Management of T2N0 Rectal CA: Overtreatment Oncologically or Undertreatment Functionally?

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Clinical Professor of Surgery, University of British Columbia

Provincial Lead Surgical Oncology, BC Cancer

Oct 26, 2024

Management of T1-3_{ab}N0 Rectal CA: TME nearly always cures BUT can alternatives avoid the morbidity?

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Disclosure

- **Ethicon** – Fellowship Support, Educational Event Funding
- **Medtronic** - Support for EBRS

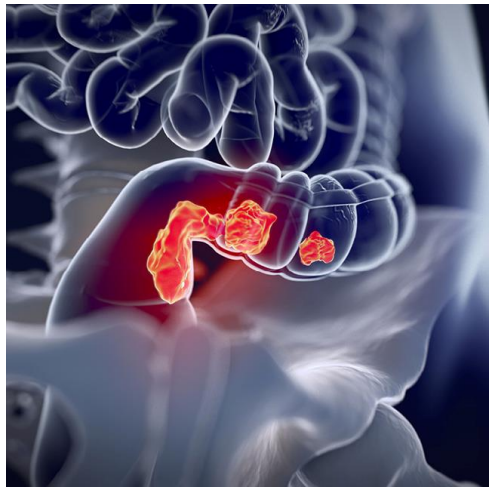
Management of Bias

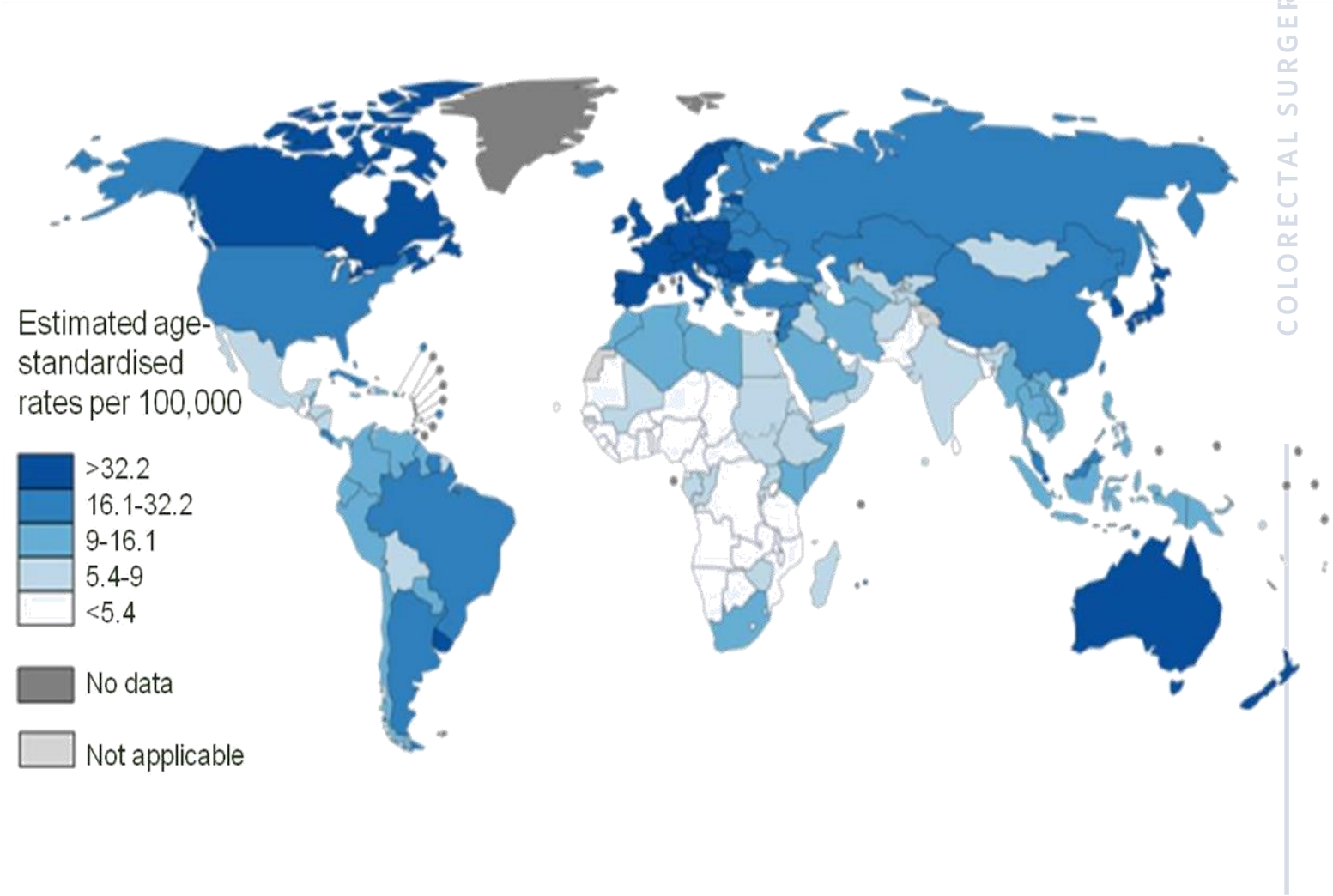
- **Ethicon** – No discussion, Not relevant to subject matter
- **Medtronic** – No discussion, Not relevant to subject matter

