

Aktuelle Altersgrenzen in der Darmkrebsfrüherkennung

Übertragbarkeit **auf** Personen mit familiärem Darmkrebs?

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Offenlegung von Interessenskonflikten

- Honorare: Amgen, Bayer, Merck, Sanofi, Roche, Falk Foundation, AstraZeneca, Servier, Takeda
- Advisory Boards: Amgen, Bayer, Biontech, Servier, AstraZeneca, Pierre Fabre, BMS, Cantargia, Olympus, Scandion, Boehringer, Novocure, Mirati
- Forschungsunterstützung: Lilly, BMS, Sanofi

Familiärer Darmkrebs – Definition der Zielgruppe

- Individuen mit familiärer Darmkrebsanamnese
 - nach Ausschluß von Lynch Syndrom und anderen hereditären Tumorsyndromen
- 20-30% der Patienten mit KRK

Das Risiko für die Entwicklung eines kolorektalen Karzinoms ist bei familiärem Darmkrebs höher

	Roos et al., 2019 [10]		Wong et al., 2018 [9]	Butterworth et al., 2006 [7]	Baglietto et al., 2006 [6]	Johns et al. 2001 [8]
	Case-control studies	Cohort studies				
1 FDR	1.92 (1.53–2.41)	1.37 (0.76–2.46)	1.82 (1.51–2.18)	–	2.03 (1.66–2.49)	–
≥1 FDR	2.22 (2.00–2.48)	1.67 (1.52–1.82)	1.76 (1.57–1.97)	2.24 (2.06–2.43)	2.26 (1.86–2.73)	2.25 (2.00–2.53)
≥2 FDRs	2.81 (1.73–4.55)	2.40 (1.76–3.28)	2.68 (1.92–3.74)	3.97 (2.60–6.06)	3.95 (2.49–6.26)	4.25 (3.01–6.02)
≥1 SDR	1.87 (1.39–2.51)	1.09 (1.03–1.15)	–	1.73 (1.02–2.94)	–	–
≥1 TDR	2.28 (0.48–10.78)	1.05 (1.02–1.08)	–	–	–	–
≥1 FDR with CRC at an age < 50 years	3.57 (1.07–11.85)	3.26 (2.82–3.77)	3.55 (1.84–6.83)	3.55 (1.84–6.83)	–	–
≥1 FDR with CRC at an age < 60 years	2.40 (2.12–2.73)	2.02 (1.59–2.57)	–	–	–	–

CRC: colorectal cancer; FDR: first-degree relative; SDR: second-degree relative.

...gerade in der jüngeren Bevölkerung, die aktuell nicht von der Vorsorge erfasst wird.

Familiärer Darmkrebs – kumulatives absolutes Risiko für die Entwicklung von Darmkrebs

	Roos et al., 2019 [10]		Butterworth et al., 2006 [7]
	Western Europe	United States	
General population at 85 years	3.5%	2.7%	2.5%
1 FDR	4.8% (2.7%–8.3%)	3.6% (2.0%–6.4%)	–
≥1 FDR	5.8% (5.3%–6.3%)	4.4% (4.0%–4.8%)	4.7% (4.0%–5.6%)
≥2 FDRs	8.2% (6.1%–10.9%)	6.2% (4.6%–8.4%)	9.6% (6.3%–14.2%)
1 FDR with CRC at an age < 50 years	11% (9.5%–12.4%)	8.3% (7.3%–9.5%)	
1 FDR with CRC at an age < 60 years	6.9% (5.5%–8.7%)	5.3% (4.2%–6.7%)	

CRC: colorectal cancer; FDR: first-degree relative.

Risk of Advanced Adenomas in Siblings of Individuals With Advanced Adenomas: A Cross-Sectional Study

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Table 3. Prevalence of Advanced Adenomas and All Colorectal Adenomas According to the Age and Sex of Exposed Siblings

	All colorectal adenomas				Advanced adenomas			
	Exposed n (%)	Unexposed n (%)	P	mOR (95% CI) ^a	Exposed n (%)	Unexposed n (%)	P	mOR (95% CI) ^a
Age								
<50 y	2/15 (13.3)	5/30 (16.7)	.968	1.05 (0.11–10.02)	0/15 (0)	0/30 (0)		
50–59 y	42/100 (42.0)	36/200 (18.0)	<.001	4.55 (2.34–8.84)	13/100 (13)	5/200 (2)		
≥60 y	34/85 (40)	35/170 (20.6)	.001	2.78 (1.56–4.96)	10/85 (11.8)	5/170 (2)		
Sex								
Male	36/90 (40.0)	39/180 (21.7)	<.001	3.00 (1.64–5.48)	13/90 (14.4)	6/180 (3)		
Female	42/110 (38.2)	37/220 (16.9)	<.001	3.42 (1.89–6.2)	10/110 (9.1)	4/220 (1)		

^aAdjusted for age and sex of proband.

