
12TH ANNUAL
NCSCG
POST-DDW
SYMPOSIUM

Colon Cancer Updates

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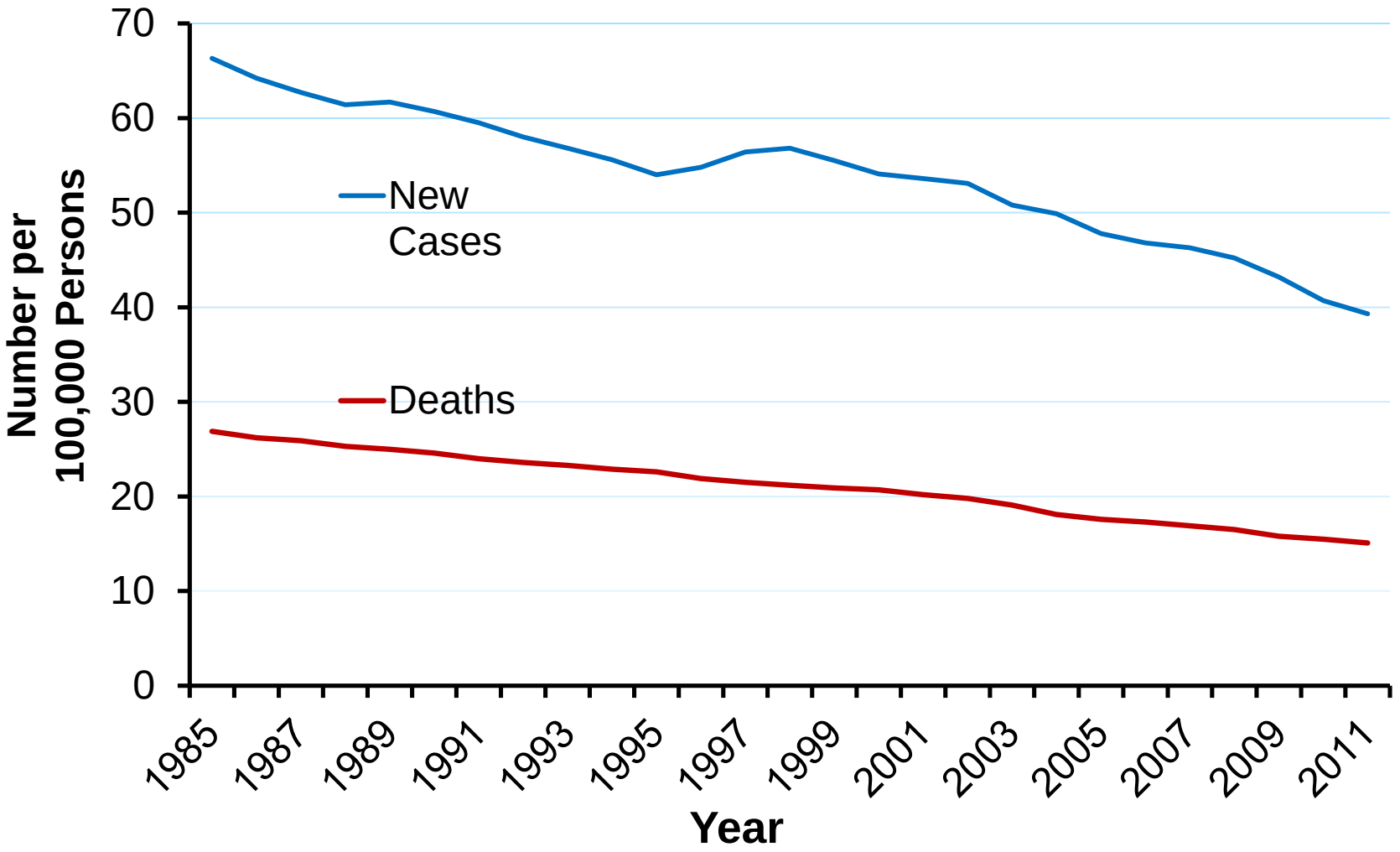
Outline

