Highlights 2016

Kolontumore
Funktionelle Erkrankungen

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Funktionelle Erkrankungen

ROME FOUNDATION

Geschichte der Rome Kriterien:

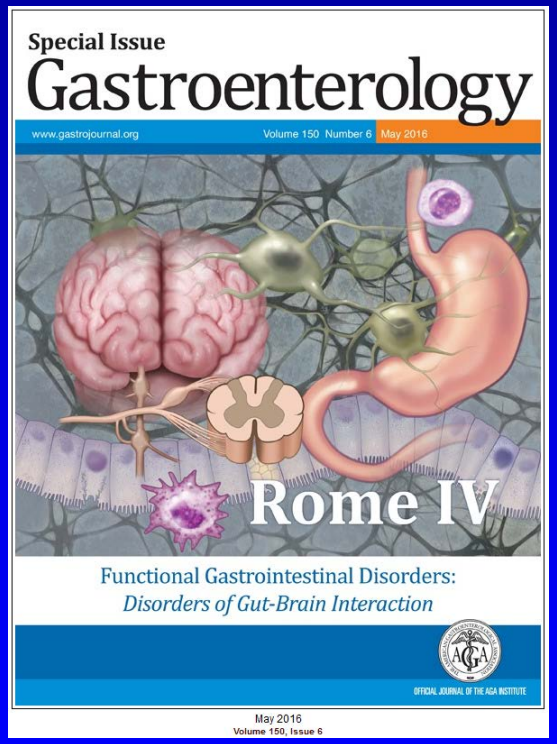
- Entwicklung seit Ende der 80er Jahre:

-> Stressbedingte od. psychiatr. Erkrankung

-> Motilitätsstörung

-> funktionelle Magendarmerkrankungen

-> ?



Erkrankungen der „Brain-Gut Interaction“

(Weitgehende) Elimination der Terminologie „funktionell“

Drossman et al. Disorders of Brain-Gut Interaction Gastroenterology May 2016 1257-1261

Rome IV: Neue Definitionen

Neu: Akzentuierung Beteiligung ZNS

Rome III

C4. Functional diarrhea

D. Functional abdominal pain syndrome

E. Functional gallbladder and Sphincter of Oddi (SO) disorders

E1. Functional gallbladder disorder

E2. Functional biliary SO disorder

→

Rome IV

IBS with predominant diarrhea (IBS-D)
IBS with mixed bowel habits (IBS-M)
IBS unclassified (IBS-U)

D. Centrally Mediated Disorders of Gastrointestinal Pain

D1. Centrally mediated abdominal pain syndrome (CAPS)
D2. Narcotic bowel syndrome (NBS)/
Opioid-induced GI hyperalgesia

E. Gallbladder and Sphincter of Oddi (SO) Disorders

Keefer et al. Centrally mediated Disorders. Gastroenterology May 2016 1408-1419

Rome IV: Neue Diagnostische Kriterien für IBS

C1. Diagnostic Criteria[a] for Irritable Bowel Syndrome

Recurrent abdominal pain, on average, at least 1 day per week in the last 3 months, associated with 2 or more of the following criteria:

1. Related to defecation
2. Associated with a change in frequency of stool
3. Associated with a change in form (appearance) of stool

[a]Criteria fulfilled for the last 3 months with symptom onset at least 6 months before diagnosis.

Neu: Entfernen «abdominal dyscomfort»
neu: Symptom mind 1/Woche
Neu: vor ODER nach Defäkation Symptomakzentuierung.

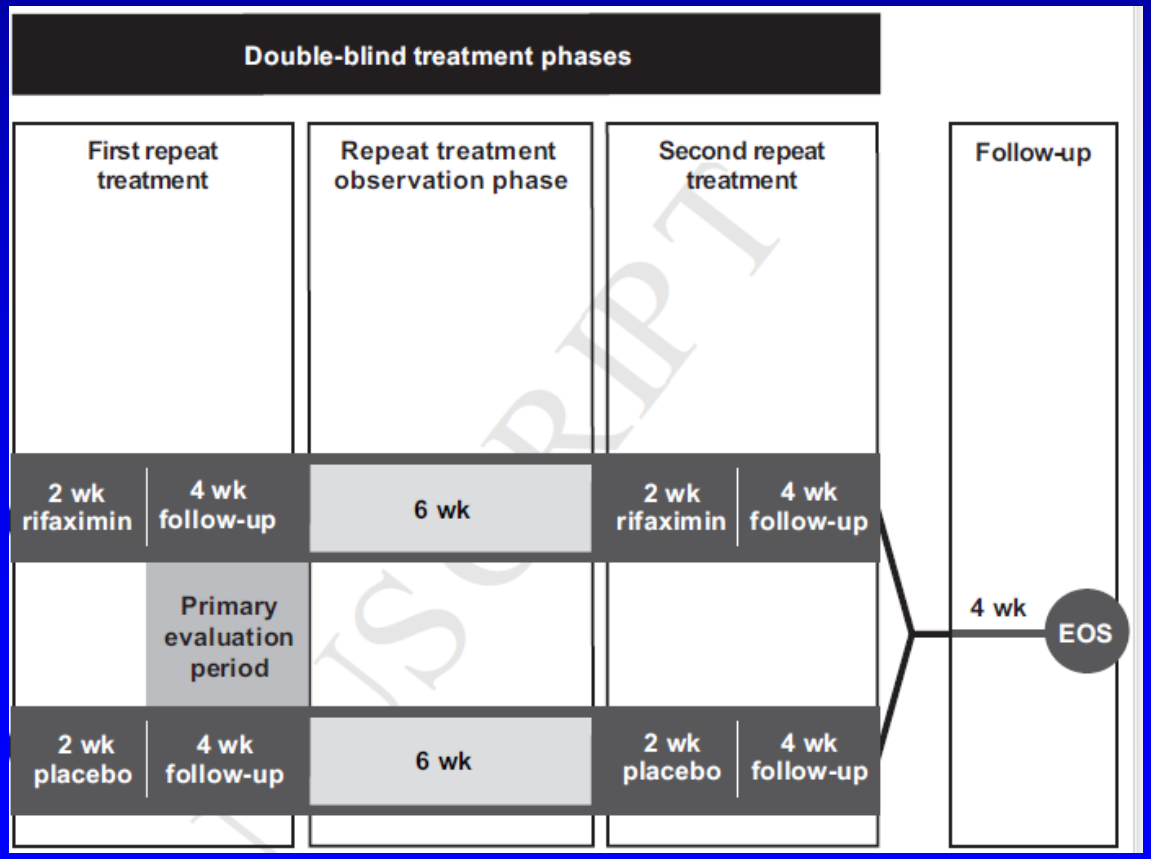
Lacy et al. Gastroenterology May 2016 1393-1407

Rifaximin – Re-Treatment bei IBS

Lembo et al. Gastroenterology Aug 2016 Epub ahead of print

randomisiert, doppel-blind, plazebo-kontrolliert (1074 Patienten)

44.1% mit positiver Symptomentwicklung nach Open-label Behandlung mit Rifaximin 550mg TID