ebrs .online EVIDENCE BASED REVIEWS IN SURGERY

Rectal Cancer

- Rectal Cancer
  - AdenoCA >85%
  - 2% lifetime risk in Canada
    - Global high risk region





History of Rectal Cancer Surgery

- Richard (Bill) Heald, 1983
  - Total Mesorectal Excision
  - Local recurrence 5%

DCCG
Dutch Colorectal Cancer Group

- Dutch Colorectal Cancer Trial Group
  - Neoadjuvant radiotherapy reduces local recurrence by 66%

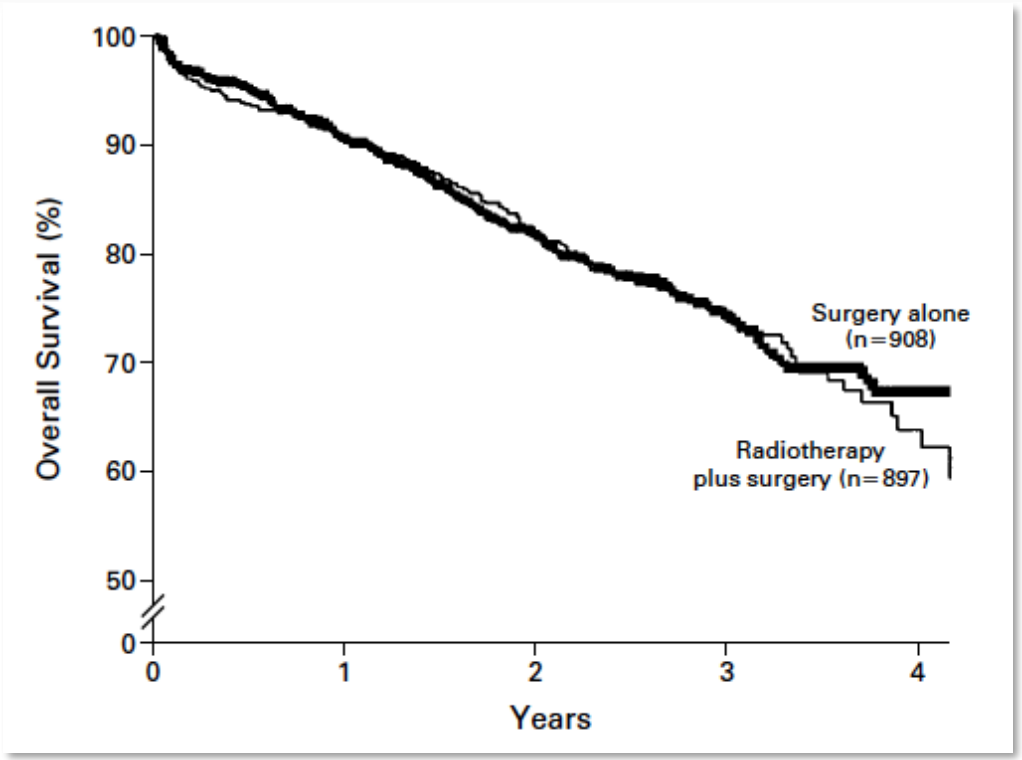
The New England Journal of Medicine