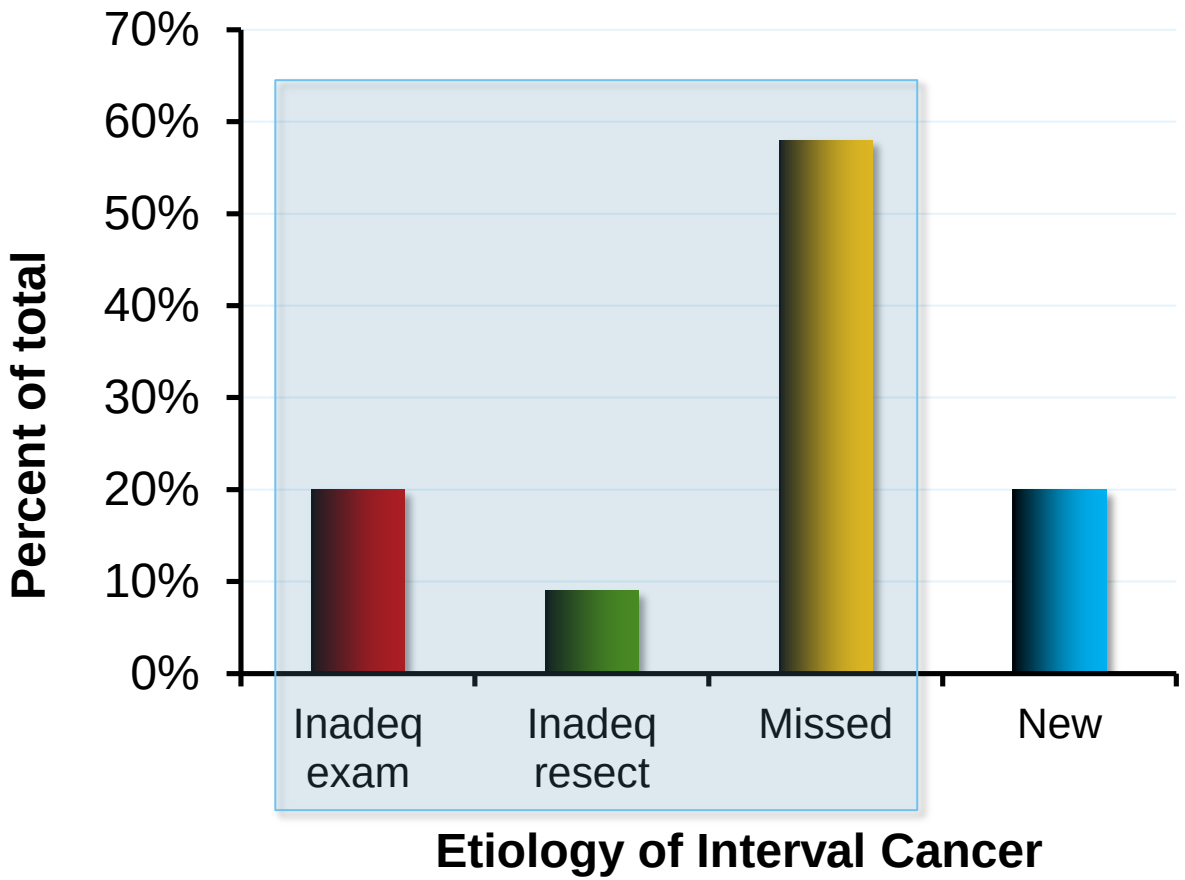
- Improving colonoscopy quality
- Landscape around screening tests
- Screening strategy & the impact of adherence
- FAP
- Discussion

New cases and deaths from CRC has steadily declined



Adapted from Surveillance, Epidemiology, and End Results (SEER) Program

Up to 75% of interval CRC might be preventable



Le Clerq et al. *Gut* 2014; Marx et al. MO498

Improvement in ADR associated with reduced interval CRC

- Polish national screening program
  - ADR increased from 14.3% to 20.2% on average
  - Improvement in ADR reduced interval CRC by 37% and death by 50%
    - Highest ADR category associated with 68% reduction in risk of CRC and death by 80%

Kaminsky et al. TU967; Kaminski MF, *NEJM* 2010; Corley D, *NEJM* 2014

How can ADR be improved?

