Colorectal Cancer in 2006: New Developments

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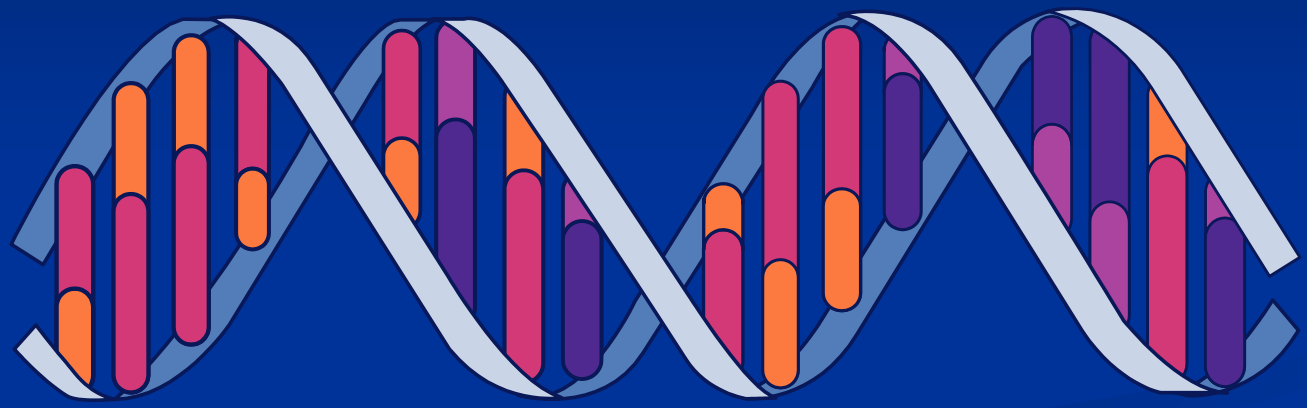
Hereditary Colon Cancer and Genetic Testing



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Who is at High Risk for Hereditary Cancer?

Hereditary cancers account for a small but important proportion of all cancer

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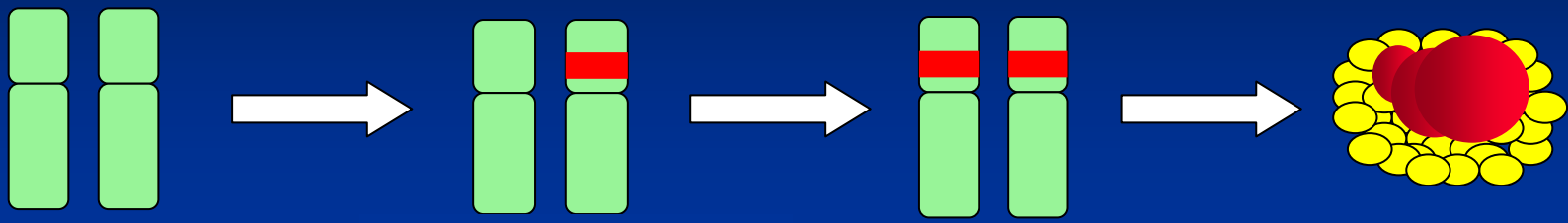
Cancer arises when both copies of genes are inactivated



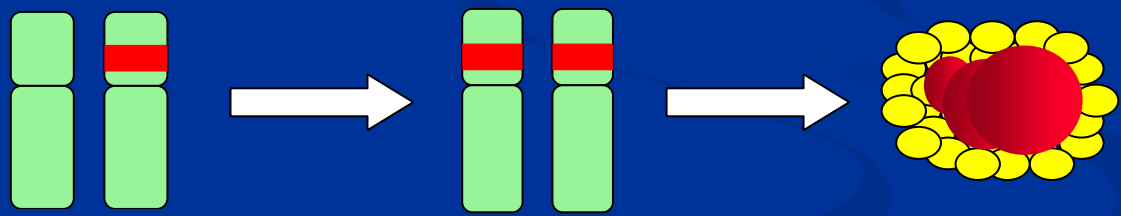
2 normal genes

1 damaged gene
1 normal gene

2 damaged genes

Tumor develops

In hereditary cancer, one damaged gene is inherited.

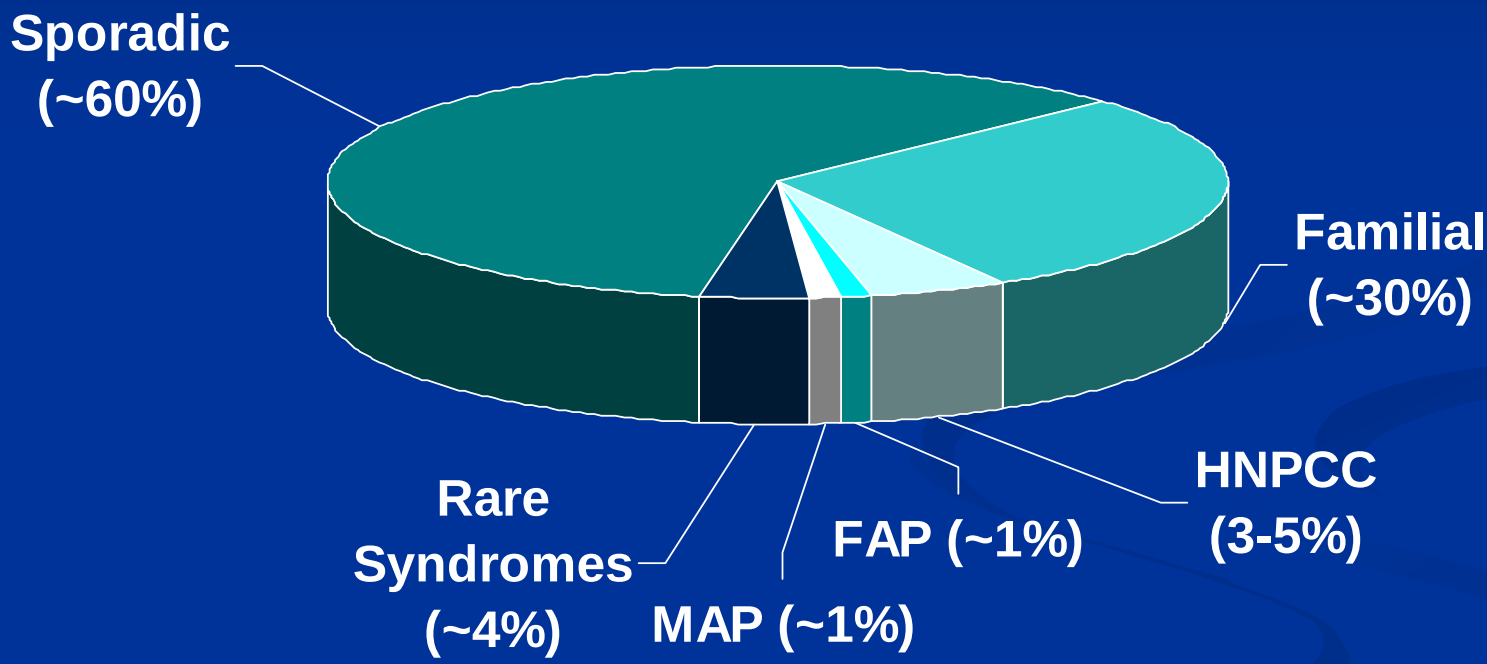


1 damaged gene
1 normal gene

2 damaged genes

Tumor develops

Colorectal Cancer



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Hereditary Colorectal Cancer (CRC) Syndromes

