

Table2. Cumulative cancer incidences for <i>MLH1</i> pathogenic variant carriers.										
Study	Gender	20y	30y	40y	50y	60y	65y	70y	75y	80y
COLORECTAL CANCER										
General population ¹										
Dominguez Valentin 2023	Male	3.3 (1.5to 7.1)	14.9 (11.1to 19.9)	32.5 (27.4to 38.3)	45.9 (40.1 to 52.3)	48.4 (42.4 to 54.8)	52.8 (46.1 to 59.8)	56.0 (48.5 to 63.7)		
	Female	0	9.0 (6.3 to 12.8)	18.2 (14.5 to 22.8)	30.6 (25.8 to 36.1)	36.3 (31 to 42.3)	42.1 (36.2 to 48.6)	48.3 (41.3 to 55.9)		
Fummey 2024	Male	4.9 (0.7 to 29.9)	22.0 (9.8 to 44.9)	34.7 (19.1 to 57.5)	48.6 (30.5 to 70.5)	53.5 (34.7 to 74.7)	53.5 (34.7 to 74.7)	64.1 (41.1 to 86.3)	64.1 (41.1 to 86.3)	64.1 (41.1 to 86.3)
	Female	0	5.0 (1.3 to 18.6)	7.6 (2.5 to 21.6)	25.6 (14.1 to 43.7)	33.7 (10.9 to 53.2)	38.2 (23.3 to 58.4)	38.2 (23.3 to 58.4)	38.2 (23.3 to 58.4)	38.2 (23.3 to 58.4)
Win 2021	Male	0.9 (0.4 to 2.1)	2.9 (1.3 to 6)	9.2 (5.6 to 16)	24 (17 to 34)		41 (30 to 55)			55 (41 to 70)
	Female	0.4 (0.2 to 1.1)	1.4 (0.6 to 3.5)	5 (2.7 to 9.7)	13 (8.3 to 21)		24 (15 to 36)			36 (24 to 52)

Data indicate the cumulative risk and 95% confidence interval.

¹ Data extracted from NCCN guideline 'Genetic/Familial High to Risk Assessment: Colorectal, Endometrial and Gastric' version 3.2024. Reflect lifetime risk data.

Table 3. Cumulative cancer incidences for <i>MSH2</i> pathogenic variant carriers.										
Study	Gender	20y	30y	40y	50y	60y	65y	70y	75y	80y
COLORECTAL CANCER										
General population ¹										
Dominguez Valentin 2023	Male		3.4 (1.4 to 8.0)	8.4 (5.2 to 13.3)	19.9 (15.3 to 25.7)	34.2 (28.3 to 40.9)		47.3 (39.9 to 55.2)	52.7 (44.4 to 61.4)	
	Female		1.7 (0.5 to 5.1)	7.1 (4.4 to 11.3)	14.9 (11.1 to 19.8)	22.1 (17.7 to 27.5)		36.5 (30.5 to 43.2)	38.4 (32.1 to 45.5)	
Fummey 2024	Male		0	0	7.7 (2.0 to 27.4)	12.7 (4.2 to 34.9)	31.0 (14.9 to 57.3)	31.0 (14.9 to 57.3)	31.0 (14.9 to 57.3)	31.0 (14.9 to 57.3)
	Female		0	4.7 (0.7 to 28.9)	14.0 (4.8 to 37.4)	24.1 (10.8 to 48.7)	24.1 (10.8 to 48.7)	32.8 (15.5 to 60.7)	32.8 (15.5 to 60.7)	32.8 (15.5 to 60.7)
Win 2021	Male		0.7 (0.3 to 1.5)	2.2 (1 to 4.3)	6.7 (4.1 to 11)	17 (12 to 25)		30 (21 to 43)		42 (29 to 58)
	Female		0.4 (0.2 to 1)	1.5 (0.7 to 3.5)	4.8 (2.6 to 9.3)	11 (6.6 to 18)		18 (11 to 30)		28 (17 to 44)

Data indicate the cumulative risk and 95% confidence interval.

¹ Data extracted from NCCN guideline 'Genetic/Familial High to Risk Assessment: Colorectal, Endometrial and Gastric' version 3.2024. Reflect lifetime risk data.