- RCT of GI to feedback alone vs. hands-on training + assessment + feedback
  - Hands-on training + assessment led to 7.1% increase in ADR
  - Feedback alone led to 4.2% increase in ADR
    - *Hawthorne effect* (aka the observer effect) - improve behavior in response to being observed

Kaminsky MO794; Tinmouth SA1516

What are other ways to increase detection?

- Optimize colonic preparation
  - Split vs. full dose
    - ADR 53% vs. 41%; Prep 96% vs. 88% adequate; more tolerable
      - » Paggi et al. SU432
      - » Fishbach et al. SU1075
- Meticulous exam (retroflex, relook)
  - *G-EYE Endoscope* → 59% ADR, shorten
    - » Hendel et al. SU435
  - *Endocuff* → mean polyp # ↑
    - » Van Doorn et al. SU434
- Imaging
  - Confocal not practical
  - Chromoendoscopy – SA1106

Measuring quality is part of practice

- Physician Quality Reporting System (PQRS)
  - CMS program
- Payment penalty to begin 2015 based on data reporting requirements, then adjustments in 2017 based on quality metrics

What are the updated quality indicators?

- Indication appropriate
- Informed consent
- Appropriate surveillance recommendations > 90%
- Prep quality adequate > 85%
- Cecal intubation > 90% overall, >95% screening
- ADR > 25%
- Mean withdrawal time = 6 minutes
- Perforation < 1:1,000
- Post-polypectomy bleeding < 1%
- Attempted endoscopic removal of polyps < 2 cm
- Others

Rex DK, *GIE* 2015

Implementing quality: GI Quality Improvement Consortium (GI QUIC)

- Compatible with G-Med, Pentax/Olympus, Provation
- Collects 84 data points and reports can be customized by user and facility; report is real-time
- Current status: 1,590,000 colonoscopies, 100,000 EGDs, 375 organizations and >3,100 physicians (of total of ~13,000 practicing GI docs)
  - Increases in ADR in a Texas group (Tom Deas) from 2009 → 2014
  - Recommended surveillance intervals often do not follow guidelines

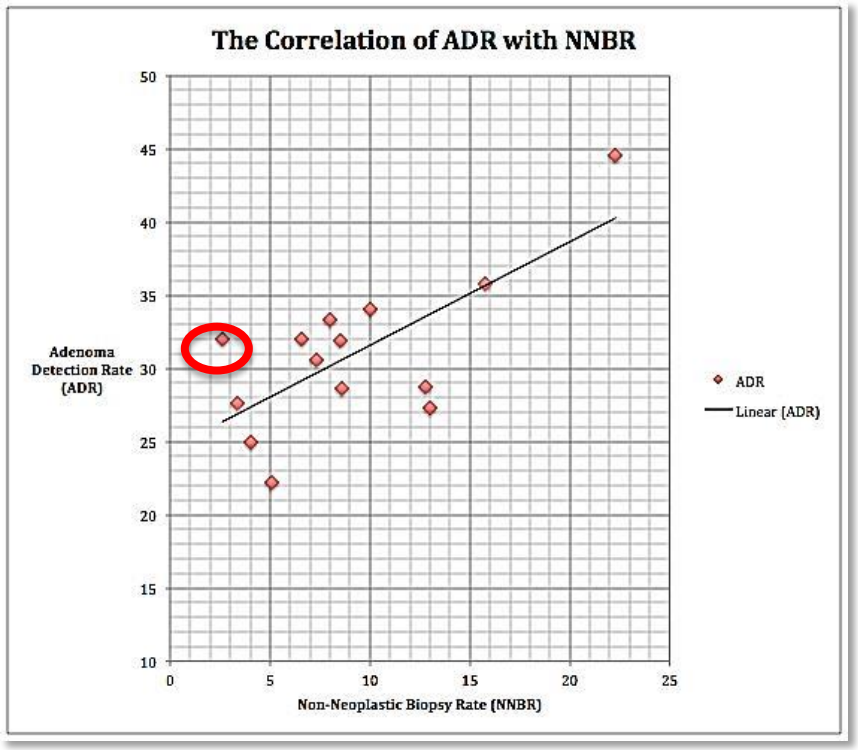
World Endoscopy Organization (WEO), Friday