Nonpolyposis (few to no adenomas)

- HNPCC – CRC and/or endometrial cancer (EC)

Polyposis (multiple adenomas)

- FAP – Severe colonic polyposis +/- CRC
- AFAP – Less severe colonic polyposis +/- CRC
- MAP – Varying degrees of colonic polyposis +/- CRC

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Features Suggestive of HNPCC

- Early onset colorectal cancer (<50y)
- Early onset endometrial cancer (<50y)
- Two or more HNPCC cancers in an individual or family*

***HNPCC cancers: colorectal, endometrial, gastric, ovarian, ureter/renal pelvis, biliary tract, small bowel, pancreas, brain, sebaceous adenoma**

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Features Suggestive of Adenomatous Polyposis Syndromes

- Multiple colorectal adenomas
- Colorectal cancer associated with multiple adenomas
- Possible extracolonic manifestations
  - Non-colonic polyps and cancers (i.e. duodenal, gastric)
  - Desmoid tumors, osteomas, soft tissue tumors, dental abnormalities, CHRPE

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Is the cancer in my family hereditary?

- Risk Assessment appointment
  - understand cancer risk specific to your history
  - learn about screening, prevention and risk reduction
  - discuss the possibility of genetic testing
  - discuss the potential impact of genetic testing

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What happens during the risk assessment appointment?

1. Collect family history information before appointment

2. Schedule an appointment with a health care provider to discuss your family history and determine if you are appropriate for genetic testing

3. Consider the pros and cons of genetic testing

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What does genetic testing involve?

1. Genetic testing is performed on a small blood sample
2. Results are available in about 4 weeks and are discussed in person with health care provider
3. Consider options for screening and prevention, based on positive or negative results
4. Contact your health care provider periodically for updates

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Costs

Risk Assessment Appointment

- Cost varies at each institution

Genetic Testing

- Most insurance companies are covering genetic testing

- Medicare and most major insurance carriers have established guidelines

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Genetic Discrimination in Health Insurance is Illegal

- Health Insurance Portability and Accountability Act (HIPAA)
  - Prohibits group health plans from discriminating on the basis of genetic information
- Most states have enacted additional protections

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Where Can I Learn More?

- Nicole Melby, RN, BSN
  757-673-5967
- Hereditary Colon Cancer Association-
  www.hereditarycc.org
- Colorectal Cancer Network
  www.colorectal-cancer.netcancer.net
- Colon Cancer Alliance
  www.ccalliance.org
- Myriad Genetic Laboratories
  www.myriadtests.com

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Colorectal Cancer Screening

T J Duntemann,MD,FACP

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Overview

- Common, lethal and preventable
- Average lifetime risk ~ 5%
- Infrequent before age of 40
- 90% of cases occur after age 50
- 2nd leading cause of cancer death both sexes
- Approx. 52,000 deaths/yr in US

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Why is Screening Effective?

- Most colon cancers develop gradually over many yrs.
- Most begin as small adenomatous polyps
- Polyps may grow then transform into malignancies and spread
- The usual progression takes at least 10 yrs
- Screening identifies polyp formers and those at risk

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Screening vs. Surveillance

- Screening- Asymptomatic w/o risk factors
- Surveillance-
  - Previous polyps
  - Previous colon cancer
  - Significant family history
- Symptom evaluation
  - Blood , anemia, etc.

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Determine the Risk

- Family history of CRC or polyps
  - 1st or 2nd degree relative?
  - Age of onset?
  - Number?
- Personal history of CRC or polyps
- Personal history of Inflammatory Bowel Disease

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Screening Tests

- FOBT
- Flexible Sigmoidoscopy
- Air Contrast Barium Enema
- Colonoscopy

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Colonoscopy-Expectations & Risk

- Evaluation of colon and removal of polyps can prevent colon cancer
- Allows inspection and treatment in 1 visit
- Low miss rate (no test is perfect)
- Requires bowel prep
- Sedation most commonly utilized
- Risk of perforation or major bleeding are ~1 / 1000 procedures

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New Technologies

- Virtual colonoscopy
- Stool DNA testing
- Both would require colonoscopic intervention for positives

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The Benefits of Minimally Invasive Surgery for Colon Cancer

Ray T. Ramirez MD, FACS, FASCRS
Tidewater Surgical Specialists - Colorectal Surgery Division
Director – Bon Secours Center for Colon & Rectal Diseases

TIDEWATER Surgical SPECIALISTS, PLLC

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Laparoscopic Surgery

- Revolution: minimally invasive surgery
- First cholecystectomy 1987
- Smaller incisions, decreased pain, shorter length of hospital stay, early return to regular activities
- Application to variety of abdominal operations

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Laparoscopic Colectomy

- 1st Laparoscopic colectomy: 1990
- Spectrum of resections described
- Benefits similar as with other procedures
- Acceptable morbidity
- 2003: < 10% of all colectomies

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LAPAROSCOPIC COLECTOMY

Clinical Outcomes of Surgical Therapy Study Group-COST

A Phase III Prospective Randomized Trial Sponsored by National Cancer Institute and NCI Cooperative Groups

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LAPAROSCOPIC COLECTOMY TRIAL
Study Aims

To test differences in

- **Cancer outcomes**

  (Overall and Disease-Free Survival)
- **Safety (morbidity; mortality)**
- **Patient-related benefits (quality of life; cost effectiveness)**

