Supplemental Material

Risk of basal cell carcinoma in a randomized clinical trial of aspirin and folic acid for the prevention of colorectal adenomas

M. N. Passarelli[1], E. L. Barry[1], D. Zhang[2], P. Gangar[3], J.R. Rees[1], R. S. Bresalier[4], G. McKeown-Eyssen[5], M. R. Karagas,[1] J. A. Baron[1,2]

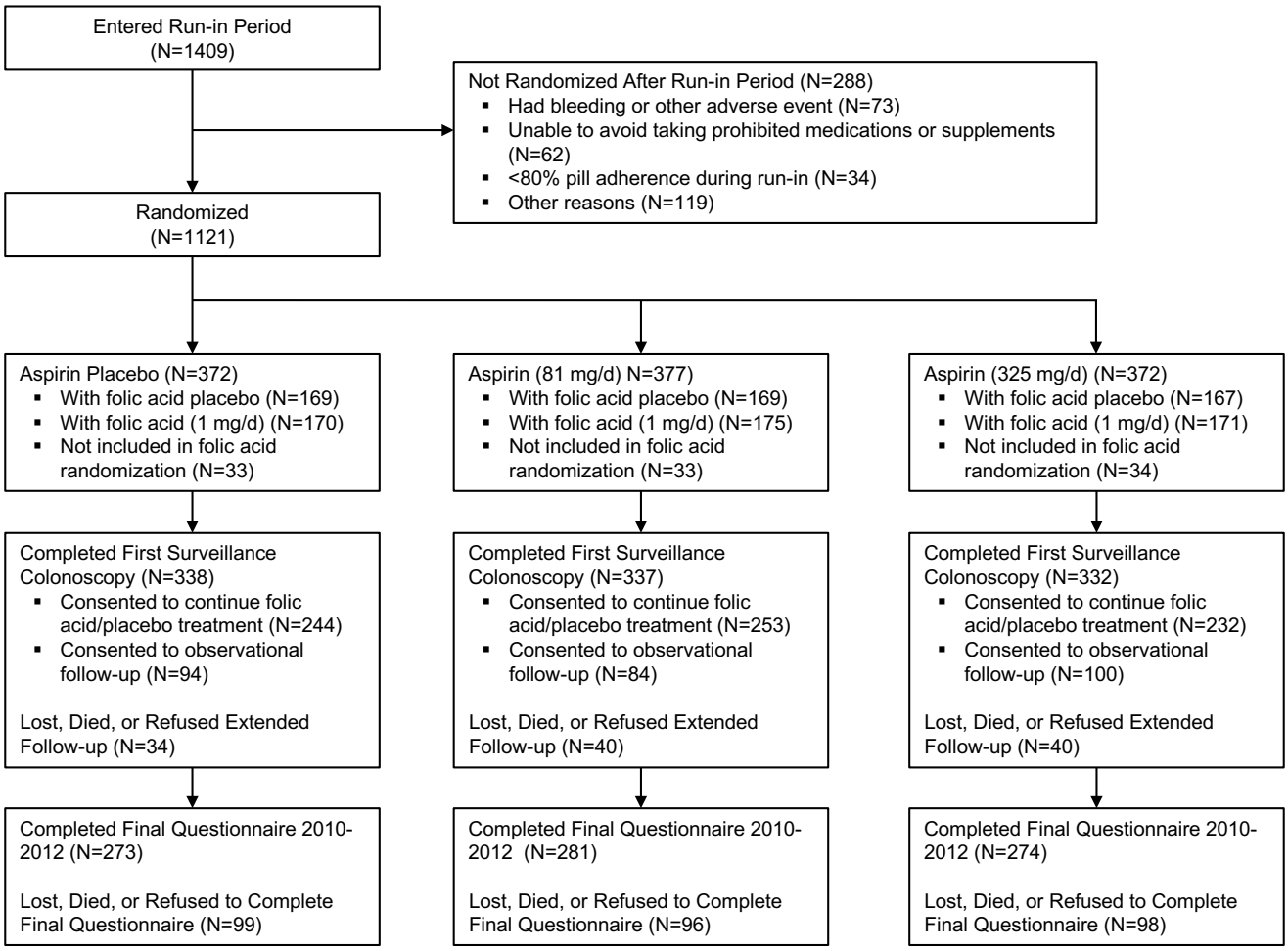
[1]Department of Epidemiology, Geisel School of Medicine at Dartmouth, Hanover, NH, U.S.A.