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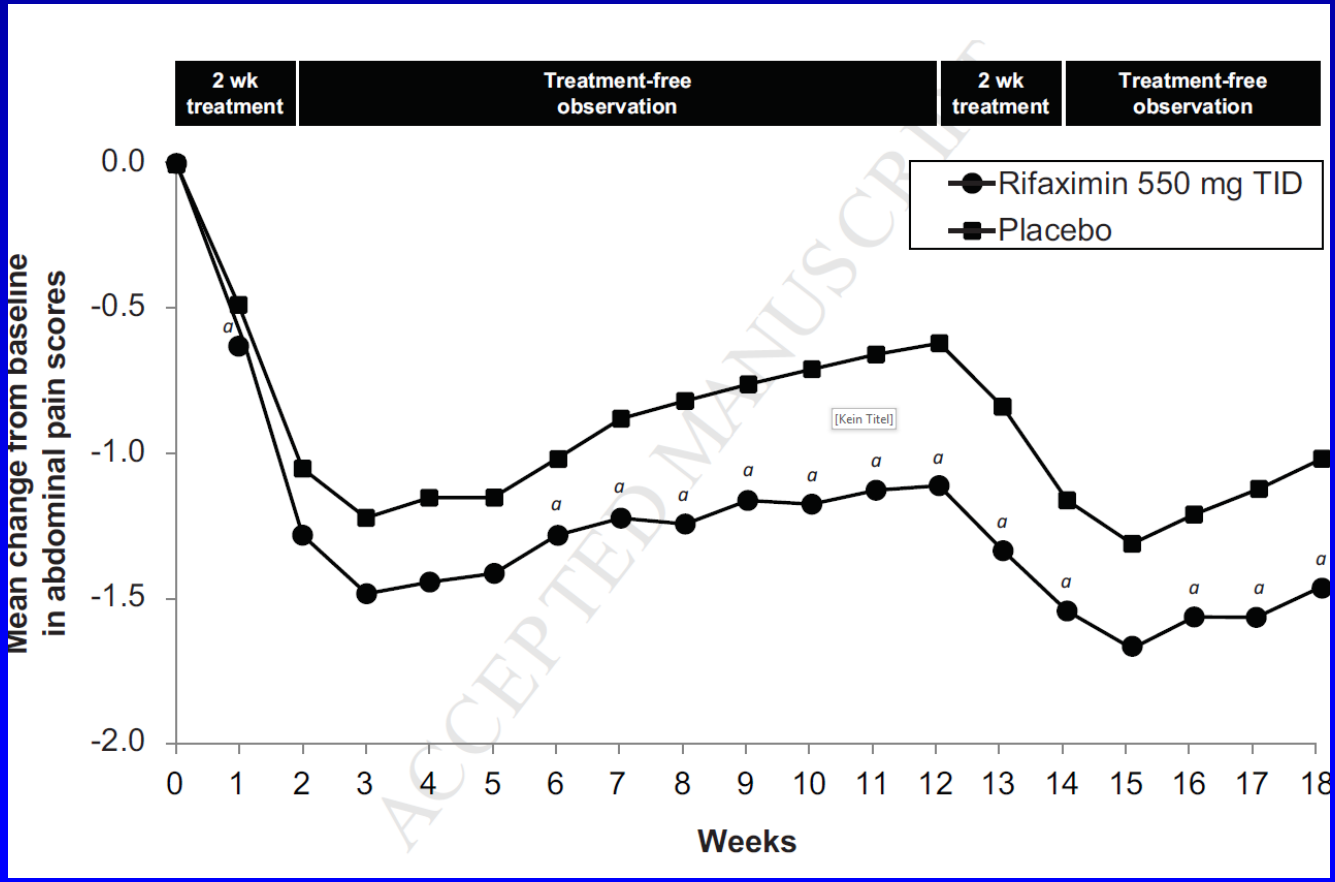
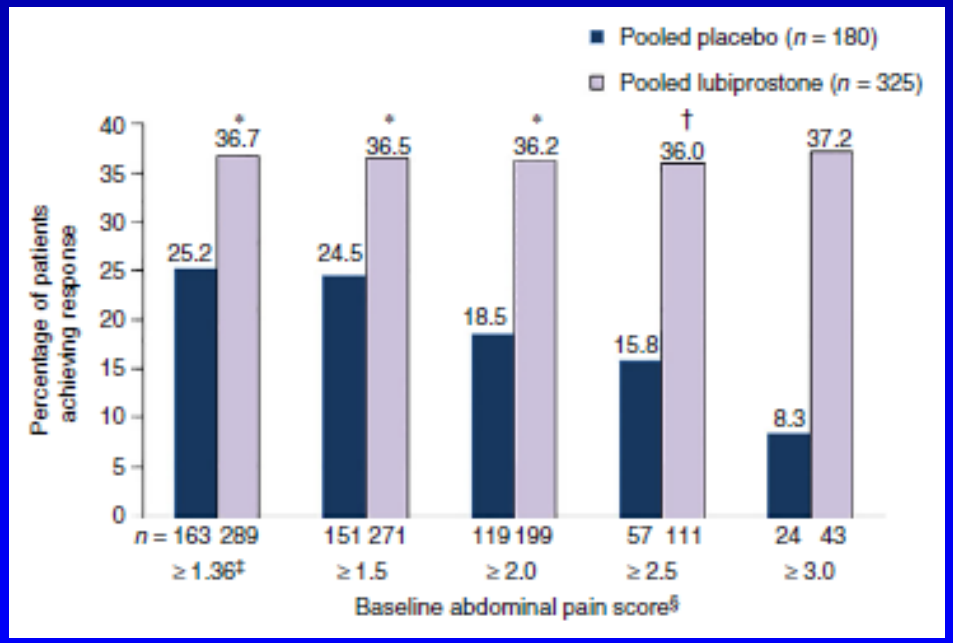
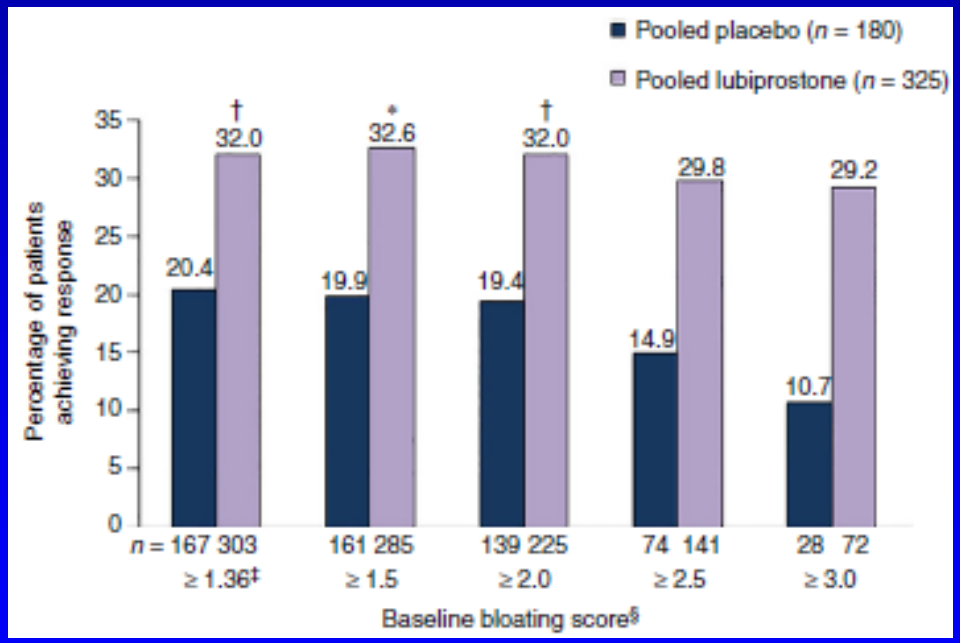


Lubiproston – IBS-C (Amitizia®)

Chang et al. Aliment Pharmacol Ther 2016; 44: 1114–1122 (USA)

Lubiprostone: activator of the ClC-2 chloride channel on the apical surface of enterocytes





Was ist am Horizont ?

Lembo et al. N Engl J Med 2016; 374:242-53: 2400 Patienten mit IBS-D

- **peripher wirksam gemischter µ-opioid receptor agonist (Eluxadoline)**
  - Besserung Abdominalschmerzen
  - Besserung Stuhlkonsistenz, - frequenz, -dringlichkeit
  - Adäquate Besserung IBS-Symptome
  - Global Symptom Score
  - IBS-QOL-Scores

Fukudo et al. Gastroenterology 2016;150:358–366: 540 Frauen mit IBS-D

- **5-hydroxytryptamine receptor 3 (5-HT3) antagonist: Ramosetron**
  - Besserung Stuhlfrequenz
  - Weniger Schmerzen
  - Bessere IBS-QOL Scores

Führt Obstipation zu Divertikeln ?

Braunschmid…Riss et al, Int J Surg 2015, 19:42-45

976 Patienten aus den Colon-Screening Program (2008 and 2009)

Obstipation: Wexner constipation score
median age: 62 years (range 22-90)
male to female ratio: 1:1

Colonic diverticular disease: 290 participants (30%)

Wexner score:	3 (0-18) n. signifkant
Risikofaktoren:	Alter BMI Diabetes
Protektiv:	Unverheiratet «Unemployed»

Kolonkarzinom-Screening

Problem Akzeptanz der Screenings: Auswahl ist gut!