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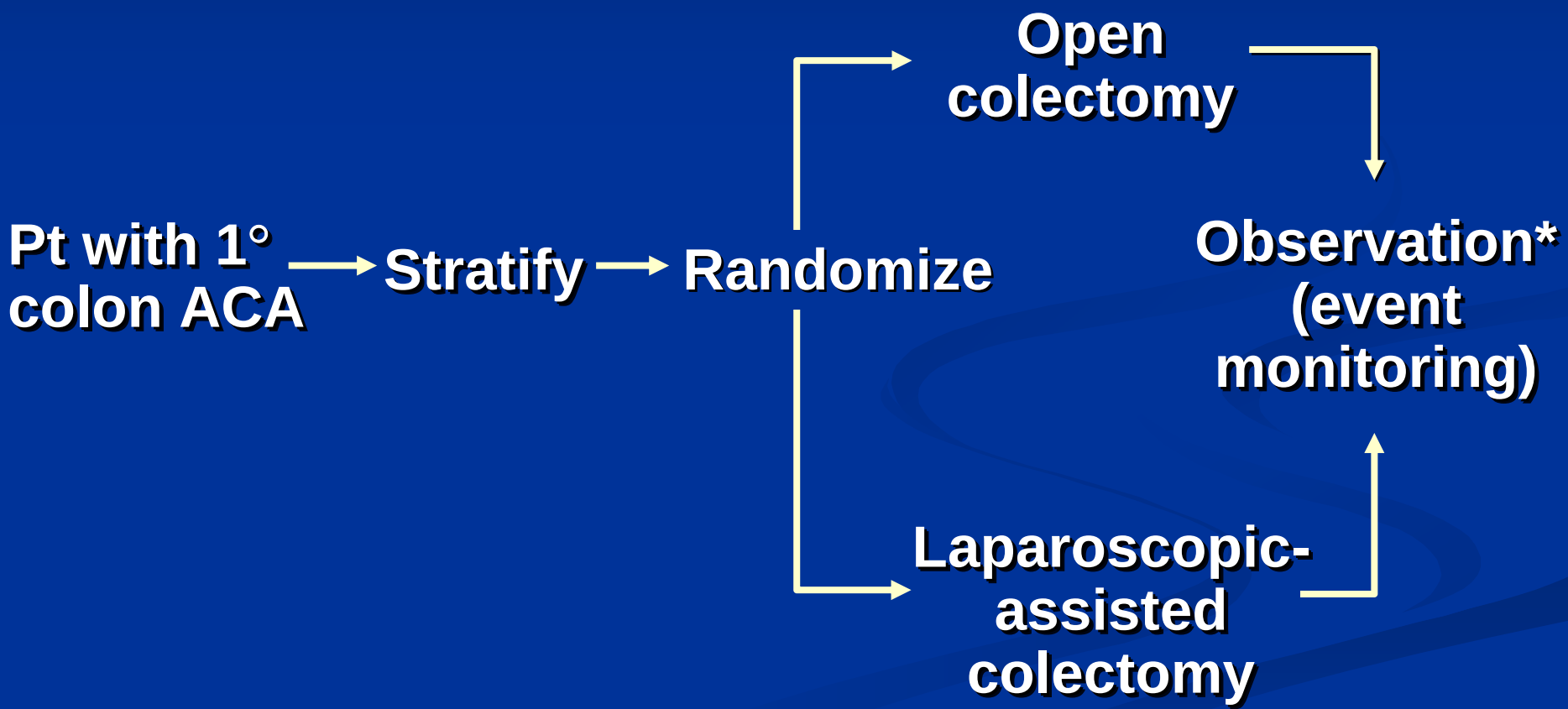
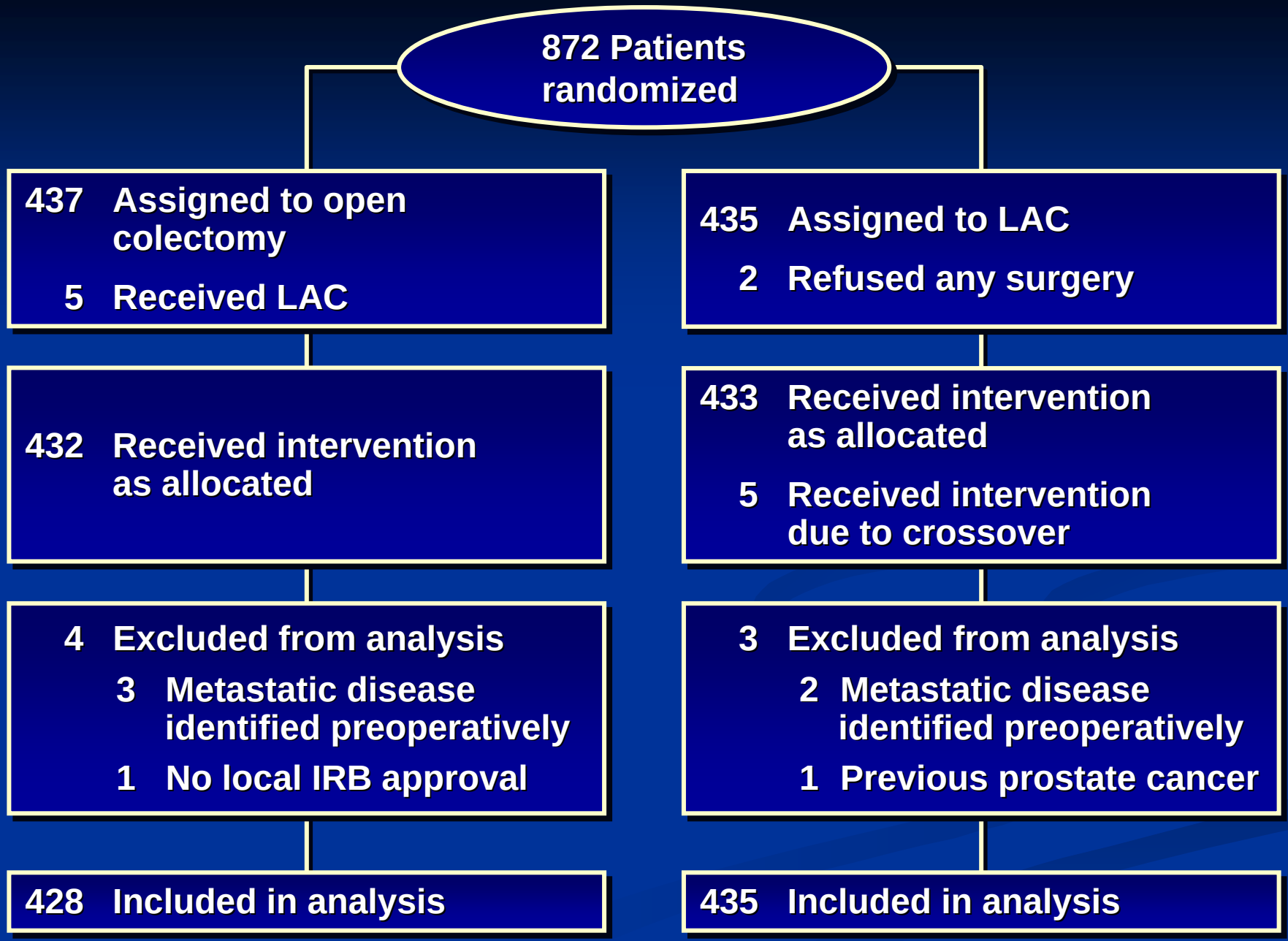
LAPAROSCOPIC COLECTOMY TRIAL
Schema




872 Patients randomized
437 Assigned to open colectomy
5 Received LAC
435 Assigned to LAC
2 Refused any surgery
432 Received intervention as allocated
433 Received intervention as allocated
5 Received intervention due to crossover
4 Excluded from analysis
3 Metastatic disease identified preoperatively
1 No local IRB approval
3 Excluded from analysis
2 Metastatic disease identified preoperatively
1 Previous prostate cancer
428 Included in analysis
435 Included in analysis

LAPAROSCOPIC COLECTOMY

COSTST Trial - Recovery Benefits*

	Open* n=428	LAC n=435
Length of stay	6 (5-7)	5 (4-6)
Narcotics	4 (3-5)	3 (2-4)
Oral analgesic	2 (1-3)	1(1-2)

*in days; median values;(interquartile range)