Quality Colonosocopy Paradox

- High ADR or quality colonoscopy → more colonoscopies
  - Guidelines 5-10 yrs, but most recommend 5 yrs
  - ADR 50+%, but lifetime CRC risk is 5% → discrepancy
- What should we recommend? How about 2 colo's with diminutive adenomas?
- *EPoS (Euro Polyp Surv)*
  - 27,500 pts with low-risk adenomas
  - RCT: Surveillance colo at 5 vs. 10 yr
  - Outcome: CRC incidence

Jover et al. NCT02319928

Trying to achieve high ADR comes at a cost



Issues around ADR

- More surveillance colonoscopy
- Societal & patient costs
- Anxiety over polyps
- Med-legal
- More is better
- Fee for service
- Open access

Berger D et al. TU971

Can we ‘diagnose and leave’ or ‘resect and discard’ diminutive polyps?

- Imaging enhancement widespread (NBI, iSCAN, FICE)
- 26 GI, 2 centers, 2770 diminutive polyps
  - » Patel SG et al. SU448

Total Diminutive Polyp Predictions	2770
High confidence	2108 (76.1%)
Low confidence	662 (23.9%)

	Overall (n=2770)
Accuracy	77.4
Sensitivity	90.0
Specificity	61.4

Desire for high ADR counters ‘resect & discard’
- Unclear how it will be implemented
- Better risk stratification warranted, but not at expense of increasing surveillance

Post-polypectomy bleeding

- Examined patients on antithrombotics
- Incidence of post polypectomy bleeding was low, 1.2% (0.91-1.54).
  - Risk factors: polyps ≥ 2cm size, multiple large polyps, early reinitiation of antithrombotics, and use of right sided cautery.
- Heparin bridge had a significant bleeding risk (15%), compared to those on warfarin alone (0.66%).
  - Consider deferred removal or IV heparin post-procedure
- The use of prophylactic clips did not influence the rate of post polypectomy bleeding.

Lin D et al. SU331

What is the risk of CRC after a FOBT+ test in patients with a prior colonoscopy?

- Retrospective Canadian study, FOBT+ → incident CRC
- Prior colonoscopy associated with 0.5% risk of CRC

FOBT groups	Percent
FOBT+ (no prior colo or colo>10yrs)	4.9
FOBT+ (prior colonoscopy < 10 years)	
Colonoscopy >0 to 2 yrs before FOBT+	1.1
Colonoscopy >2 to 5 yrs before FOBT+	1.4
Colonoscopy >5 to 10 yrs before FOBT+	2.1

Indication for FOBT unclear (potential confounding) but performing colonoscopy may be warranted

Tinmouth et al. #TU968

Innovation around CRC screening tests

- Stool-based
  - Fecal immunochemical test (FIT)
  - Cologuard: Stool DNA + FIT
- CT colonography
- Capsule endoscopy
- Blood-based
  - Methylated Septin 9 (ColoVantage, Epi proColon)
  - Cologic by Phenomenome
  - Liquid Biopsies: circulating tumor DNA/cells

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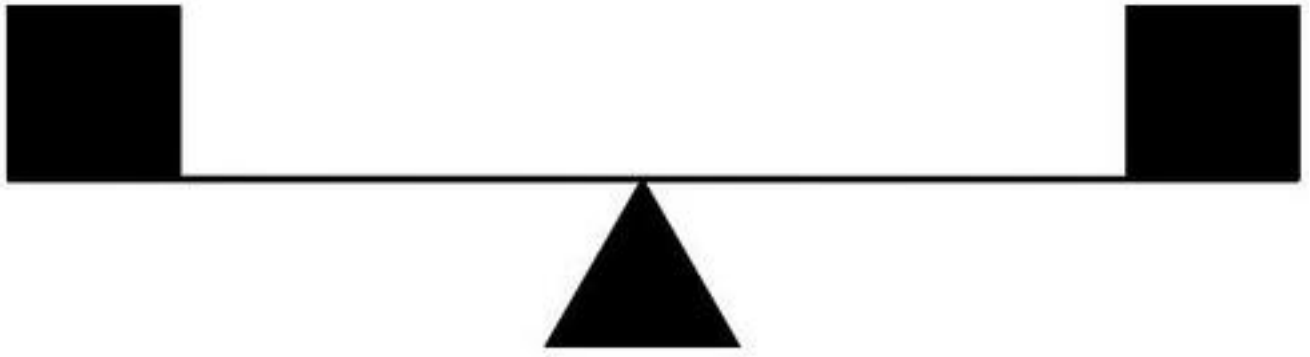
What did the Deep-C (stool DNA) trial teach us?