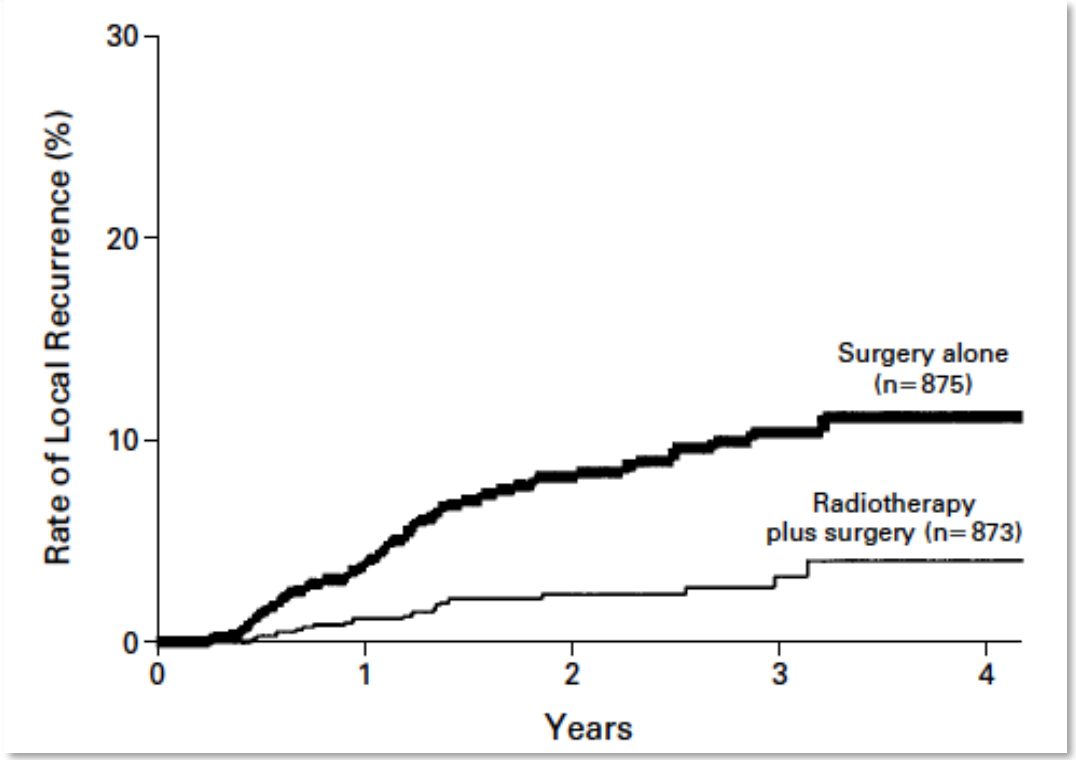
PREOPERATIVE RADIOTHERAPY COMBINED WITH TOTAL MESORECTAL EXCISION FOR RESECTABLE RECTAL CANCER

ELLEN KAPITEIJN, M.D., CORRIE A.M. MARIJNEN, M.D., IRIS D. NAGTEGAAL, M.D., HEIN PUTTER, PH.D., WILLEM H. STEUP, M.D., PH.D., THEO WIGGERS, M.D., PH.D., HARM J.T. RUTTEN, M.D., PH.D., LARS PAHLMAN, M.D., PH.D., BENGT GLIMELIUS, M.D., PH.D., J. HAN J.M. VAN KRIEKEN, M.D., PH.D., JAN W.H. LEER, M.D., PH.D., AND CORNELIS J.H. VAN DE VELDE, M.D., PH.D., FOR THE DUTCH COLORECTAL CANCER GROUP*