[2]Department of Epidemiology, University of North Carolina, Chapel Hill, NC, U.S.A.

[3]Department of Pediatrics, University of Arizona, Tucson, AZ, U.S.A.

[4]Department of Gastroenterology, Hepatology, and Nutrition, University of Texas MD Anderson Cancer Center, Houston, TX, U.S.A.

[5]Dalla Lana School of Public Health, University of Toronto, ON, Canada.



Supplemental Fig 1. Flow of participants in aspirin/placebo arms of the Aspirin/Folate Polyp Prevention Study. Exclusions for skin cancer analysis based on race/ethnicity not shown.

Supplemental Table 1 Counts of non-Hispanic white participants diagnosed with basal cell carcinoma and/or cutaneous squamous cell carcinoma during the Aspirin/Folate Polyp Prevention Study. Only lesions identified at the time of first diagnosis after randomization shown.

Anatomic location	BCC Only (N=102)	SCC Only (N=29)	BCC & SCC (N=2)
1 lesion			
Head/neck	61	12	—
Torso	22	2	—
Lower limbs	2	5	—
Upper limbs	4	8	—
Missing	1	0	—
>1 lesion			
All head/neck	3	2	1
All torso	4	0	1
All lower limbs	0	0	0
All upper limbs	0	0	0
Head/neck & torso	2	0	0
Torso & upper limbs	3	0	0

Abbreviations: BCC, basal cell carcinoma; SCC, squamous cell carcinoma.

Supplemental Table 2 Hazard ratios of cutaneous squamous cell carcinoma (SCC) for aspirin and folic acid treatment assignment.

Treatment Assignment	SCC Events/At Risk[a] (%)	HR[a] (95% CI)	P
Aspirin Placebo	8/307 (3)	1 (Reference)	
Aspirin 81 mg/d	11/329 (3)	1.31 (0.52, 3.25)	0.57
Aspirin 325 mg/d	12/322 (4)	1.38 (0.56, 3.38)	0.48
Folic Acid Placebo[b]	11/431 (3)	1 (Reference)	
Folic Acid 1 mg/d	19/443 (4)	1.65 (0.78, 3.46)	0.19

Abbreviations: CI, confidence interval; HR, hazard ratio; SCC, squamous cell carcinoma; UV, ultraviolet radiation.

[a] HR adjusted for age at randomization (<60 vs ≥60 years), sex (male vs female), study center (high vs low UV).

[b] Excludes 84 participants randomized to aspirin/placebo only, of whom 1 was diagnosed with SCC over follow-up.

Supplemental Table 3 Self-reported use of non-protocol aspirin and NSAIDs according to study year.

Average use after randomization	Placebo Users/At risk* (%)	Aspirin 81 mg/d Users/At risk* (%)	Aspirin 325 mg/d Users/At risk* (%)
Year preceding end of study treatment			
Aspirin			
>4 days/month	8/289 (3)	14/309 (5)	18/310 (6)
>4 days/week	3/289 (1)	12/309 (4)	7/310 (2)
Non-aspirin NSAIDs			
>4 days/month	7/289 (2)	8/309 (3)	7/310 (2)
>4 days/week	1/289 (<1)	1/309(<1)	1/310 (<1)
Year 2 following end of study treatment			
Aspirin			
>4 days/month	62/283 (22)	66/288 (23)	72/291 (25)
>4 days/week	36/283 (13)	48/288 (17)	39/291 (13)
Non-aspirin NSAIDs			
>4 days/month	24/283 (8)	30/288 (10)	28/291 (10)
>4 days/week	9/283 (3)	11/288 (4)	8/291 (3)
Year 5 following end of study treatment			
Aspirin			
>4 days/month	76/257 (30)	82/261 (31)	79/262 (30)
>4 days/week	51/257 (20)	56/261 (21)	56/262 (21)
Non-aspirin NSAIDs			
>4 days/month	23/257 (9)	28/261 (11)	17/262 (6)
>4 days/week	11/257 (4)	13/261 (5)	7/262 (3)

Abbreviations: BCC, basal cell carcinoma; NSAID, nonsteroidal anti-inflammatory drug.
[a] Participants lost to follow-up or no longer at risk for first BCC before the end of the given year are excluded. Restricted to non-Hispanic white participants.