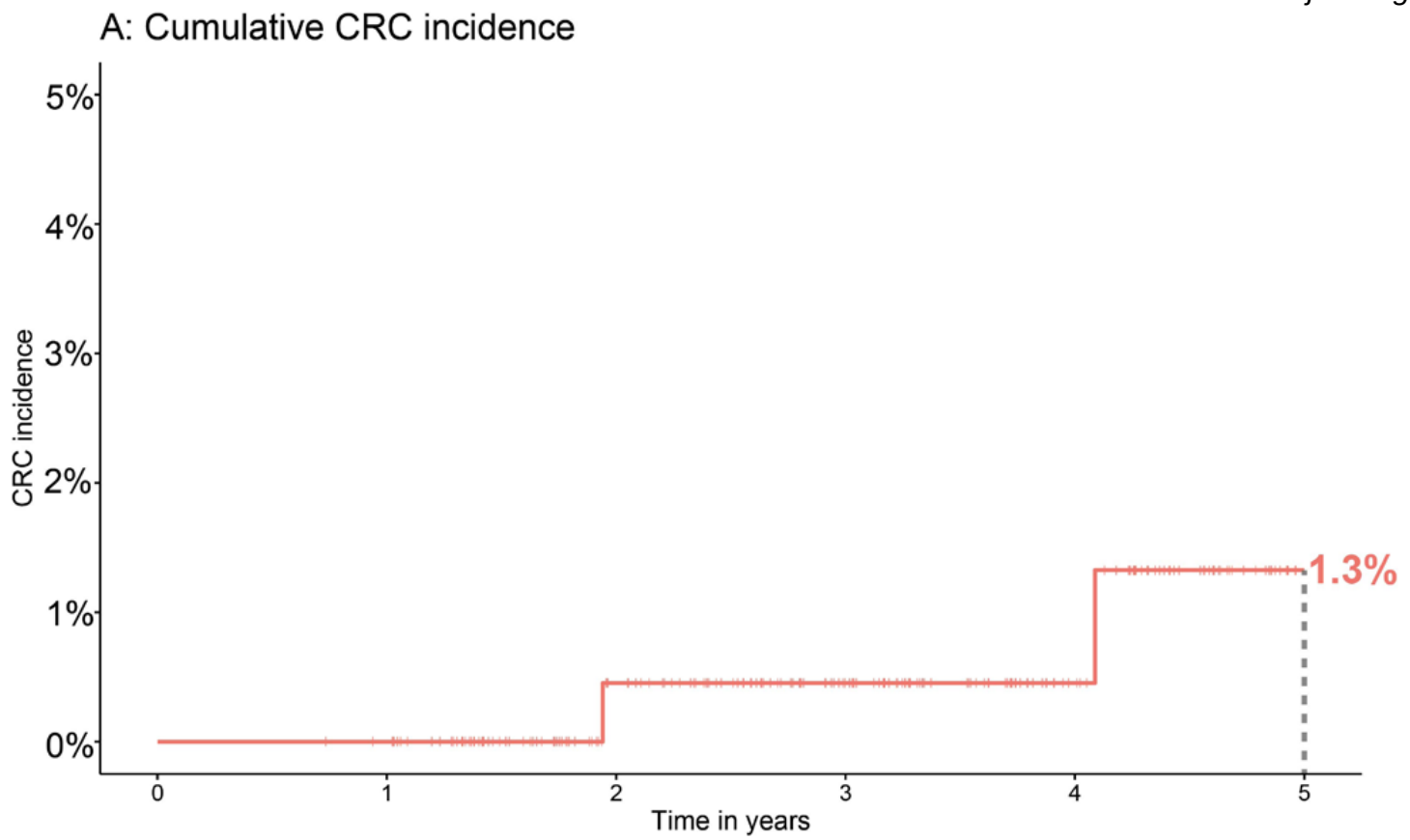
Findings include at least one of the following:
- **≥1** advanced SP (TSA and/or ≥10mm and/or containing dysplasia)
- **≥1** advanced adenoma (≥10mm and/or high-grade dysplasia and/or ≥25% villous histology)
- **≥5** SSL (irrespective of size) and/or adenomas (irrespective of size) and/or HPs ≥ 5mm

Bleijenberg, et al. Gut 2019



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Serrated polyposis syndrome

- High-risk:
  - Serrated polyp with dysplasia
  - Number of serrated polyps
  - Size of serrated polyp
  - Proximally located serrated polyp
  - Advanced adenoma
  - WHO criteria I and III

Serrated polyposis syndrome

- For the proband

- *Current recommendation:*
  - Yearly colonoscopy with extension to 2-yearly if no high-risk features on two consecutive examinations

Serrated polyposis syndrome

- For the first-degree relatives

- *Current recommendation:*
  - 5-yearly colonoscopy from the age of 40y or 10y before diagnosis of proband

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