Aktuelle internationale Altersgrenzen in der Darmkrebsfrüherkennung bei Personen mit familiärem Darmkrebs

	Year of publication	DEFINITION		SCREENING	SURVEILLANCE	FAMILY HISTORY OF ADVANCED POLYPS
ESGE [11] 	2019	≥ 1 FDR with CRC at age <50 yr	≥ 2 FDRs with CRC at any age	Colonoscopy screening at age 40 yr	•F020 After a <u>normal</u> high quality baseline colonoscopy → 5-year interval • After <u>polyp excision</u> → surveillance guidelines for the general population	Not included
British Society of Gastroenterology [12] 	2020	<u>Moderate risk:</u> •1 FDR with CRC at age <50 yr • 2 FDRs with CRC at any age	<u>Moderate risk:</u>	<u>Moderate risk:</u> •F020 Colonoscopy screening at age 55 yr	<u>Moderate risk:</u> •F020 Normal → National screening •F020 Polyps → Surveillance guidelines for the general population	Not included
		<u>High risk:</u> •F020 3 FDRs with CRC across >1 generation	<u>High risk</u>	<u>High risk</u> •F020 Colonoscopy screening from age 40 yr until age 75 yr	<u>High risk</u> •F020 5-yearly colonoscopy	

	Year of publication	DEFINITION	SCREENING	SURVEILLANCE	FAMILY HISTORY OF ADVAN POLYPS
American College of Gastroenterology [13] 	2021	1 FDR with CRC at age <60 yr ≥2 FDRs with CRC at any age 1 FDR with CRC at age ≥60 yr	Colonoscopy screening at age 40 yr or 10 yr before the youngest affected relative CRC screening at age 40 or 10 yr before the youngest affected relative and then resuming average-risk screening recommendations	5-yearly colonoscopy	1 FDR with CRC at age <60 yr ≥2 FDRs with CRC at any age 1 FDR with advanced adenomas at age ≥60 yr
United States Multi-Society Task Force [14] 	2017	1 FDR with CRC at age <60 yr 2 FDRs with CRC at any age 1 FDR with CRC at age ≥60 yr	Colonoscopy screening at age 40 yr or 10 yr before the age at diagnosis of the youngest affected relative Screening test as per average-risk recommendations at age 40 yr	5 yr colonoscopy Intervals are as per average-risk recommendations	1 FDR with advanced adenomas at age <60 yr 2 FDRs with advanced adenomas at any age 1 FDR with advanced adenomas at age ≥60 yr
Canadian Association of Gastroenterology Banff Consensus [15] 	2018	1 FDR with CRC ≥2 FDRs with CRC	Colonoscopy screening at age 40–50 yr or 10 yr younger than the age of diagnosis of the FDR Colonoscopy screening at age 40 yr or 10 yr younger than the age of diagnosis of the FDR	5–10 yr intervals 5 yr interval	≥1 FDR with advanced adenoma