Liang et al. Am J Gastroenterol online, 3 November 2015; doi: 10.1038/ajg.2015.367 (USA)

997 Personen, 3 Jahre f/u

Coloscopie	Jährlich FOBT	Freie Wahl
38%	14%	42%
	1. Jahr: 231/332	1. Jahr: 122/321
	2. Jahr: 94/332	2. Jahr: 58/321
	3. Jahr: 49/332	3. Jahr: 37/321

FIT Stuhl-Test: US Ergebnisse

Jensen et al. Ann Intern Med. doi:10.7326/M15-0983

323 349 Personen 50 - 70 (2007 or 2008); OC Sensor

Kaiser Permanente Northern and Southern California

f/u 4 Jahre:

- FIT positivity rate (5.0%)
- positive predictive values adenoma: 51.5%
- positive predictive values CRC: 3.4%
- FIT screening detected 80.4% of patients with CRC diagnosed within 1 year of testing

Meta-Analysis für Stuhltest: M2-PK

Uppara et al. World Journal of Surgical Oncology (2015) 13:48 (St. Marks)

- M2-PK: pyruvate kinase isoenzyme

- 2,654 patient data
- 407 patients colorectal cancer
- Sensitivity: 79% (CI 73%–83%)
- Specificity: 80% (CI 73%–86%)

- Polypen?
- Selection Bias
- Hohe falsch Pos bei IBD
- Cut off nicht standardisiert

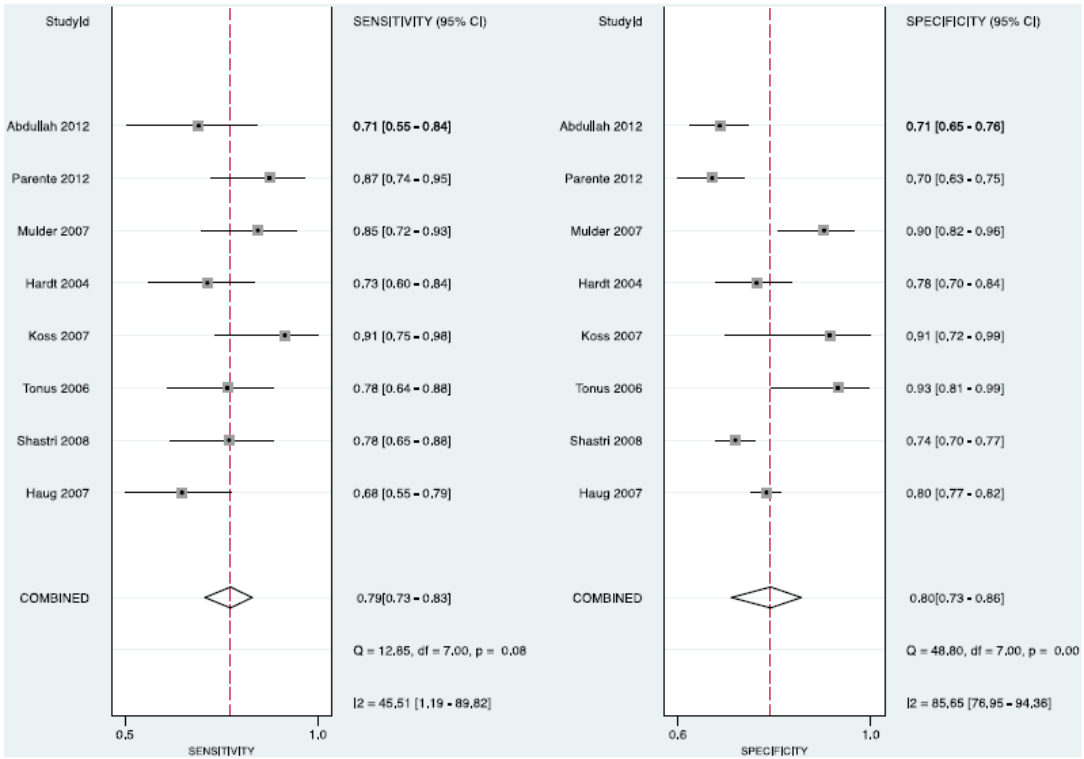


Figure 3 Forest plots showing the sensitivity and specificity for individual studies with their 95% confidence intervals, combined sensitivity and combined specificity from all the included studies.

FDA approves first blood test for colorectal cancer

April 13, 2016

READ/SUBMIT COMMENTS EMAIL PRINT SAVE

The FDA has approved the Epi proColon blood-based screening test for the early detection of colorectal cancer, the manufacturer announced.

See Also

Time to colonoscopy following positive fecal blood test varies ...

Clinical Genomics secures $15 million to commercialize ...

Multifaceted intervention improved colorectal cancer ...

Featured

Highlights from International Liver Congress

MORE FEATURED:

Highlights from AIBD 2015

Highlights from The Liver Meeting 2015

The Epi proColon (Epigenomics) "is a blood test that detects methylated Septin9 DNA, a differential blood biomarker found to be specifically hypermethylated in colorectal cancer, and not normal colon tissue," according to materials from an FDA medical device advisory committee. "Hypermethylated Septin9 tumor DNA shed into the bloodstream displays a unique and discriminating methylation pattern that is detectable in plasma by real-time PCR."

The test is indicated for colorectal cancer screening in average-risk patients who opt not to be screened by colonoscopy or stool-based fecal immunochemical tests, as recommended by current guidelines, according to a press release. It requires a blood sample to be analyzed at a local or regional diagnostic laboratory, and does not require dietary restrictions or changes in medications.

The approval follows safety and efficacy data from three clinical studies, and the demonstrated potential of increasing colorectal cancer screening rates.

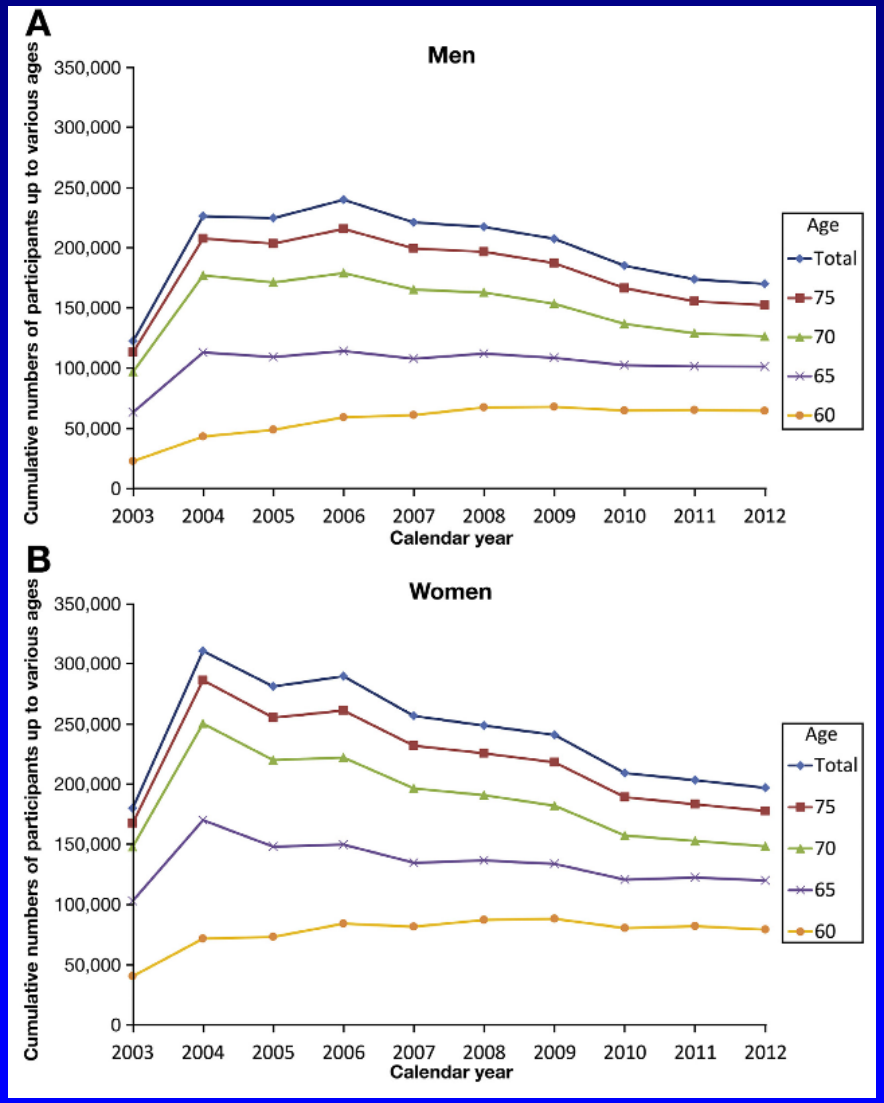
The test will be made available in the U.S. under a joint commercialization agreement between Epigenomics and Polymedco, and Epigenomics will begin a post-approval study of the test's long-term benefits, according to the press release.