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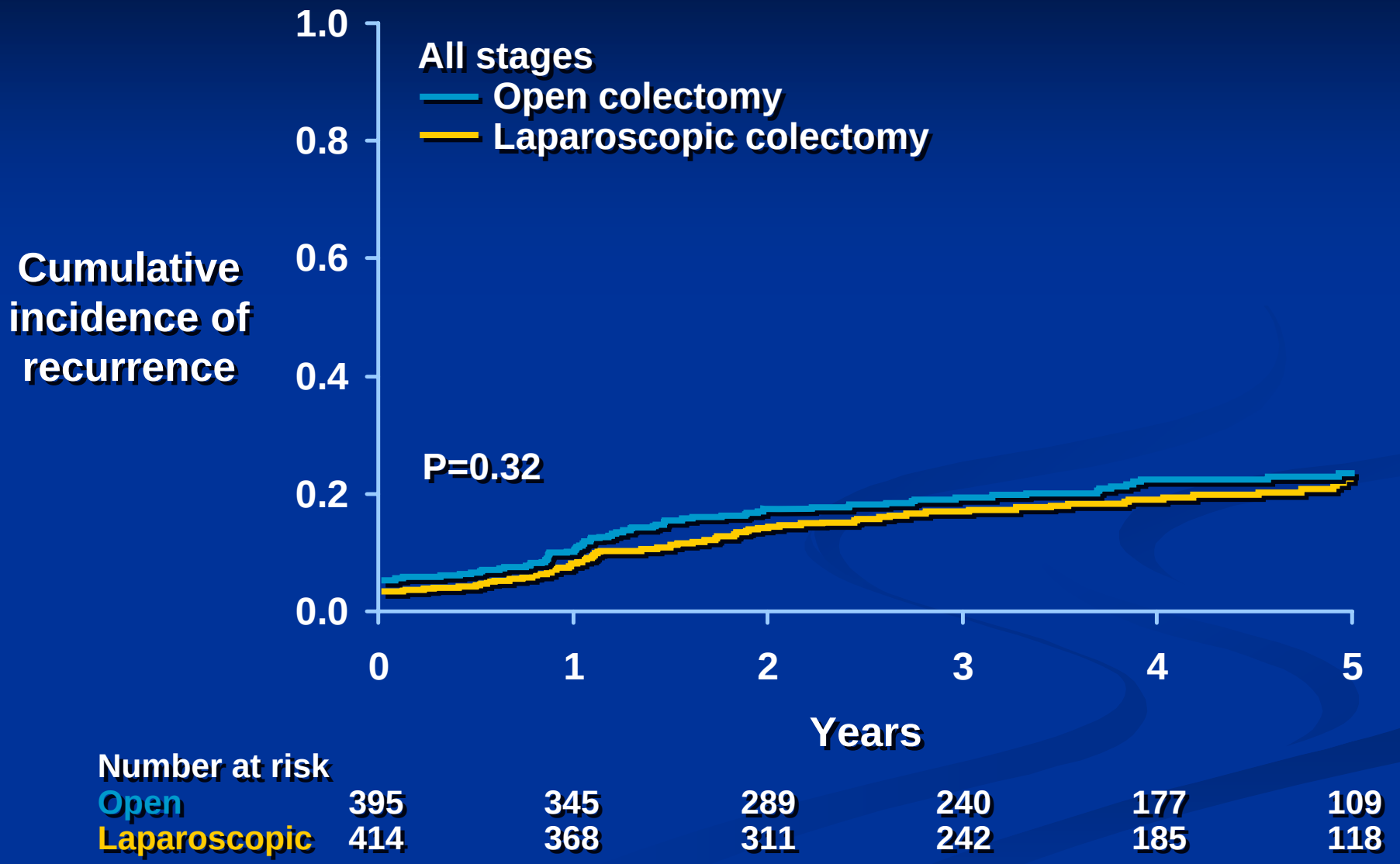
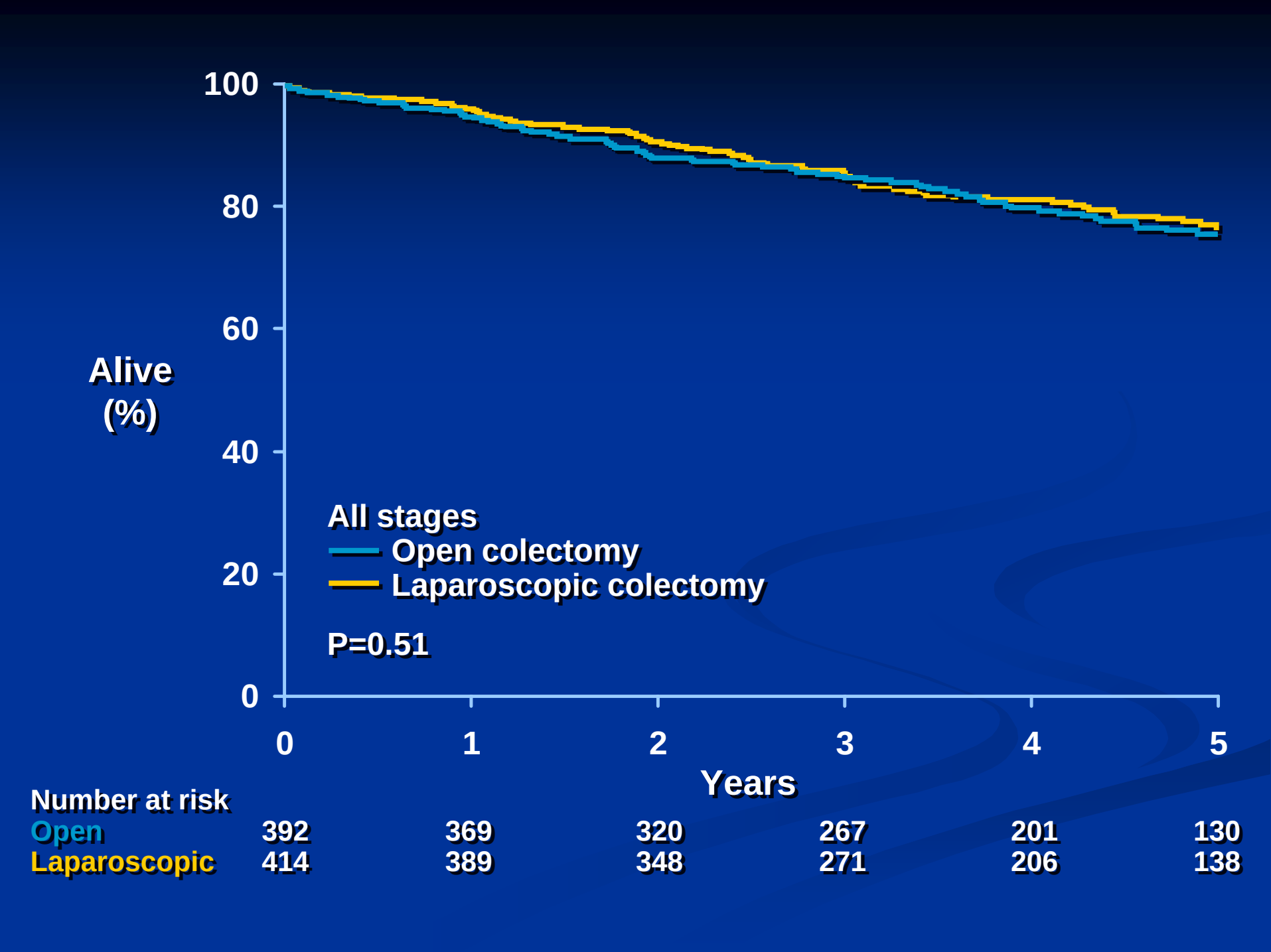
LAPAROSCOPIC COLECTOMY
COSTSG Trial - Morbidity/Mortality

	Open* n=428	LAC * n=435
30-day mortality		
no.(%)	4 (0.9)	2 (0.5)
Complications		
Overall	85 (20)	92 (21)
Intraoperative	8 (2)	16 (4)
Postoperative	80 (19)	81 (19)