Table 4. Cumulative cancer incidences for <i>MSH6</i> pathogenic variant carriers.										
Study	Gender	20y	30y	40y	50y	60y	65y	70y	75y	80y
COLORECTAL CANCER										
General population ¹										
Dominguez Valentin 2023	Male		2.7 (0.4 to 17.7)	5.8 (1.8 to 17.6)	6.9 (2.5 to 18.3)	11.8 (5.9 to 22.8)	12.7 (6.8 to 23.1)	13.5 (7.1 to 24.8)	16.4 (8.8 to 29.4)	
	Female		0	1.2 (0.2 to 8.1)	4.0 (1.5 to 10.3)	8.6 (4.7 to 15.5)	10.1 (5.8 to 17.1)	17.3 (11.2 to 26.3)	17.3 (11.2 to 26.3)	
Fummey 2024	Male		0	0.7 (0.1 to 5.1)	2.9 (1.1 to 7.6)	5.2 (2.5 to 10.7)	11.2 (6.6 to 18.7)	14.6 (9.1 to 23.0)	18.7 (11.7 to 28.9)	18.7 (11.7 to 28.9)
	Female		0	0	3.3 (1.4 to 7.7)	7.0 (3.8 to 12.6)	9.8 (5.7 to 16.4)	11.0 (6.6 to 18.1)	12.9 (7.7 to 21.2)	12.9 (7.7 to 21.2)
Suerink 2019	Male							10 (1.8 to 24.5)		
	Female							11.7 (2.1 to 26.5)		
Win 2021	Male		0.4 (0.1 to 1.3)	1.2 (0.4 to 3.7)	3.6 (1.3 to 9.5)	8 (4 to 17)		14 (7.5 to 26)		21 (11 to 36)
	Female		0.05 (0.01 to 0.2)	0.2 (0.05 to 0.7)	0.8 (0.3 to 2.2)	2.6 (1.3 to 5.7)		5.9 (2.9 to 12)		11 (5.3 to 22)
Werf – 't Lam 2025 ²	Male		0 (0 to 0.1)	0.2 (0 to 0.7)	1.6 (0.9 to 3.7)	8.9 (5.6 to 14.4)		22.2 (14.8 to 32)		35.7 (25.4 to 47.7)
	Female		0.1 (0 to 0.3)	0.9 (0.3 to 2.5)	3.4 (1.4 to 8)	7.7 (4.3 to 14.3)		13.5 (8.3 to 21.8)		21 (13.4 to 32)

Data indicate the cumulative risk and 95% confidence interval.

¹ Data extracted from NCCN guideline 'Genetic/Familial High to Risk Assessment: Colorectal, Endometrial and Gastric' version 3.2024. Reflect lifetime risk data.

² Dutch cohort study under review (online available in the repository); a retrospective cohort study of 360 families with 1117 known *MSH6* LP/P carriers identified in the Netherlands between 1995 and 2020. Cumulative risks (CRs) were estimated using segregation analysis, appropriately adjusted for ascertainment

Table 5. Cumulative cancer incidences for PMS2 pathogenic variant carriers.									
Study	Gender	30y	40y	50y	60y	65y	70y	75y	80y
COLORECTAL CANCER									
General population ¹									
Dominguez Valentin 2023	Male	0	0	0	10.5 (2.7 to 36.0)	9.5 (2.5 to 32.9)	10.5 (2.7 to 36.0)	32.8 (12.7 to 68.6)	
	Female	0	0	0	0	2.8 (0.4 to 18.2)	8.5 (2.1 to 31.5)	8.5 (2.1 to 31.5)	
Fummeij 2024	Male	0	0	0	0.7 (0.1 to 4.7)	1.5 (0.4 to 5.8)	3.4 (1.3 to 9.0)	6.5 (2.9 to 14.4)	6.5 (2.9 to 14.4)
	Female	0	0	0.4 (0.1 to 2.7)	1.2 (0.4 to 3.8)	1.2 (0.4 to 3.8)	5.0 (2.5 to 9.9)	5.0 (2.5 to 9.9)	5.0 (2.5 to 9.9)
Suerink 2019	Male						9.9 (4.9 to 15.3)		
	Female						5.9 (1.6 to 11.1)		
Ten Broeke 2018 ²	Male	0.1 (0.03 to 0.4)	0.5 (0.2 to 1.8)	1.8 (0.7 to 5.4)	3.9 (2.1 to 9.6)	5.3 (3.2 to 11)	7.2 (4.5 to 13)	9.7 (6.0 to 17)	13 (7.9 to 22)
	Female	0.1 (0.04 to 0.3)	0.5 (0.2 to 1.4)	1.6 (0.7 to 4.2)	3.4 (1.9 to 7.3)	4.6 (2.7 to 8.9)	6.4 (3.8 to 12)	8.6 (5.1 to 15)	12 (6.7 to 21)
Win 2021	Male	0.2 (0.04 to 0.7)	0.5 (0.1 to 2.1)	1.7 (0.6 to 5.8)	4.3 (2 to 11)		8.1 (3.9 to 17)		13 (6.4 to 25)
	Female	0.02 (0.003 to 0.1)	0.07 (0.01 to 0.4)	0.5 (0.2 to 1.6)	2.5 (1.2 to 5.5)		6.5 (3.1 to 13)		12 (6.1 to 23)

Data indicate the cumulative risk and 95% confidence interval.

¹ Data extracted from NCCN guideline 'Genetic/Familial High to Risk Assessment: Colorectal, Endometrial and Gastric' version 3.2024. Reflect lifetime risk data.

² The following hazard ratios were presented by Ten Broeke (2018). Age specific incidences were retrieved from authors records.

Type of cancer	Hazard ratio (95% confidence interval)
Colorectal	Males <40 years: 6.51 (2.03 to 20.9) Males >70 years: 1.70 (0.89 to 3.24) Females <40 years: 6.48 (2.24 to 18.8) Females >70 years: 2.23 (1.21 to 4.12)