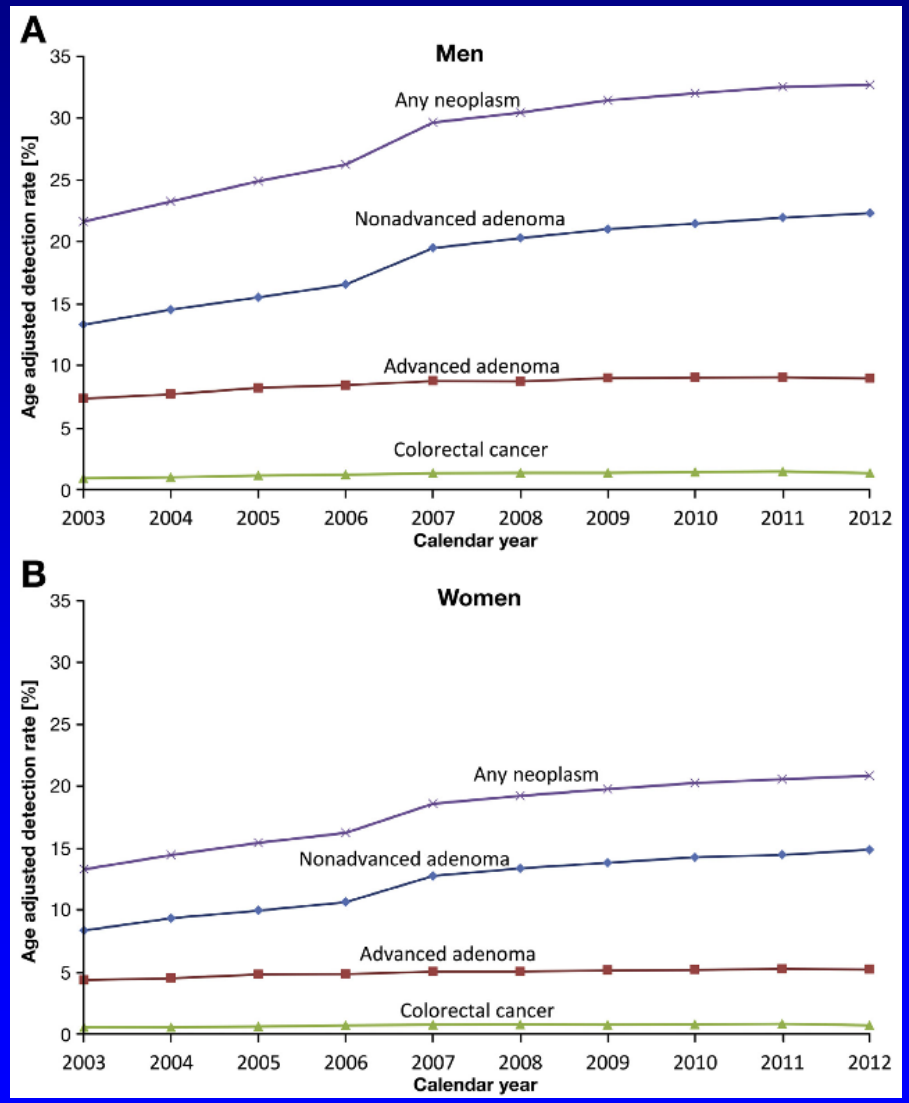
An FDA panel previously recommended that the benefits of Epi proColon

Screening Kolonoskopie

Adenom-Detektiosrate in der D Screening Kohorte

Brenner Gastroenterology 2015 149:356





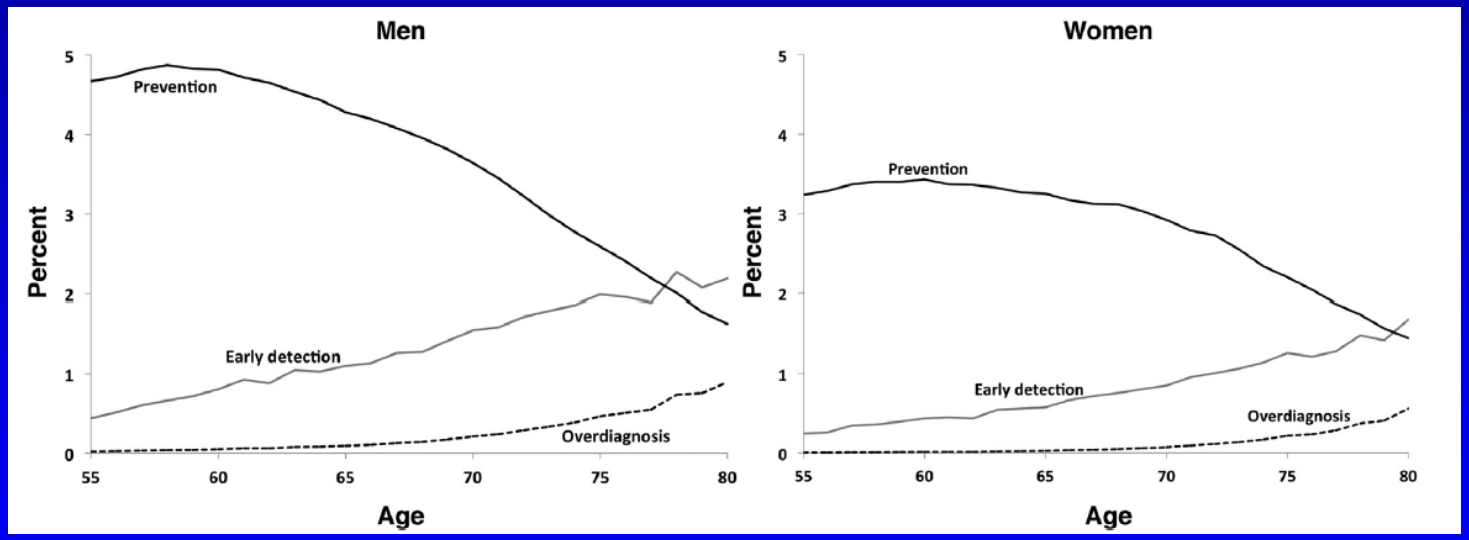
Rechnerische Wirksamkeit des Kolonkarzinomscreening in D

Brenner et al. Clin. Gastroenterol and hepatol 2015, 13:717-723

2003-2012: 4.4 million screening colonoscopies (55–79 years)

At least 1 neoplasm (adenoma or cancer): 28.5% of men and 17.6% of women

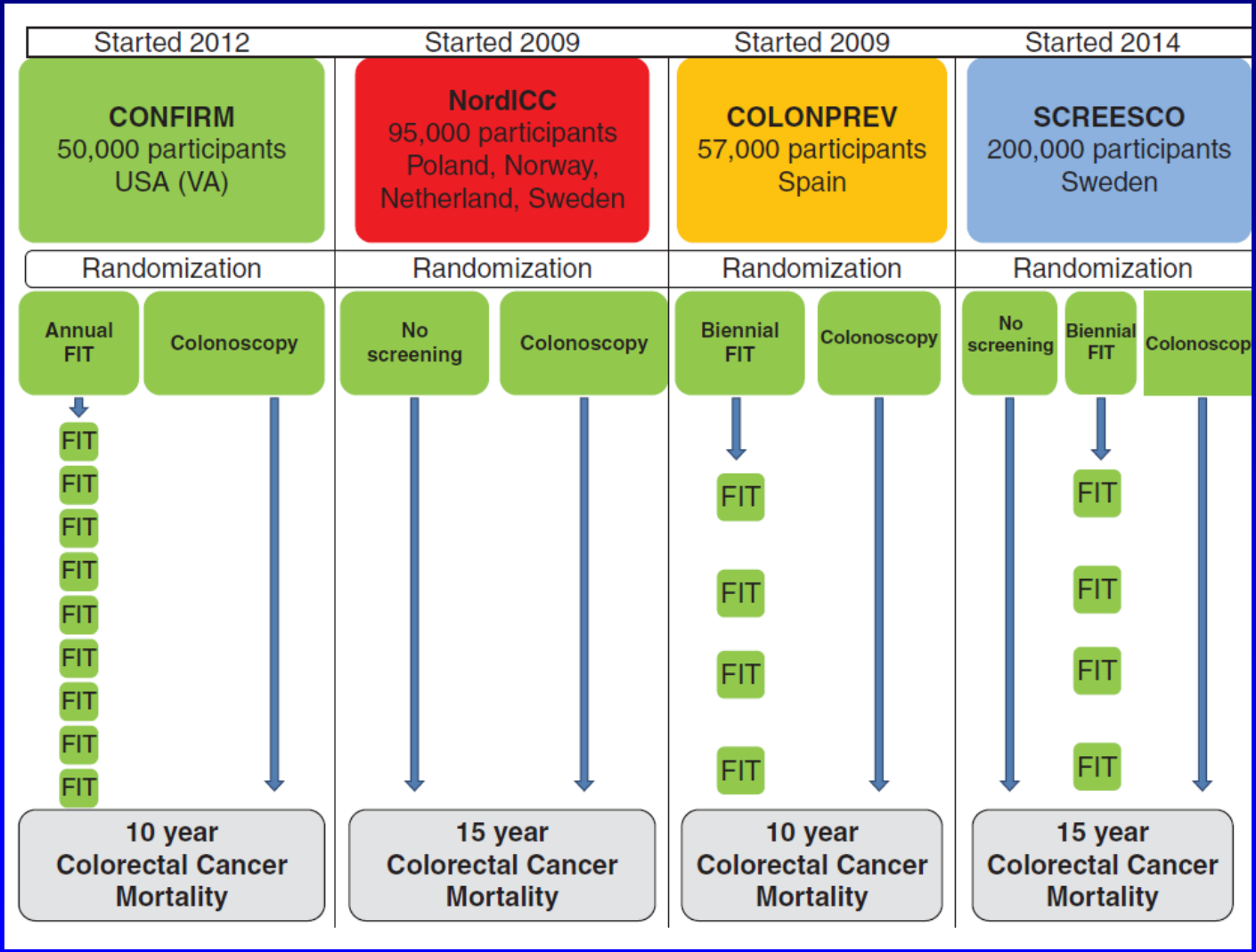
Probability of having CRC prevented or early detected or having overdiagnosis of CRC