* p=ns for all comparisons


All stages
Open colectomy
Laparoscopic colectomy
Cumulative incidence of recurrence
1.0
0.8
0.6
0.4
0.2
0.0
P=0.32
0
1
2
3
4
5
Years
Number at risk
Open 395 345 289 240 177 109
Laparoscopic 414 368 311 242 185 118


100
80
60
40
20
0
Alive (%)
All stages
Open colectomy
Laparoscopic colectomy
P=0.51
0
1
2
3
4
5
Years
Number at risk
Open 392 369 320 267 201 130
Laparoscopic 414 389 348 271 206 138

LAPAROSCOPIC COLECTOMY
Summary

- **Cancer Outcomes**
  - **No differences in**
    - **Overall Survival**
    - **Disease-free survival**
    - **Wound recurrences**

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LAPAROSCOPIC COLECTOMY
Summary

- Safety
  - Equivalent morbidity
  - Equivalent mortality
- Patient Related Benefits
  - Faster recovery
  - Significant differences

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Patients Now Have a Choice !

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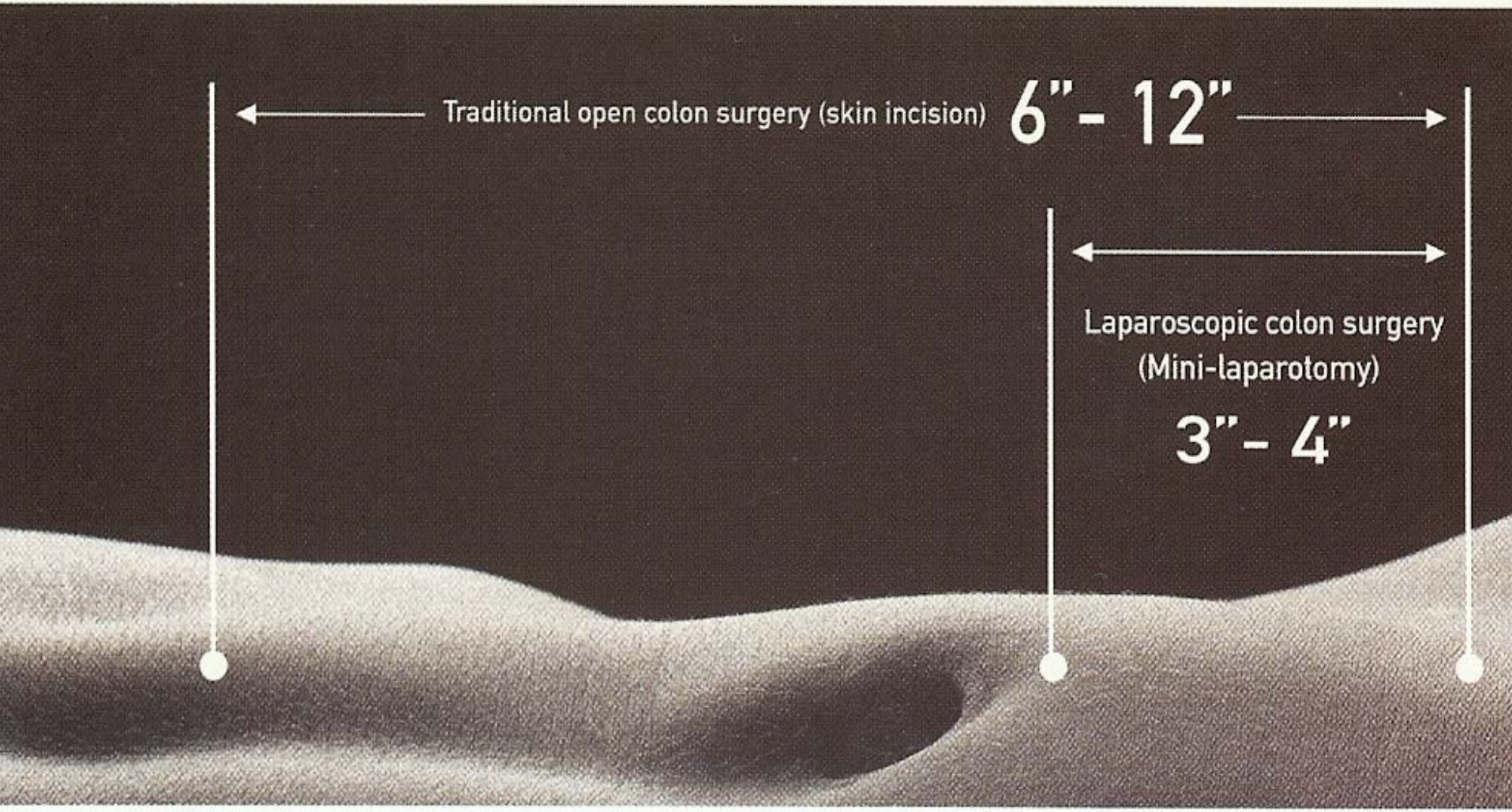
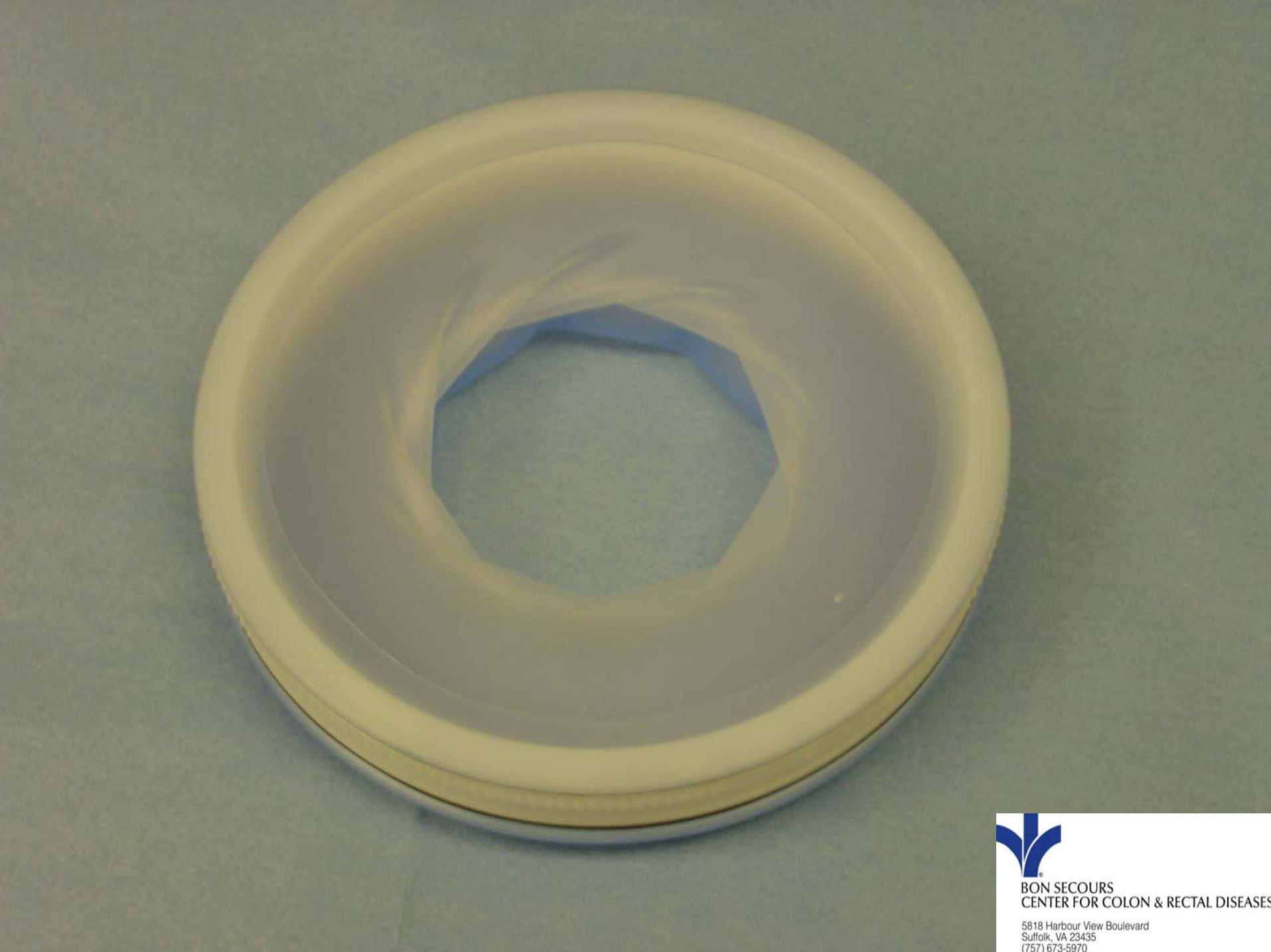