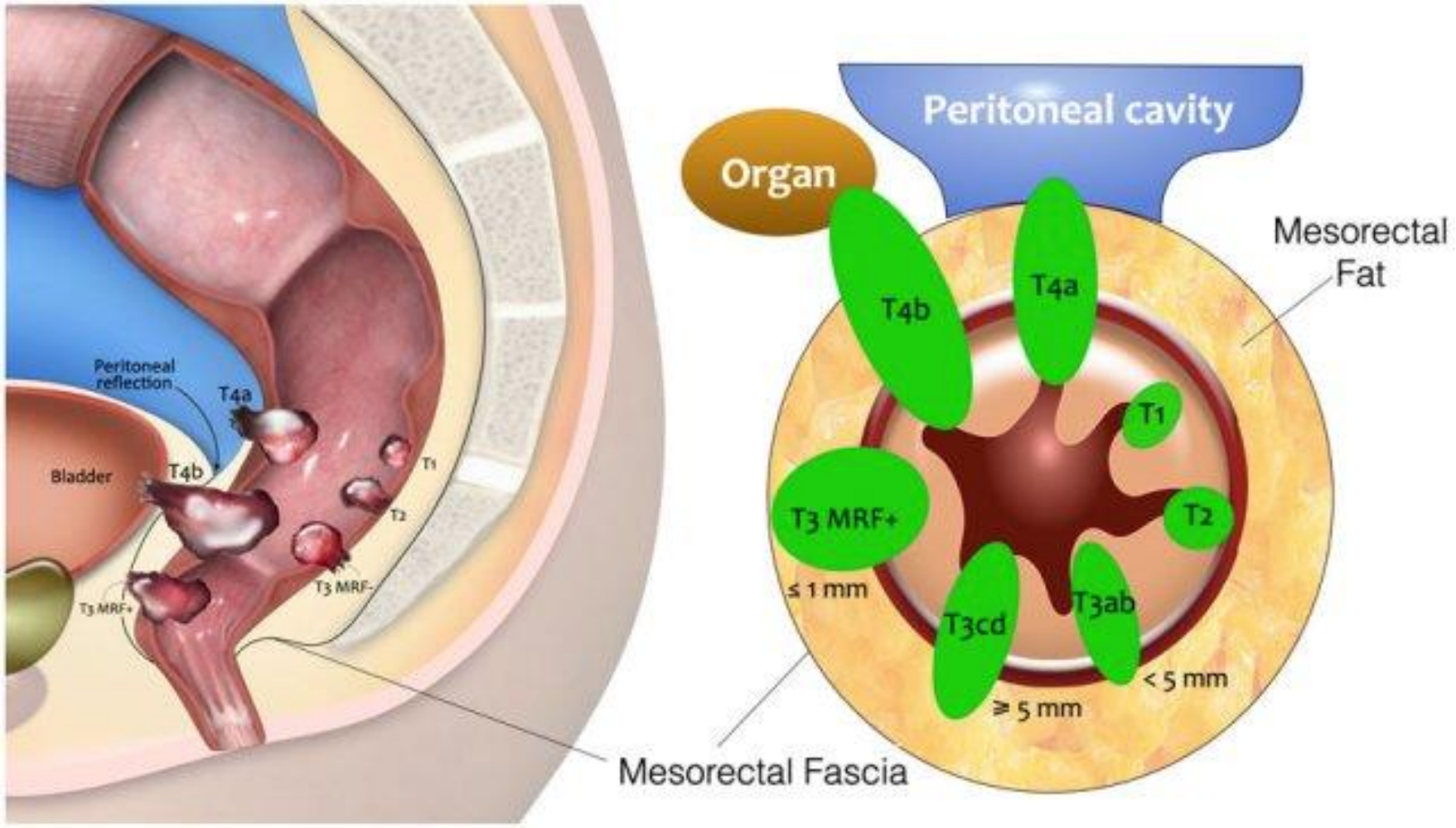
N Engl J Med, Vol. 345, No. 9 · August 30, 2001