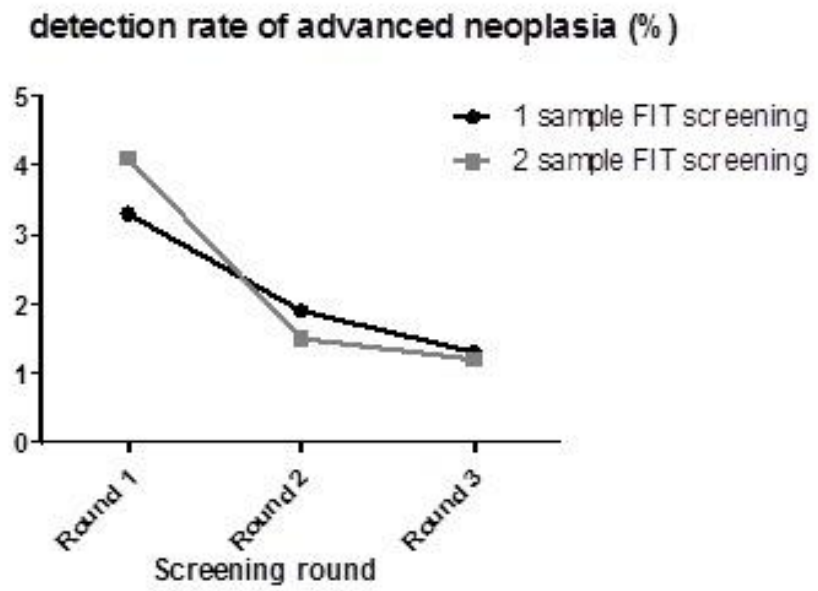
Stool DNA + FIT	FIT
Very good for cancer (92%)	Good for cancer (74%)
Fair for large polyps (42%)	Poor for large polyps (24%)
Fair for serrated lesions (42%)	Useless for serrated polyps (5%)
Lower specificity (86%)	High specificity (95%)
Expensive ($500)	Inexpensive ($22)
Failed samples (6%)	Unanalyzable (< 1%)