THE SHORTEST DISTANCE BETWEEN A PATIENT AND RECOVERY

Laparoscopic Colorectal Surgery
- Benefits -

- Smaller incision and scar
- Reduced operative trauma and stress
- Reduced post-op pain and narcotic use
- Early feeding
- Early return of bowel function
- Shorter hospital stay
- Diminished blood loss and morbidity
- Earlier return to work and activities of daily living
- Decreased physiologic and immunologic compromise



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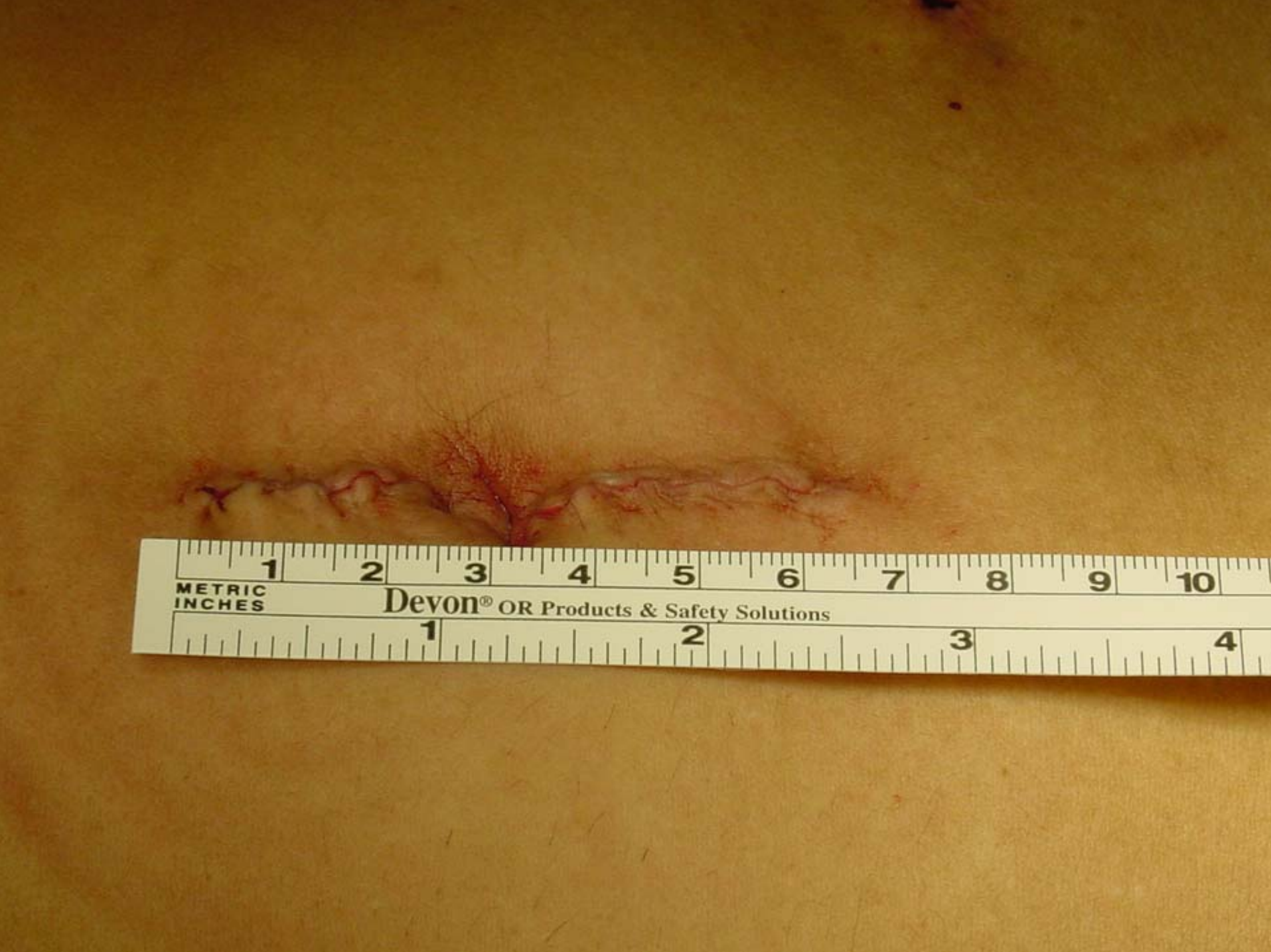
METRIC
INCHES
Devon® OR Products & Safety Solutions

Laparoscopic Colon Resection

- Summary
  - Less pain
  - Shorter hospital stay
  - Faster recovery
  - Why have colon surgery any other way???

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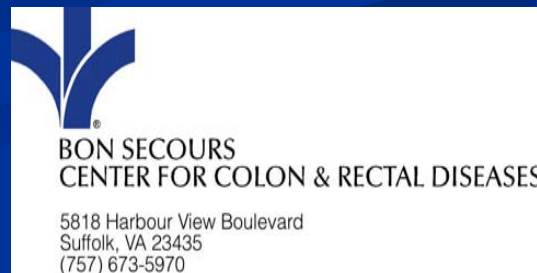
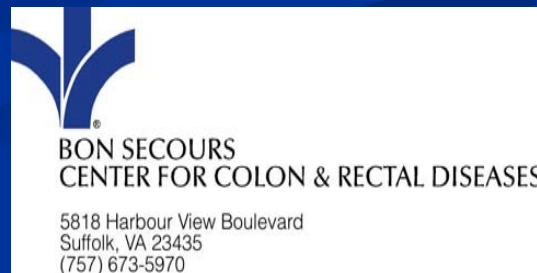
Bon Secours Center for Colon and Rectal Diseases

- Harbour View Campus
- Nicole Melby
  - On-site Clinical Coordinator
  - 673-5970



Questions?