DCCG
DUTCH COLORECTAL CANCER GROUP





Rectal Cancer Staging – Tumour



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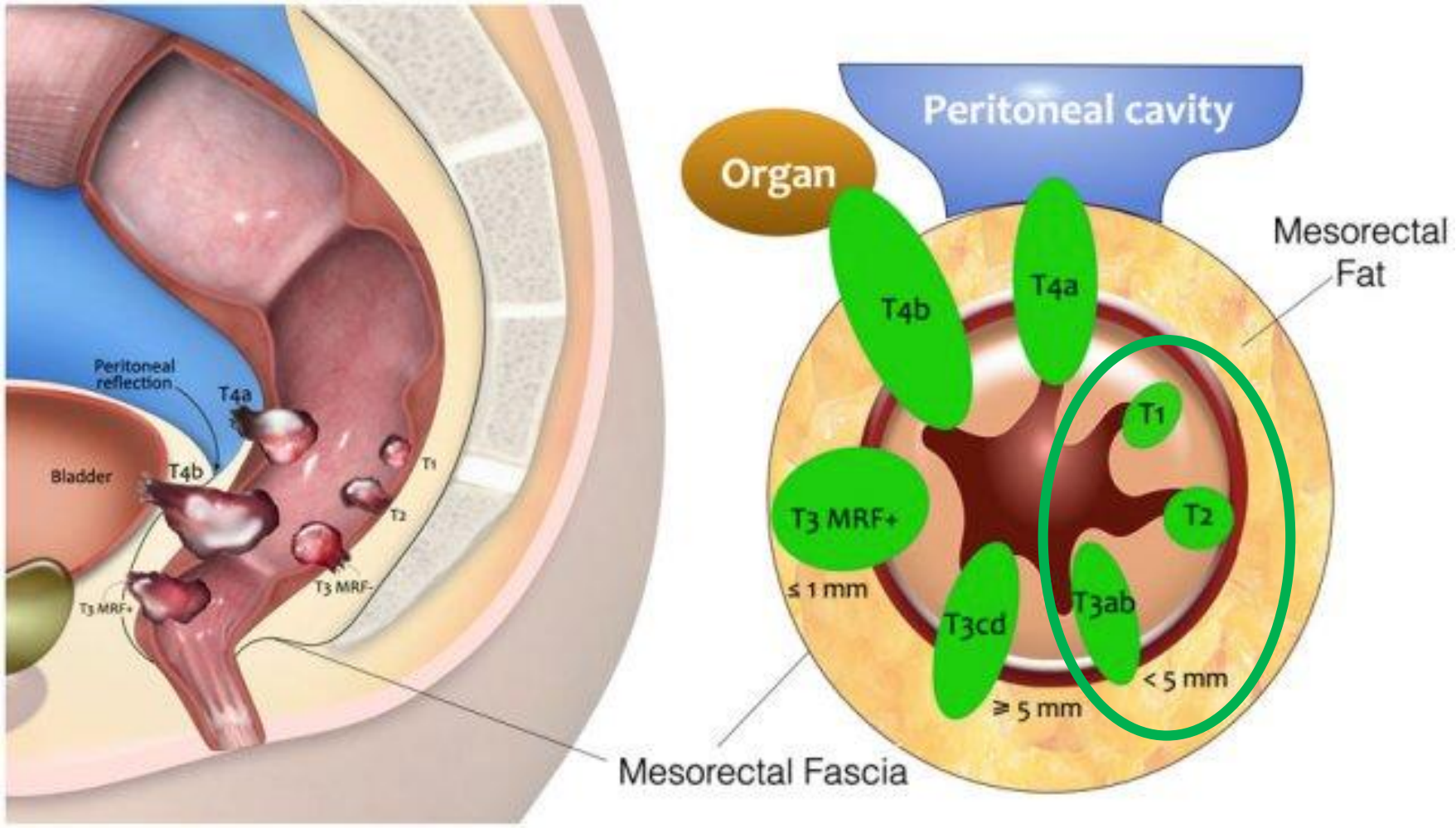
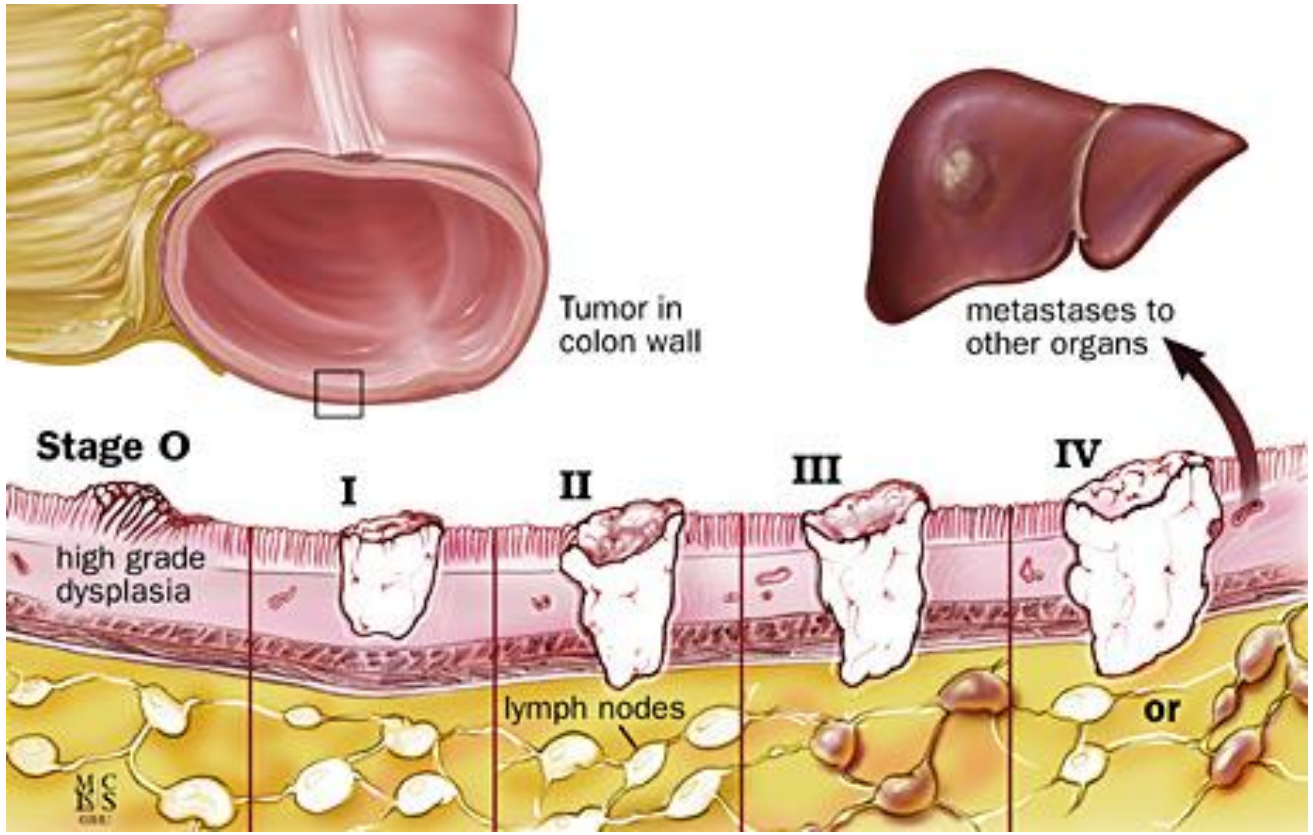