Prevented CRC: 180,000	(1/28 screening colonoscopies)
Detected CRC: 40,000	(1/121 screening colonoscopies)
Overdiagnoses: 4500	(1/1089 screening colonoscopies)

Randomisierte Studien zu Screening-Koloskopie

Robertson DJ, et al. Gut 2015;64:982–990

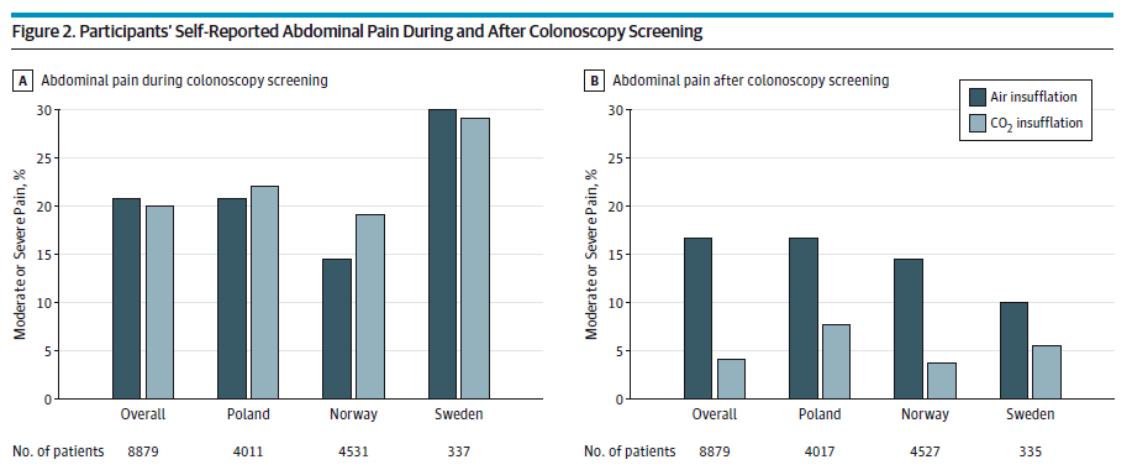


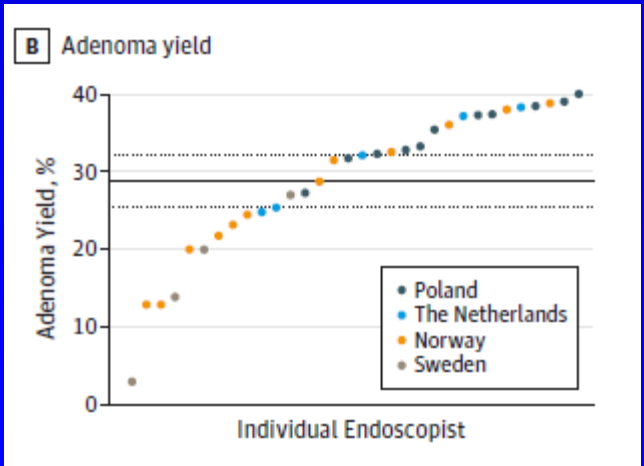
Randomisierte Studien zu Screening-Koloskopie

Bretthauer et al. JAMA Intern Med. doi:10.1001/jamainternmed.2016.0960
Published onlineMay 23, 2016.

94959	Individuals identified as eligible in population registries
54927	From Poland
26588	From Norway
9780	From the Netherlands
3664	From Sweden

	Total Participants	Norway	Poland	Sweden	The Netherlands
Screening participation					
Total	12 574 (40.0)	5354 (60.7)	6004 (33.0)	486 (39.8)	730 (22.9)
Sedation given	2848 (22.7)	579 (10.8)	1389 (23.1)	223 (45.9)	657 (90.0)





Conclusions:
satisfactory participation….
Air insufflation should be abandoned in favor of insufflation with CO2 in colonoscopy screening

Qualitätsverbesserung Koloskopie

Zorzi M et al. Gut 2015;64:1389–1396 (Italien)

75 569 colonoscopies for positive FIT
Age: 61.3 years
Men: 57%
479 endoscopists
79 centres

Adenoma detection rate (ADR): 13.5% to 75 (mean: 44.8%)

Kriterien für hohe Adenoma Detection Rate (ADR):

- Gastroenterology specialty (OR: 0.87 for others)
- Number of screening colonoscopies (OR: 1.51 for endoscopists >600 colonoscopies)
- Higher rates of sedation (OR: 0.47 if occasional; 95% CI 0.24 to 0.92)

Intervallkarzinome nach Screening

leClercq et al. Gastrointest Endosc 2015,82:325-33 (NL)

5157 patients with CRC (2001-2010):

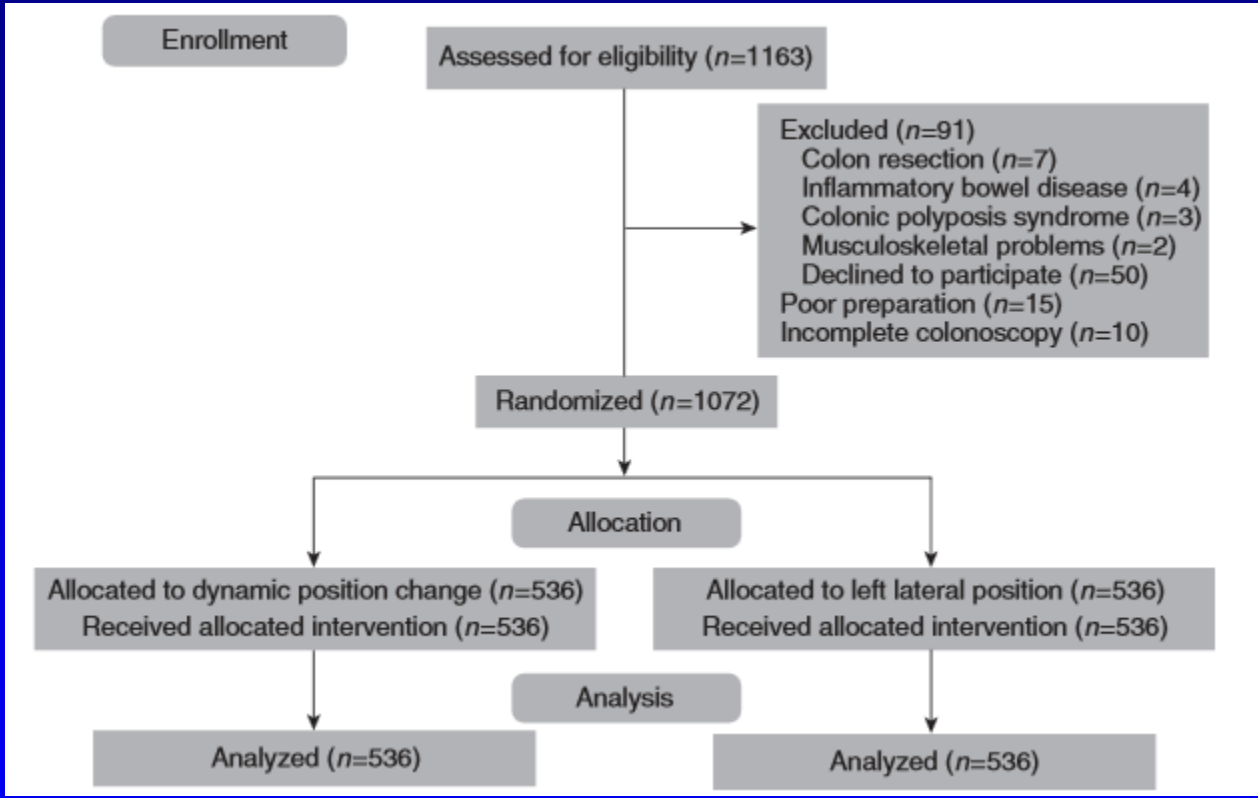
93 (1.8%) had mCRCs 81 months (range 7-356 months)

Gründe für Intervallkarzinome:

43.0% non-compliance
43.0% missed lesions
5.4% incompletely resected lesions
3.2% inadequate examination
5.4% newly developed cancers

Lagewechsel und ADR

Lee et al. Am J Gastroenterol 2016 111:63-9 (Korea)



ADR 42.4 vs. 33.0% (*P* =0.002)

Risikogruppen
Primärprophylaxe

Familienanamnese: Erhöhtes Risiko auch bei „alten“Indexpatienten

Samadder et al. Clin Gastroenterol Hepatol 2015, 13: 2305-11(Salt Lake City)

Utah Krebsregister 1980-2010:
18‘208 Indexpatienten

Alter des Indexpatienten:
<40j: HR 2,53
>80j: HR 1,76

Shoen et al. Gastroenterology 2015, 149:1438-45 (Pittsburg)

144‘768 Personen (55-74j):

- 10,3% positive FA für CRC
- 2090 CRC
- 538 verstorben an CRC

Positive FA:
1x 1.gradig: HR 1.2
≥2x 1.gradig: HR 2,04

Alter des Indexpatienten:
<60j: HR 1.27
60-70j: HR 1,33
>70j: HR 1,14

Brustkrebs und Kolonkarzinom

Lu et al. Cancer Epidemiology 41 (2016) 57–62 (Schweden)

Table 1
Basic characteristics of colorectal cancer in the breast cancer patients.