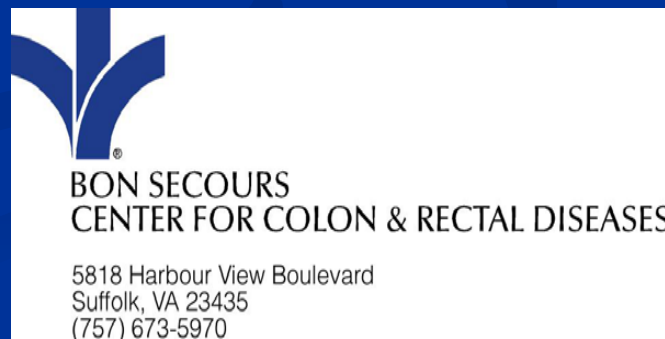
Thank You



Updates in Medical Oncology of Colon Cancer: Adjuvant Chemotherapy

James J. Stark, MD, FACP
Medical Director, Cancer Program
Maryview Medical Center

Professor of Medicine,
Eastern Virginia Medical School



Adjuvant Chemotherapy

- Given soon after surgery for cancer to try to eradicate tiny amounts of cancer that may have escaped the primary tumor before surgery
- Abundant animal experimental and human evidence of a substantial reduction in mortality using this approach

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Adjuvant Chemotherapy for Colorectal Cancer

- Relatively late development
  - Only about 15 years of successful data, probably because of previously relatively weak drugs
  - Newer drugs have improved outcome at the cost of additional toxicity and a financial burden on the health care system
    - "FOLFOX" regimens most active, use Oxaliplatin, an expensive and toxic drug

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Additional Factors Affecting Outcome

- Colorectal screening programs identify patients with earlier-stage disease
- Better surgical techniques
- Better pathological staging
  - The Will Rogers Phenomenon….

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- "When the Okies left Oklahoma and moved to California, they raised the average intelligence levels in both states."
  - -- Will Rogers, commenting on geographic migration during the economic depression of the 1930s.

Additional Factors Affecting Outcome

- Better surgical techniques
- Better pathological staging
  - The Will Rogers Phenomenon….

- As pathologists get better at finding lymph nodes, patients who would have been scored as “node negative” now have positive nodes and the prognosis of both groups improves
- Implications for data analysis….

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Adjuvant Chemotherapy: Bottom Line

- As more patients get diagnosed early, have better surgery and have a better outcome, we need a better way to select which patients should *not* be treated with adjuvant chemotherapy: who doesn't need treatment, and who won't benefit from it

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Better Selection of Patients: Molecular Markers of Prognosis

- New technology can identify thousands of genes in a tiny specimen of tumor: c-DNA microarray technology
- Tumors can be analyzed retrospectively to see which gene mutations can predict for a good or bad outcome
- This approach has recently been taken in colorectal cancer…

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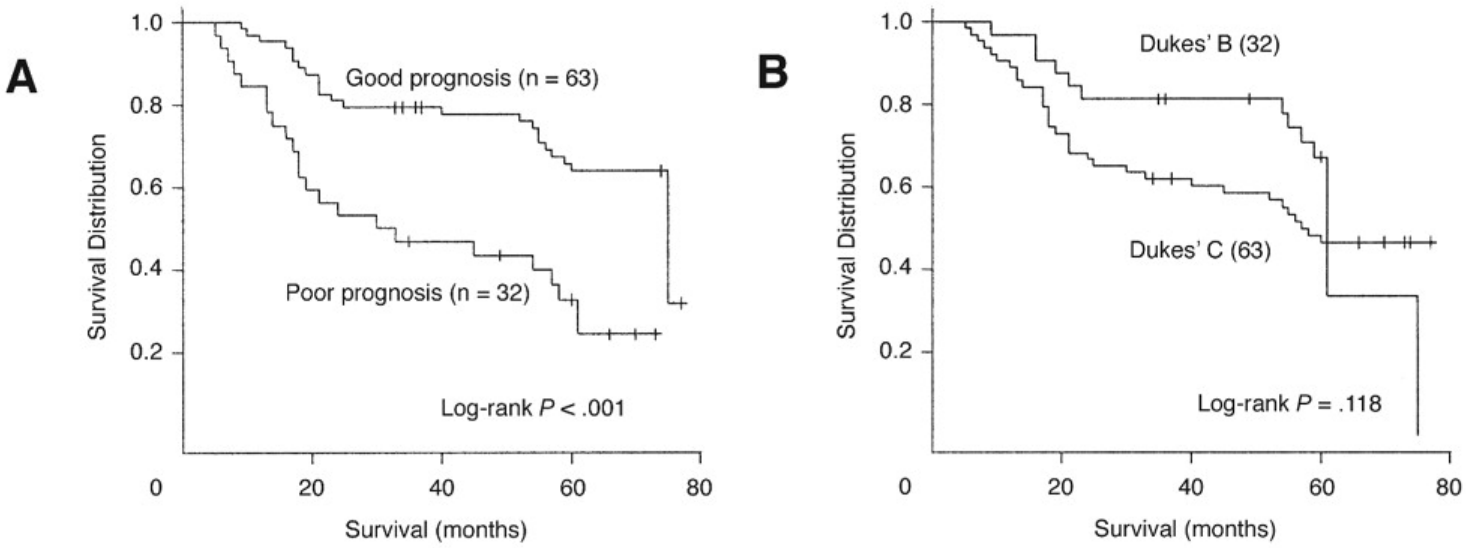
The Eschrich Study:

Identified 43 genes out of 32,000 studied:



Eschrich et al, JCO 23:3526, 2005

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Another Variable: Microsatellite Instability

- Looks at ability of tumor genes to repair themselves
- 15% of colon cancers have “MSI” which means they cannot repair defective genes
- Leads to a relative inability of the tumor to survive additional mutations
- May be a marker for a better outcome…