Leitlinie KRK

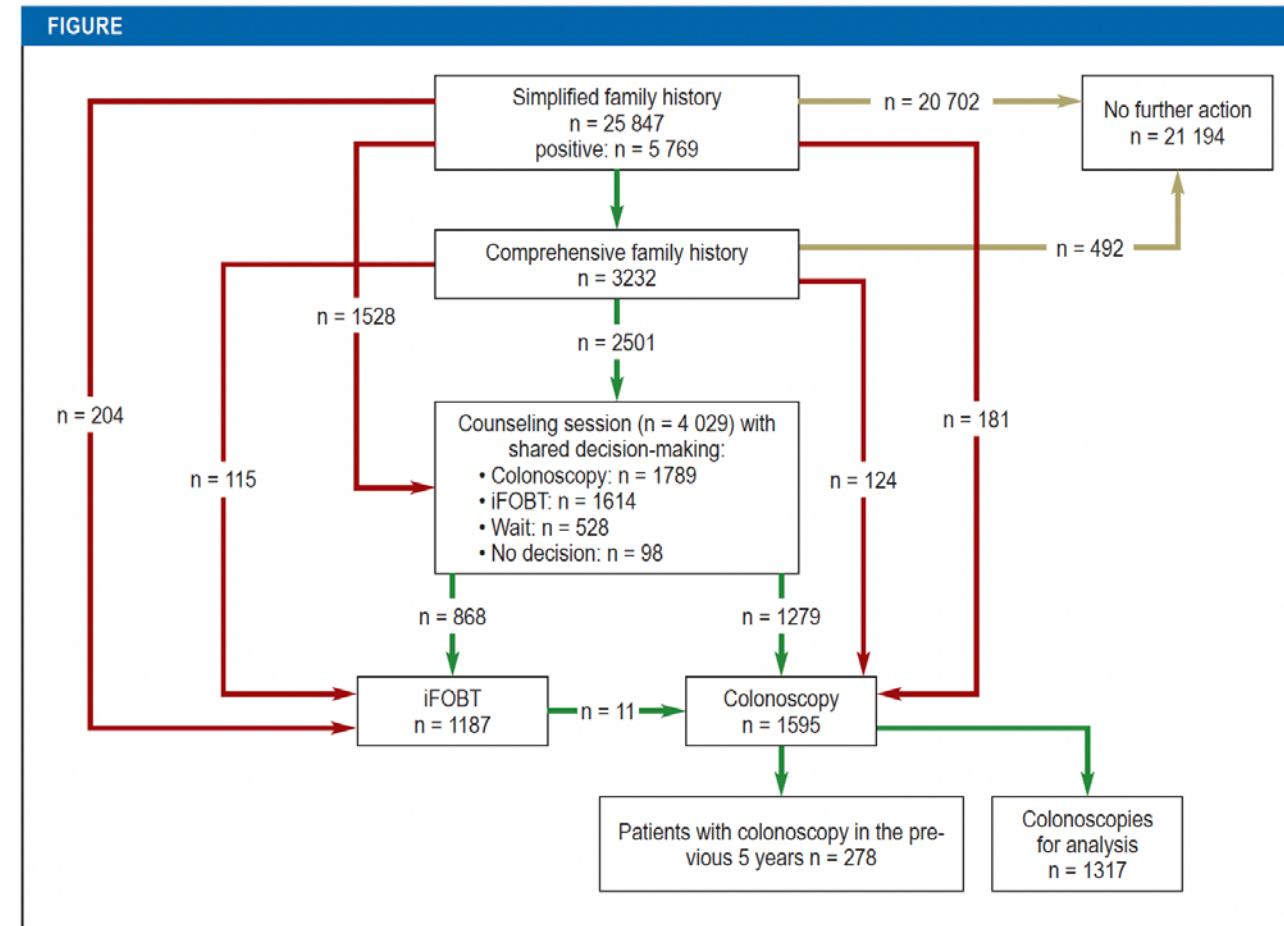
5.1.3. Vorsorgeuntersuchungen

5.1.3.1. Verwandte ersten Grades von Patienten mit kolorektalem Karzinom

5.7.	Konsensbasierte Empfehlung	2013
EK	Verwandte ersten Grades von Patienten mit kolorektalem Karzinom sollten in einem Lebensalter, das 10 Jahre vor dem Alterszeitpunkt des Auftretens des Karzinoms beim Indexpatienten liegt, erstmals komplett koloskopiert werden, spätestens im Alter von 40-45 Jahren. Die Koloskopie sollte bei polypenfreiem Darm in der initialen Koloskopie mindestens alle 10 Jahre wiederholt werden.	
	Starker Konsens	

Durchführbarkeit eines (früheren) Screenings bei familiärem Risiko für KRK- FARKOR Studie

- Risiko-adjustiertes Screening in der Gruppe der 25-50 Jährigen
- 2018-2021; Machbarkeit, Efficacy, Sicherheit
- Ziel: Rate an Adenome und Karzinomen nicht niedriger als in konventioneller Screeningpopulation (10%); nicht-Unterlegenheits-Design
- Shared decision making (Koloskopie, iFOBT, Warten)
- Screening bei ähnlichem Risiko wie in der aktuell in der KFE-RL vorgesehen
- 69.9% Frauen



Durchführbarkeit eines (früheren) Screenings bei familiärem Risiko für KHK- FARKOR Studie

TABLE 2

Results of the screening colonoscopies in the FARKOR program: detection rates* (for comparison: detection rates from the established screening program, according to the Central Research Institute for Ambulatory Health Care in Germany)