Imperiale et al. *NEJM* 2014

FIT: Positivity, participation, & usability

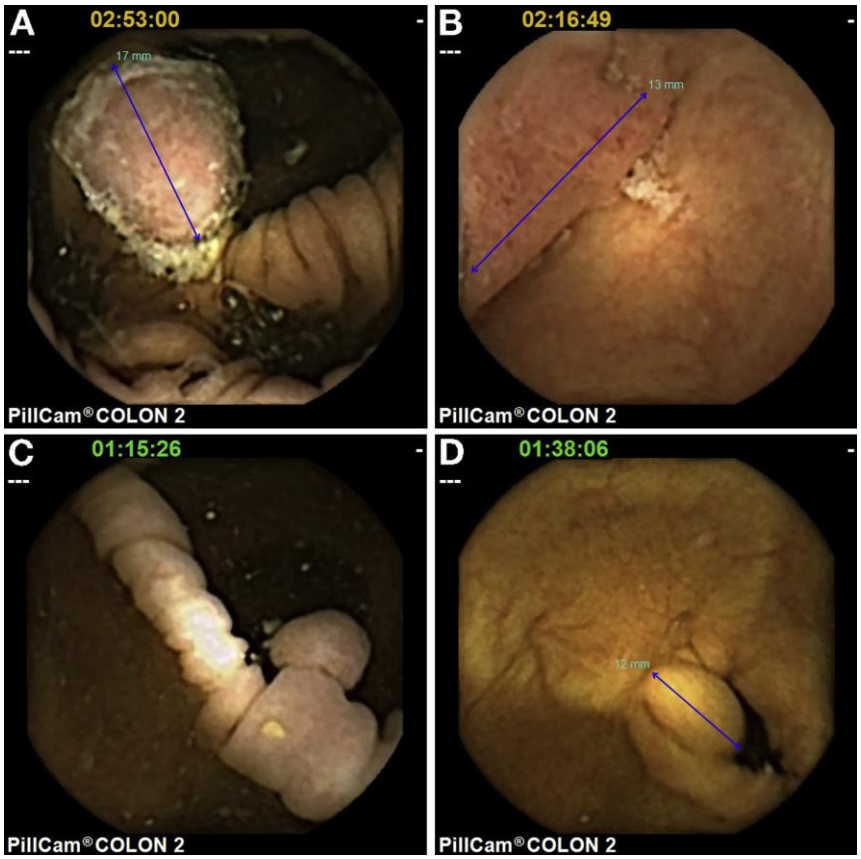
- Optimal strategy
  - » MO1984; MO1944
- Performance varies by FIT brand
  - – FOB-Gold vs. OC-Sensor
  - – Not analyzable
    - 1.9% with FOB-Gold
      - » Grobbee et al. TU820



Which side does the patient open?

Capsule endoscopy continues to improve

- Given Imaging → PillCam COLON2
  - Prep/instructions are extensive → 9% of procedures excluded
  - Adenomas > 10 mm
    - Sens 92%
  - Adenomas 6-9 mm
    - Sens 88%
  - Sessile polyps
    - Sens 74%



Romero MO1985; Rex et al. Gastro 2015

CT Colonography endorsed by …

CT Colonography

- Currently, used in 0.03% of Medicare beneficiaries (MO1949) – high risk & incomplete colonoscopies
- Endorsed in Multi-Society Task Force since 2008 and FDA in 2013
- US Preventative Services Task Force had concerns in 2008
  - Extracolonic lesions and radiation (very low < 5 mSv)
  - Variable colonoscopy referral rate (8% - 39%)
    - » Sehgal MO1955
  - One-third of sessile serrated polyps (n=91) will be missed
    - » Singla et al. MO552
- USPSTF updated statement is expected this year