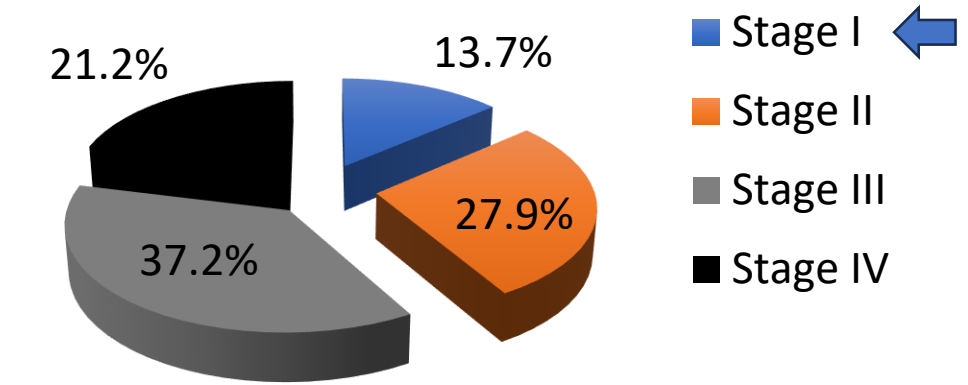
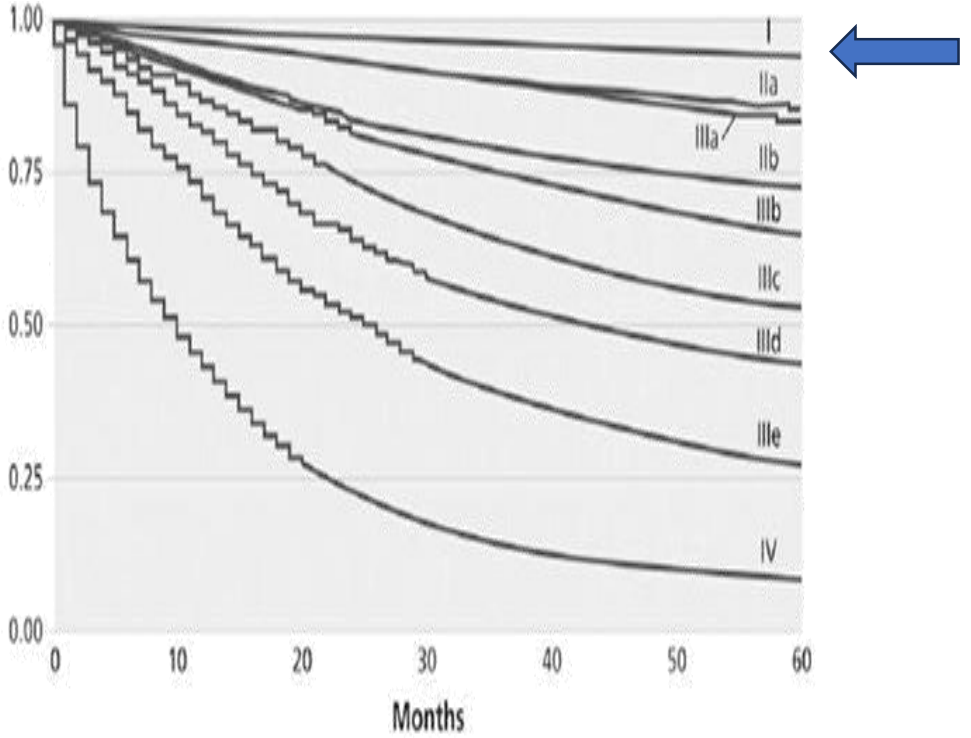