Risk group		Polyps	All adenomas	Advanced adenomas	Cancers
FARKOR		n = 132	n = 232	n = 78	n = 4
Age 25–40 years	n = 698	9.2 [7.2; 11.6]	13.8 [11.3; 16.6]	3.3 [2.1; 5.0]	0.0 [0.0; 0.7]
Age 41–50 years	n = 626	10.2 [8.0; 12.9]	21.2 [18.1; 24.7]	5.9 [4.3; 8.1]	0.6 [0.2; 1.7]
Men	n = 576	11.5 [9.0; 14.4]	19.8 [16.7; 23.3]	5.2 [3.6; 7.4]	0.3 [0.1; 1.4]
Women	n = 748	8.3 [6.5; 10.6]	15.4 [12.9; 18.2]	4.0 [2.8; 5.7]	0.3 [0.0; 1.1]
First-degree relatives with CRC	n = 701	10.3 [8.2; 12.8]	19.3 [16.4; 22.4]	6.6 [4.9; 8.7]	0.6 [0.2; 1.6]
Second-degree relatives with CRC	n = 749	9.3 [7.4; 11.7]	16.0 [13.5; 18.9]	4.9 [3.5; 6.8]	0.1 [0.0; 0.9]
Young relatives with CRC (age under 60 years)	n = 486	8.4 [6.2; 11.4]	18.5 [15.2; 22.3]	6.4 [4.4; 9.0]	0.2 [0.0; 1.3]
More than two relatives with CRC or relatives with multiple cancers	n = 252	11.1 [7.6; 15.8]	17.1 [12.7; 22.4]	7.1 [4.4; 11.2]	0.8 [0.1; 3.1]
Participants with SFH and CFH	n = 612	7.0 [5.2; 9.4]	16.2 [13.4; 19.4]	5.1 [3.5; 7.2]	0.2 [0.0; 1.1]
Participants without CFH	n = 705	12.6 [10.3; 15.4]	18.9 [16.1; 22.0]	6.7 [5.0; 8.8]	0.4 [0.1; 1.3]
Total	n = 1317	10.0 [8.5; 11.8]	17.6 [15.6; 19.8]	5.9 [4.7; 7.4]	0.3 [0.1; 0.8]
For comparison: 2018 annual report of Central Research Institute for Ambulatory Health Care in Germany (age group 55–59 years)					
Men		14.4	22.5	7.6	0.5
Women		13.3	14.5	4.9	0.3
Overall		13.8	18.2	6.1	0.4

Aktuelle Altersgrenzen in der Darmkrebsfrüherkennung Übertragbarkeit auf Personen mit familiärem Darmkrebs?

Fazit:

- Aktuell verwendete Altersgrenzen in der Darmkrebsfrüherkennung sind nicht auf Personen mit familiärem Darmkrebs übertragbar
- Bei Individuen mit familiärer Darmkrebsanamnese:
 - V.a. bei ≥ 2 EGV mit CRC oder 1 EGV mit Beginn CRC < 50 Jahre
 - -> Start des Screenings im Alter von 40 Jahren oder 10 Jahre früher als Indexpatient
 - Ausschluß Lynch Syndrom
- 5- Jahres-Screeningintervalle (Koloskopie) bei negativer Indexkoloskopie, ggf. jährliche FIT
- Verfahren ist durchführbar (FARKOR), erfordert aber Schulung (Risikoadjustierung)

New insights on familial colorectal cancer type X syndrome

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- Keimbahn-Exomsequenzierung identifiziert in 17,65% pathogene Varianten bei familiärem kolorektalen Karzinom

Family	Criteria fulfilled	Proband tumour	Diagnostic age (in years)	Germline variant	Tumour location	Tumour differentiation
3	Amsterdam-2	CRC	34	<i>ATR</i> :c.3043C>T	Rectum	Moderate
5	Amsterdam-2	CRC	38	<i>PARK2</i> :c.758G>A	Left colon	Moderate
5	Amsterdam-2	CRC	38	<i>SLX4</i> :c.4259dupC	Left colon	Moderate
6	Amsterdam-2	CRC	54	<i>OGG1</i> :c.30dupC	Rectum	Poor
13	Amsterdam-1	CRC	37	<i>TREX1</i> :c.506G>A	Rectum	Moderate
22	Amsterdam-2	CRC	77	<i>ASXL1</i> :c.1927dupG	Rectum	Moderate
33	Amsterdam-1	CRC	37	<i>CHEK2</i> :c.470T>C	Right colon	Moderate
33	Amsterdam-1	CRC	37	<i>FAN1</i> :c.356_357del	Right colon	Moderate

Vielen Dank für Ihre Aufmerksamkeit!

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