Variables		Value
1	Number of cohort members (breast cancer cases)	179,733
2	Total person-years of follow-up	1,740,482
3	Average age at entry, years	60.54 + 12.69
4	Average follow-up, years	9.68
5	Total number of colorectal adenocarcinoma (incidence)	2571 (147.72 per 10,000 person year)
6	Adenocarcinoma in the proximal colon (incidence)	1008 (57.91 per 10,000 person year)
7	Adenocarcinoma in the distal colon (incidence)	590 (33.90 per 10,000 person year)
8	Adenocarcinoma in the rectum (incidence)	808 (10.92 per 10,000 person year)
9	Adenocarcinoma in the unspecified colon (incidence)	190 (46.42 per 10,000 person year)

Risiko für colorectales Adenocarcinoma erhöht bei Brustkrebs: SIR = 1.59, 95% CI: 1.53, 1.65

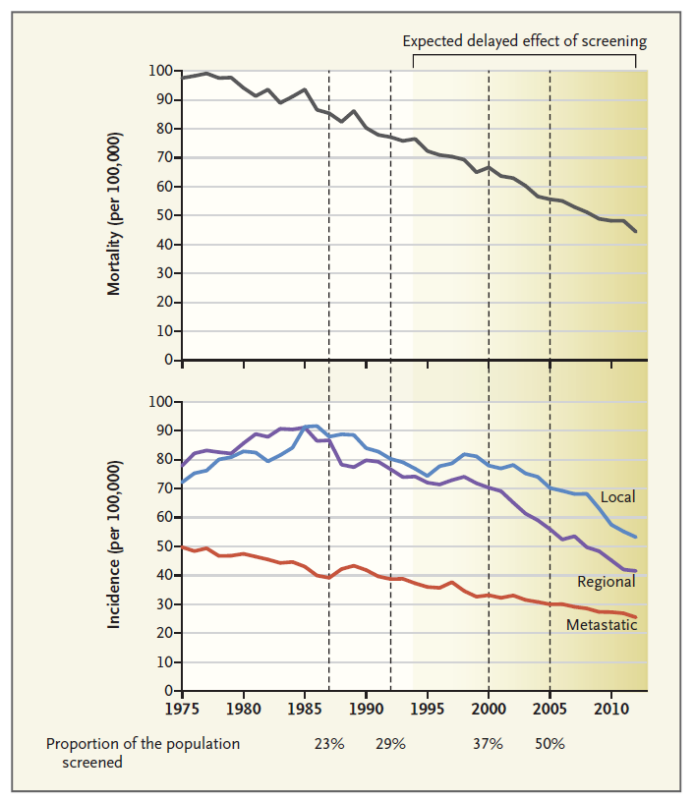
Proximal colon: SIR = 1.72, 95%CI: 1.61, 1.82
Distal colon: SIR = 1.46, 95%CI: 1.34, 1.58

Kolonkarzinom: Mortalität und Screening sinkt

Colorectal Cancer on the Decline — Why Screening Can't Explain It All

H. Gilbert Welch, M.D., M.P.H., and Douglas J. Robertson, M.D., M.P.H.

N ENGL J MED 374;17 NEJM.ORG APRIL 28, 2016



Erklärung:

- Bessere Ergebnisse der Behandlung
- Bessere Primärprophylaxe
- Aspirin

Primärprävention Darmkrebs: Aspirin

Bibbins-Domingo Ann Intern Med. doi:10.7326/M16-0577

Annals of Internal Medicine

CLINICAL GUIDELINE

Aspirin Use for the Primary Prevention of Cardiovascular Disease and Colorectal Cancer: U.S. Preventive Services Task Force Recommendation Statement

Kirsten Bibbins-Domingo, PhD, MD, MAS, on behalf of the U.S. Preventive Services Task Force*

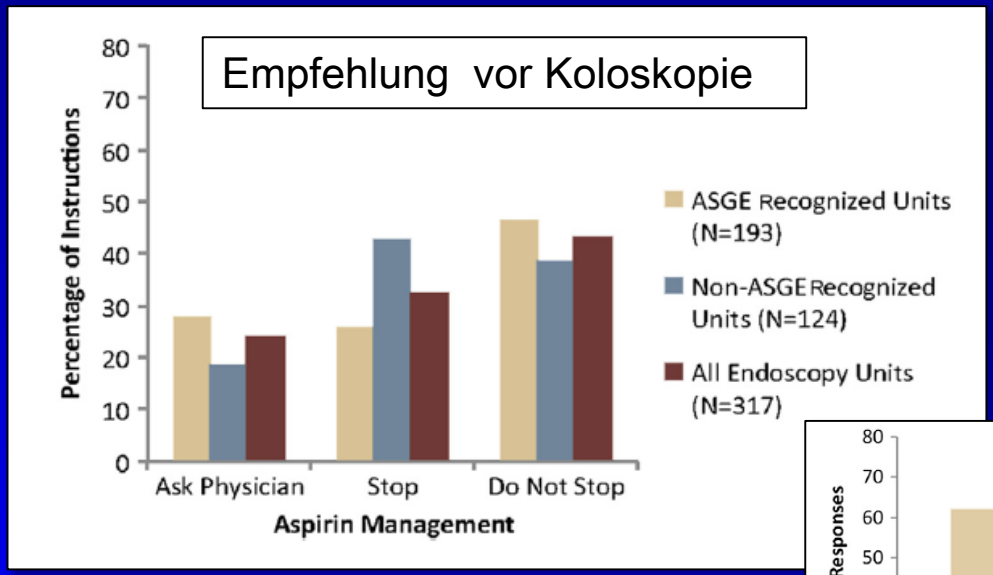
The USPSTF recommends:

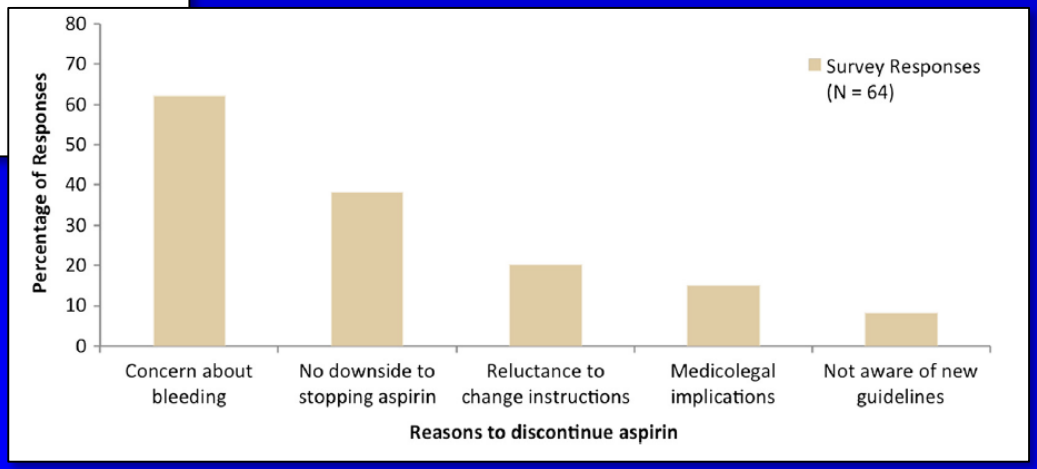
Lowdose aspirin use for the primary prevention of CVD and CRC in adults aged 50 to 59 years who have a 10% or greater 10-year CVD risk, are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years.

ASS, Anticoagulation

Absetzen von Aspirin vor Koloskopie

Robbins R et al. Gastrointest Endosc 2015; 82; 895-900





ESGE & BSG guidelines Endoscopy 2016;48:385-402
ASGE guidelines Gastrointestinal Endoscopy 2016;83:3-16

Risiko für Blutung nach Polypektomie unter Antikoagulation

Shalman Gerson Aliment Pharmacol Ther 2015, 42:949-56

1490 articles:

- Aspirin and/or NSAIDs:……. 3 papers and 1 abstract
- Warfarin:…….. 1 paper
- Clopidogrel:……. 2 abstracts
- Clopidogrel & ASS and/or NSAID:.. 2 papers

Ergebnis für Post Polypectomie Blutung (PPB):

Aspirin and/or NSAIDs:	sofortige Blutung OR 1.1	
	verzögerte Blutung OR 1.7 (n.s.)	