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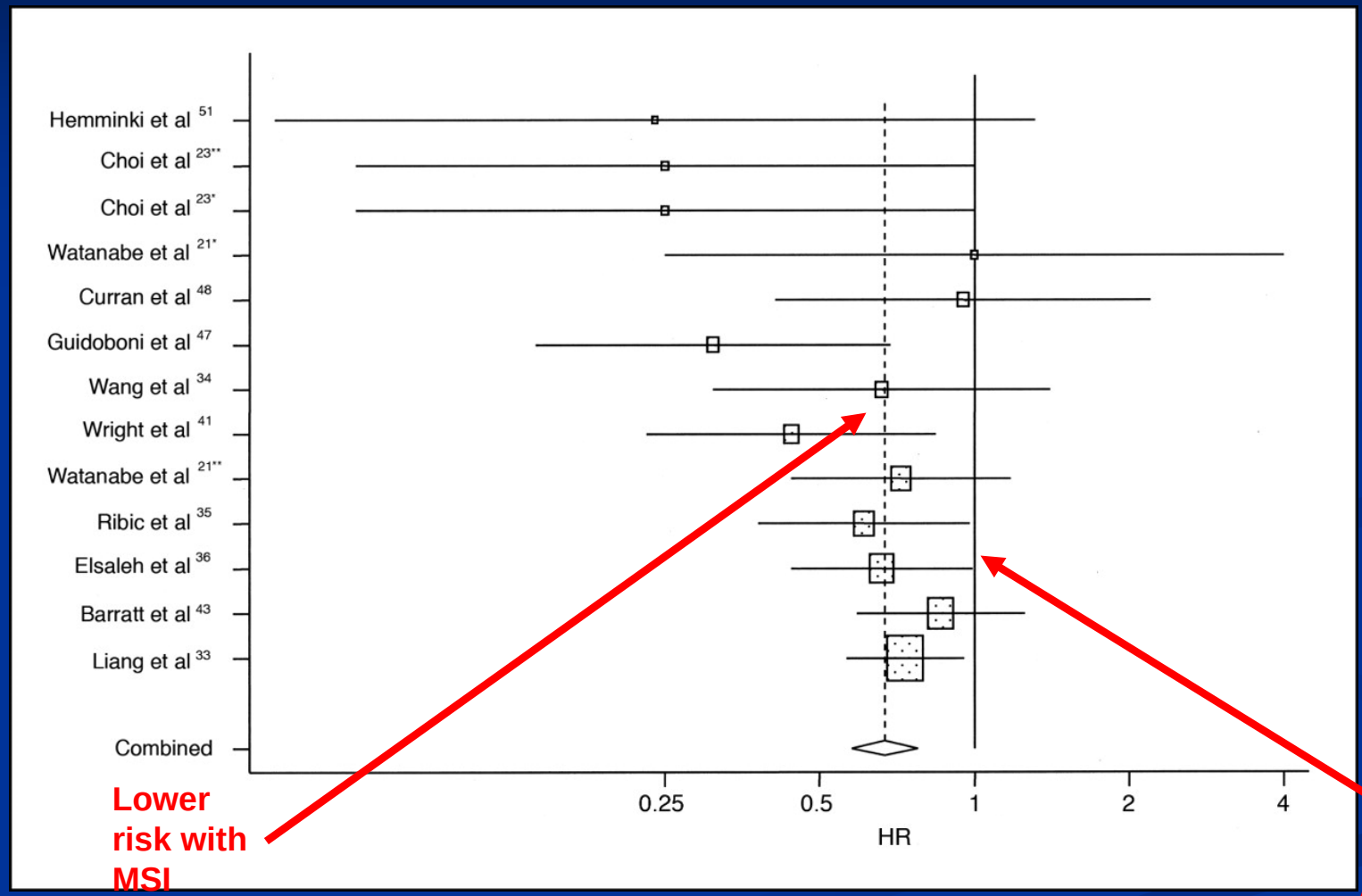
Hazard ratios (HRs) of overall survival in studies of all stage II-III colorectal cancer associated with microsatellite instability



Popat, S. et al. J Clin Oncol; 23:609-618 2005

Final Variable: P-53 status

- P-53 is a tumor suppressor gene: helps us *not* to get cancer
- When altered (mutated) cancers may develop more easily and may be more aggressive
- Colon cancer specimens examined retrospectively for this gene…

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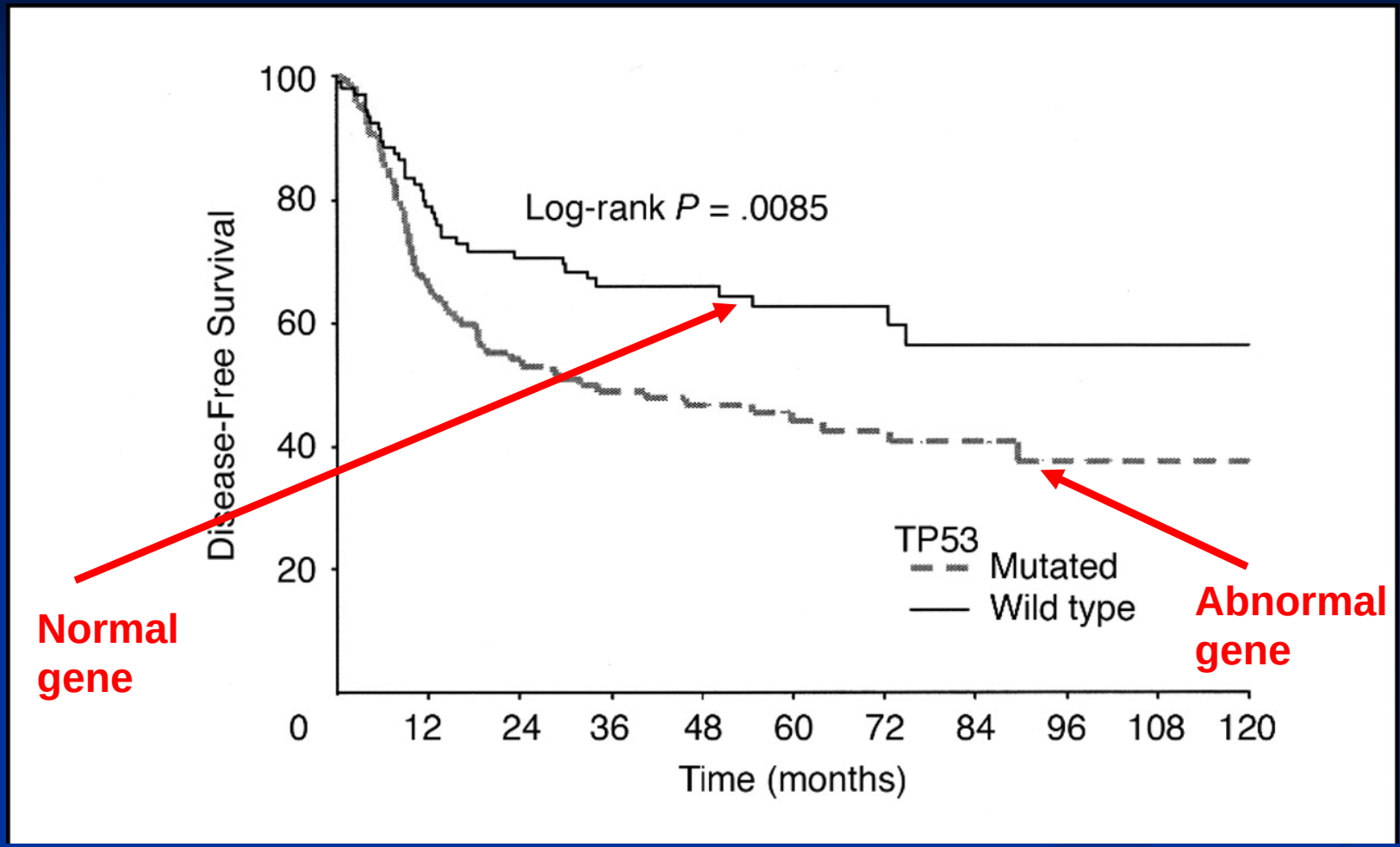
Disease-free survival of 220 patients according to TP53 status (mutated v wild type)



Westra, J. L. et al. J Clin Oncol; 23:5635-5643 2005

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Conclusions

- With better surgery and better staging colon cancer survival is better even without chemotherapy
- With newer drugs regimens are more effective but more toxic and much more expensive
- Decision on who to treat becomes very important
- Newer markers may predict outcome more precisely allowing better estimate of risk/reward ratio with chemo
- Patients with poorest predicted outcome will then get the most effective therapy

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Any Questions?

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