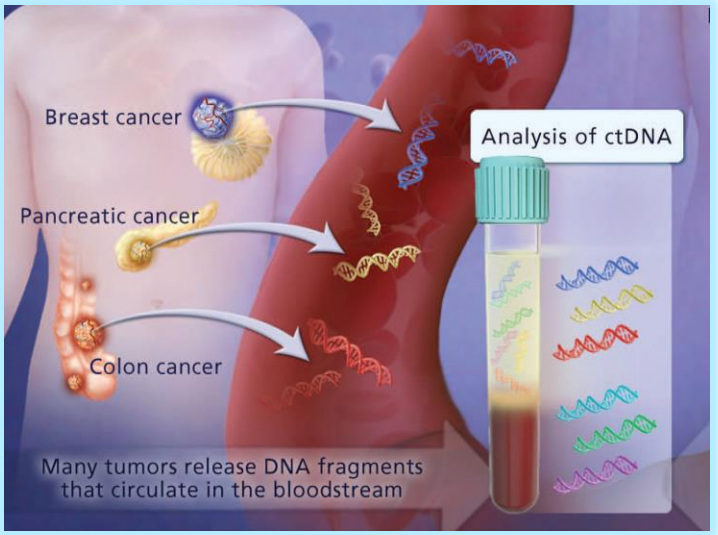
Cash B, *WEO* conference pre-DDW

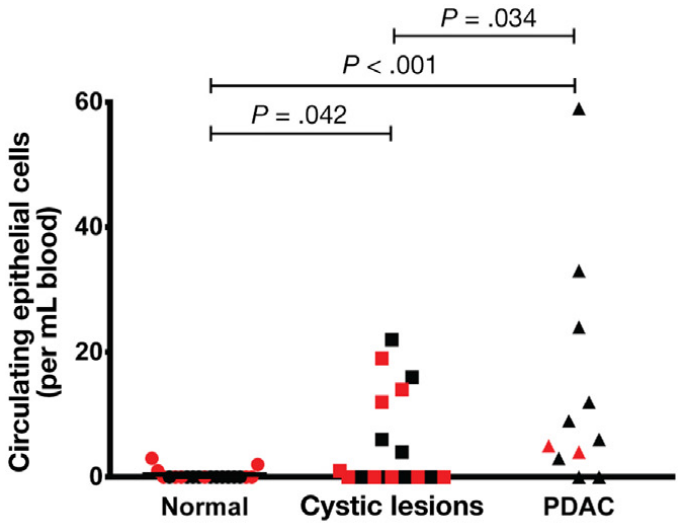
Blood-based test … holy grail

- Methylated Septin 9 (Epi *pro*Colon)
  - Sens. 70%, Spec. 73%
    - » Leung et al. MO1931
  - Other DNA markers → performance may improve
    - » Guery et al. MO1939
- GTA-446 (Cologic) by Phenomenome
  - Limited data but sens. ~80%, spec. 80%
    - » Goodenowe et al. MO1962

Liquid biopsy

- Oncology space
  - Response to chemo
- Blood sample
  - PCR detects DNA
  - Microfluidics platform to identify cancer cells





Rhim A et al. SA239, also see Gastro 2014

Which screening strategy is more effective?

- CONFIRM trial (VA system) – Dominitz
  - FIT (OC Sensor, 100 ng/mL) vs. colonoscopy
  - 28,000/52,000 enrolled, more preferred FIT
  - Colonoscopy quality: 97% cecal intubation, 11 minute withdrawal, 62% split prep & 89% adequate
  - FIT: 5% out of window (mail issues)
- ColonPrev trial (Spain) - Quintero
  - Colonoscopy vs. biennial FIT; 53,000 enrolled
  - Findings: Participation 34.2% FIT vs. 24.6% Colonoscopy → similar CRC detected.
    - FIT+ rate was 7.2%, colonoscopy follow up was 86%

In the end, adherence a major issue

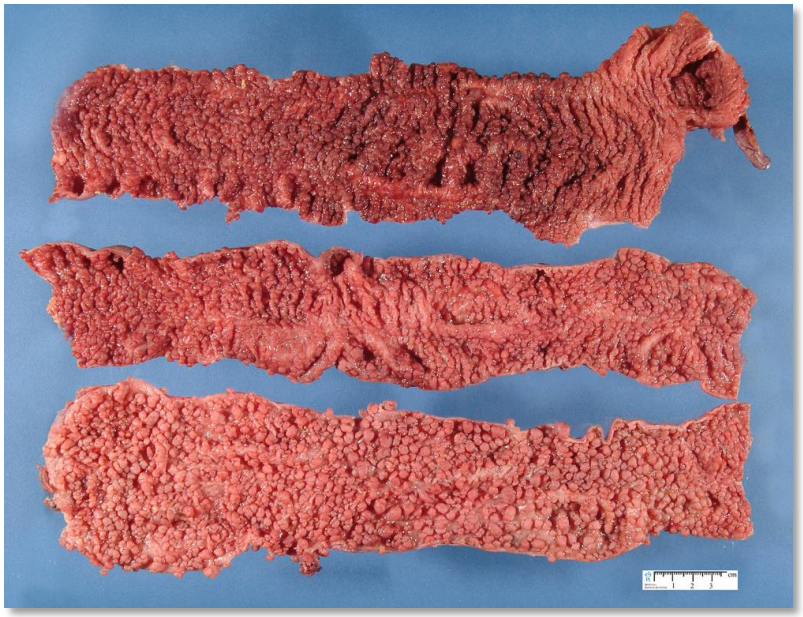
- Mathematical simulation
  - Goal: Achieve 80% adherence by 2018
    - 58%-80% reduction in CRC incidence and mortality compared to no screening
    - 33% reduction when compared to 60% adherence
- *Message*: get the test done → and if positive, you'll need a colonoscopy