Warfarin:	sofortige Blutung	cold snare 6%, hot snare 23%
	verzögerte Blutung	cold snare 0%, hot snare 14%

Risiko für Blutung nach Polypektomie unter Antikoagulation

Shalman Gerson Aliment Pharmacol Ther 2015, 42:949-56

Ergebnis für Post Polypectomie Blutung (PPB):

Clopidogrel:

Table 2 | Post-polypectomy bleeding in patients on clopidogrel therapy

Author, country	Study type	No pts polypectomy	No pts clopidogrel; dosage	% Male	No pts on clopidogrel with bleed/no pts on clopidogrel (%)	Non-clopidogrel with bleed/non clopidogrel users (%)
Grossman, USA[20]	Retrospective case–control	3191	70 (2%) Dosage – N/A	N/A	3/70 (4%) Immediate 3/70 (4%) Delayed[8]	8/2380 (0.3%) Immediate 15/2380 (0.6%) Delayed*
Rodino, Italy[22]	Retrospective case–control	425	25 (6%) Dosage – N/A	261 (65%)	1/25 (4%)† Delayed	4/400 (1%) Delayed

* Not all patients available for 30-day follow-up period.

† Bleeding within 15 days of polypectomy. Application of hemoclips occurred after all polypectomy cases.

Conclusion:

Warfarin and Clopidogrel should be discontinued !

Endoskopischen Resektion von grossen Polypen

Hassan C,et al Gut 2016;65:806–820

ORIGINAL ARTICLE

Efficacy and safety of endoscopic resection of large colorectal polyps: a systematic review and meta-analysis

C Hassan,[1] A Repici,[2] P Sharma,[3] L Correale,[4] A Zullo,[1] M Bretthauer,[5,6] C Senore,[7] C Spada,[8] Cristina Bellisario,[9] P Bhandari,[10] D K Rex[10]

50 studies: 6442 patients and 6779 large polyps

Surgery due to non-curative endoscopic resection: 8%
Surgery due to adverse events: 1%

Endoscopic perforation: 1.5%
Bleeding: 6.5%

Endoscopic recurrence: 13.8%, invasive cancer in (0.3%)
Endoscopic treatment successful in: 90.3%

Mortality: 0.08%

≥ 2 cm

Mean size:

33 mm (range:20–51)

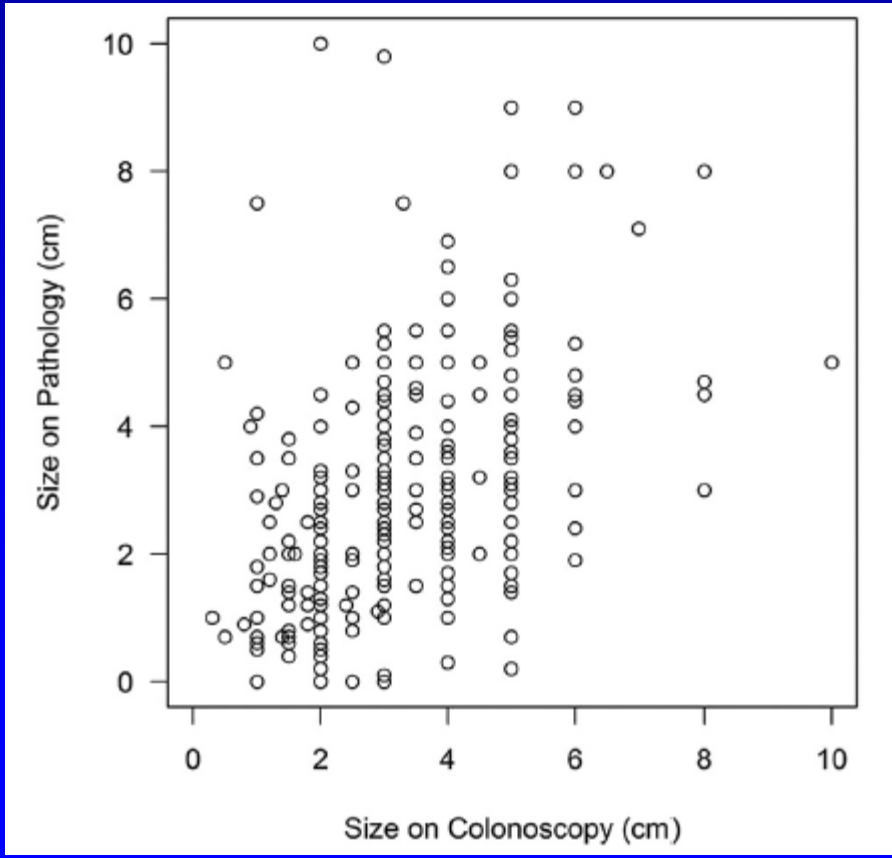
Welche Polypen sollten operiert warden?

Gorgun et al. J Am Coll Surg 2016;223:478-484

346 Patienten mit grossen Polypen:

- Right colon (89.7%)
- Sessile (57.4%), pedunculated (24.8%), flat (17.8%)
- High-grade dysplasia (20%)

Surgery:
cancer in 37 patients (8%).
stage I (23), stage II (11), and stage III (3)



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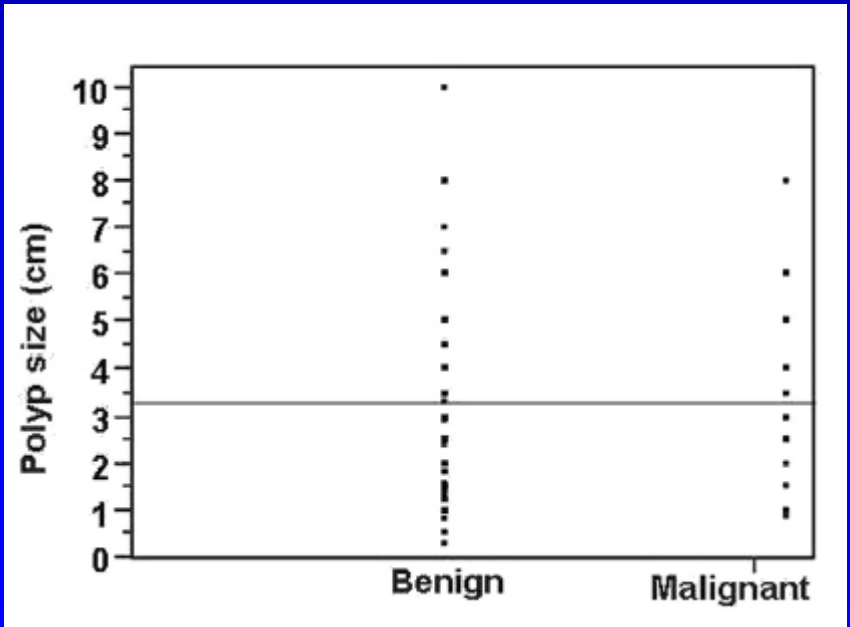
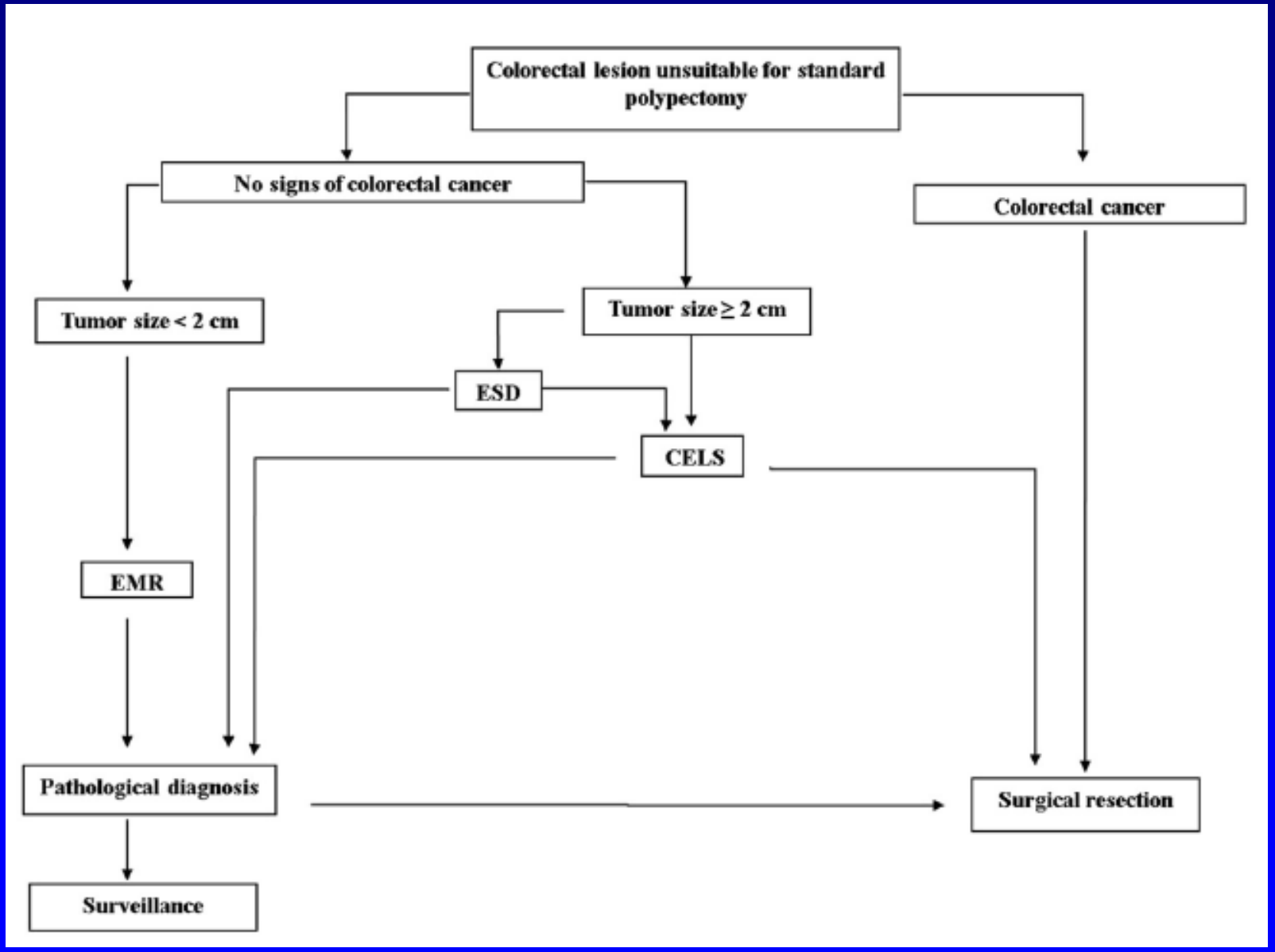


CONCLUSIONS:
For the majority of endoscopically benign colonic polyps, an oncologic colonic resection may be unnecessary…

Welche Polypen sollten operiert warden?

Gorgun et al. J Am Coll Surg 2016;223:478-484



Rektumkarzinom: operieren notwendig ?

Renehan et al. Lancet December 16, 2015 http://dx.doi.org/10.1016/S1470-2045(15)00467-2

431 primary non-metastatic rectal cancers

45 Gy & fluoro pyrimidine-based chemotherapy

↓

Complete clinical response

↓

Propensity-score matching: (T stage, Age, Performance status)

↙ ↘

109 with surgical resection

109 Watch and Wait

Rektumkarzinom: operieren notwendig ?

Renehan et al. Lancet December 16, 2015 http://dx.doi.org/10.1016/S1470-2045(15)00467-2

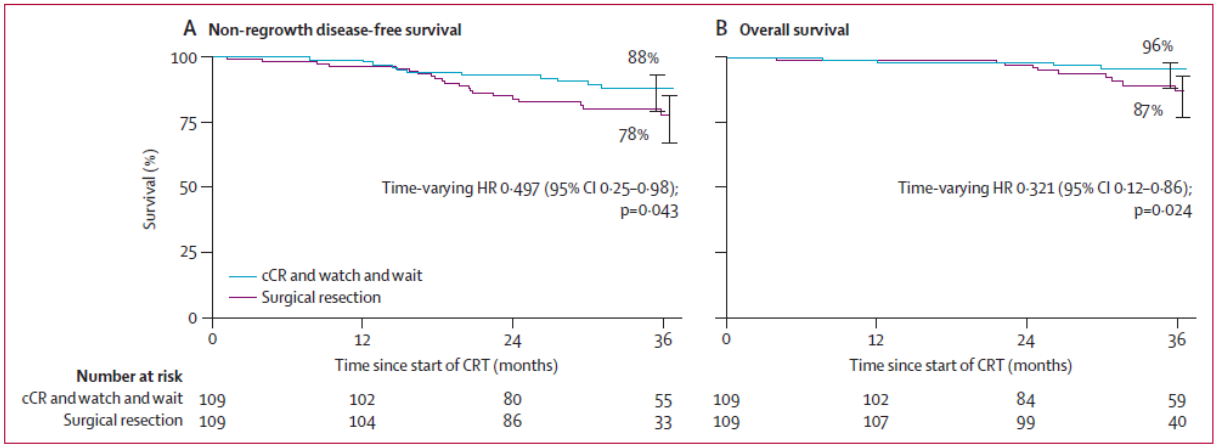


Figure 3: **Non-regrowth disease-free survival (A) and overall survival (B) in the 218 patients in the matched analysis cohort**
Percentages shown on the graphs are 3-year non-regrowth disease-free survival (A) and 3-year overall survival (B); vertical lines show 95% CIs. We included propensity score as a covariate in the models. cCR=clinical complete response. CRT=chemoradiotherapy. HR=hazard ratio.

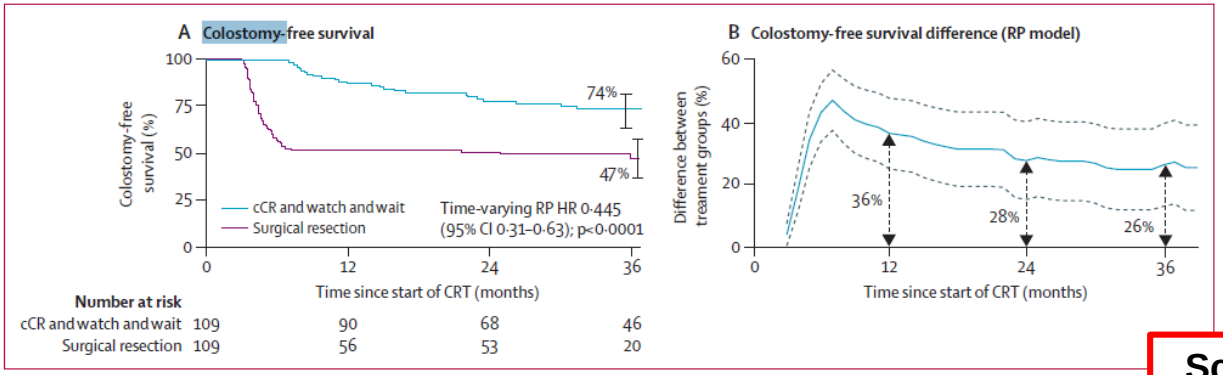


Figure 4: **Colostomy-free survival for the 218 patients in the matched analysis cohort**
(A) Kaplan-Meier curves of colostomy-free survival with effect modelled in a time-varying covariate RP model; percentages shown on the graph are 3-year colostomy-free survival; vertical lines show 95% CIs. (B) Differences in colostomy-free survival between the two treatment groups with time, based on the RP percentages show difference at 12, 24, and 36 months and dotted curves show 95% CI. We included propensity score as a covariate in the models. cCR=clinica complete response. CRT=chemoradiotherapy. HR=hazard ratio based on the time-varying covariate RP model. RP=Royston-Parmar.

Mehr N1 und mehr T4 Stadien in der OP Gruppe

Schlussfolgerung: klinisch relevant

es braucht randomisierte Studien

Kolonkarzinomrisiko bei seratierten Adenomen

Holme et al. GUT 2015, 64:929-36 (Norwegen)

Studienpopulation: 12‘955 Personen, 50-64j
Sigmoidoskopie

≥ 1 x ≥ 1cm serratiertes Adenom	Nicht fortgeschrittenes Adenom	fortgeschrittenes Adenom
81	1488	701
HR: 2.5	HR: 0.6	HR: 2.0

f/u 10.9 Jahre

Kontrollpopulation:
78‘220 Personen
50-64j

NB! 23 grosse serratierte Adenome: Nicht reseziert - > keiner wurde zum Karzinom !

Serrated Polyposis Syndrome SPS

WHO Definition:

(I) ≥ 5 serrated polyps proximal to the sigmoid colon, two measure at least 10 mm in diameter

and/or

(I) Any number of serrated polyps occurring proximal to the sigmoid colon in an individual who has a first-degree relative with SPS

and/or

(I) more than 20 serrated polyps spread throughout the colon

Carballal S, et al. Gut 2015:	296 patients: 47 with CRC (15.8%)
IJspeert JEG, et al. Gut 2015:	434 patients: 127 with CRC (29.3%)