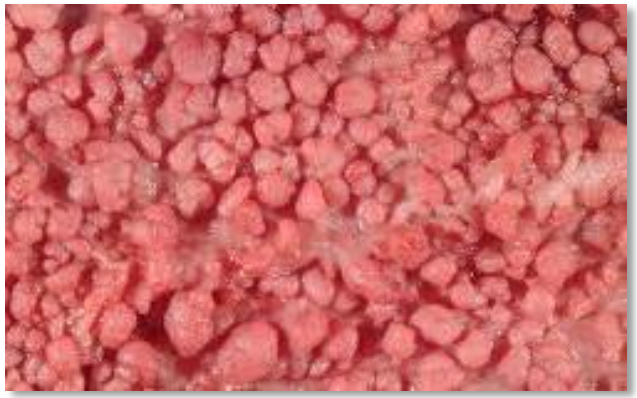
Meester et al. TU969

Conclusions

- Quality and reporting is here to stay
- Colonoscopy ADR can be improved
  - Prep quality is critical
  - Feedback alone improves performance
- Take caution in patients on heparin bridge
- FOBT+ after colonoscopy still incurs increased CRC risk
- Dominant strategies remain dominant
  - CTC, capsule, and likely stool DNA for subset
- Adherence is critical and colonoscopy remains vital in all strategies
- Unanswered questions
  - How do we do a better job at risk stratification?
  - How do we do a better job of polypectomy?

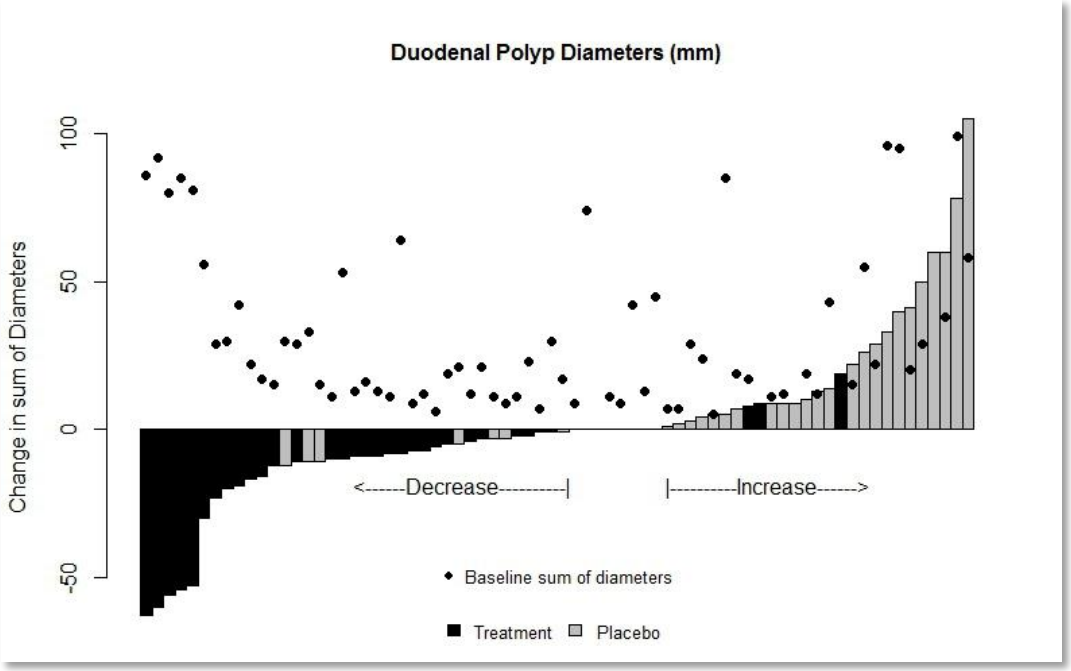
What's new in familial adenomatous polyposis?





Novel regimen to decrease duodenal adenomas

- Patients with FAP at high risk for other cancers
- Duodenal adenomas > 50% and cancer > 15%
  - RCT: sulindac (Cox-2) 150 mg BID + Erlotinib (epidermal growth factor inhibitor) 75 mg QD x 6 mo versus placebo.



Sammader J et al. SU447