Rectal Cancer Staging





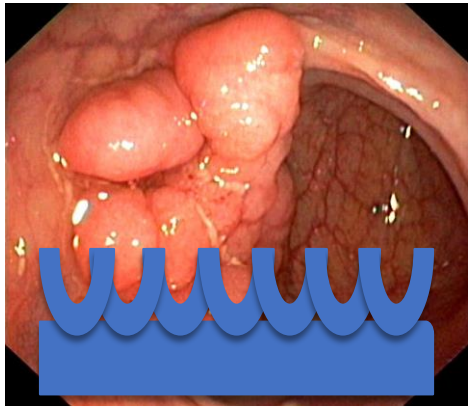


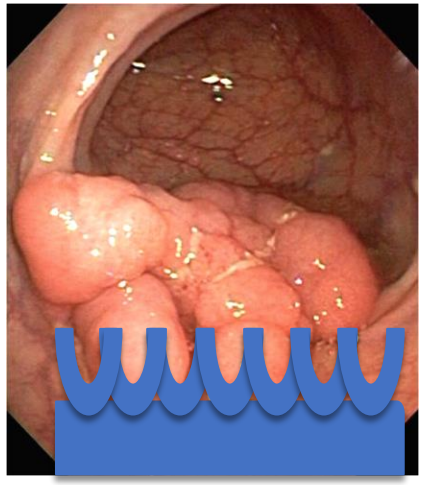
COLORECTAL SURGERY

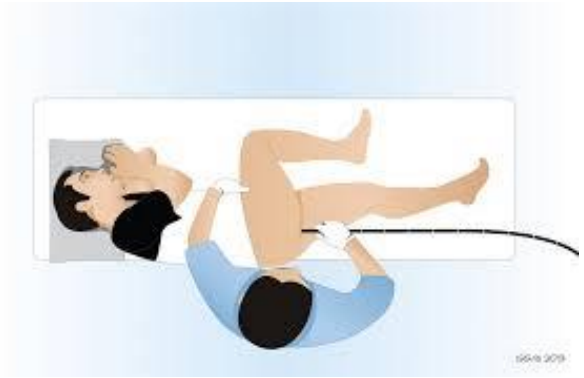
"Standard" Management T2N0 Rectal CA

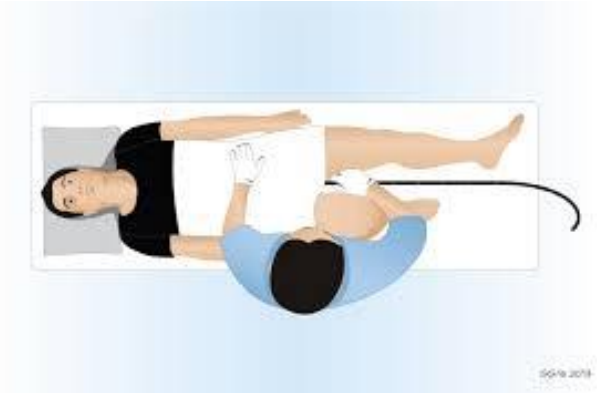
Early Rectal Cancer

- **Additional endoscopic assessment**
  - Determine the location
  - Ideally, use water to facilitate
  - Anterior/Posterior/Lateral
- **Biopsy, Biopsy, Biopsy**



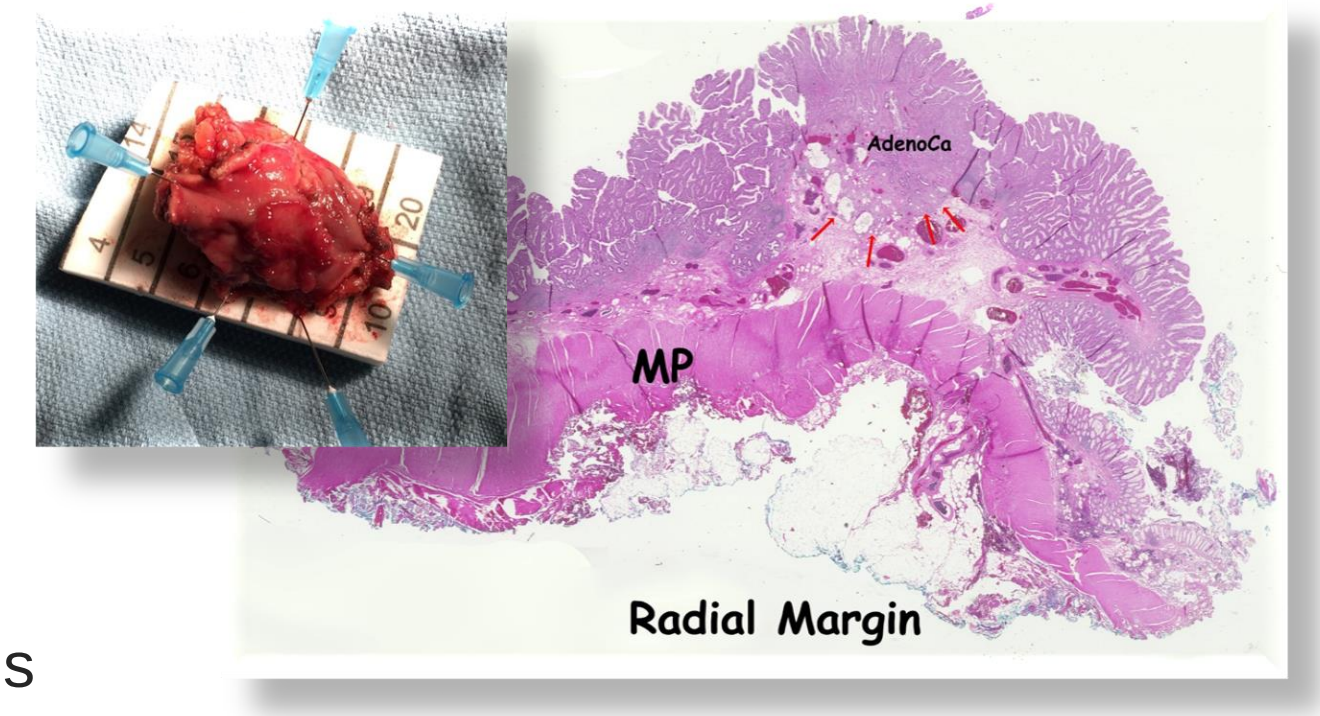


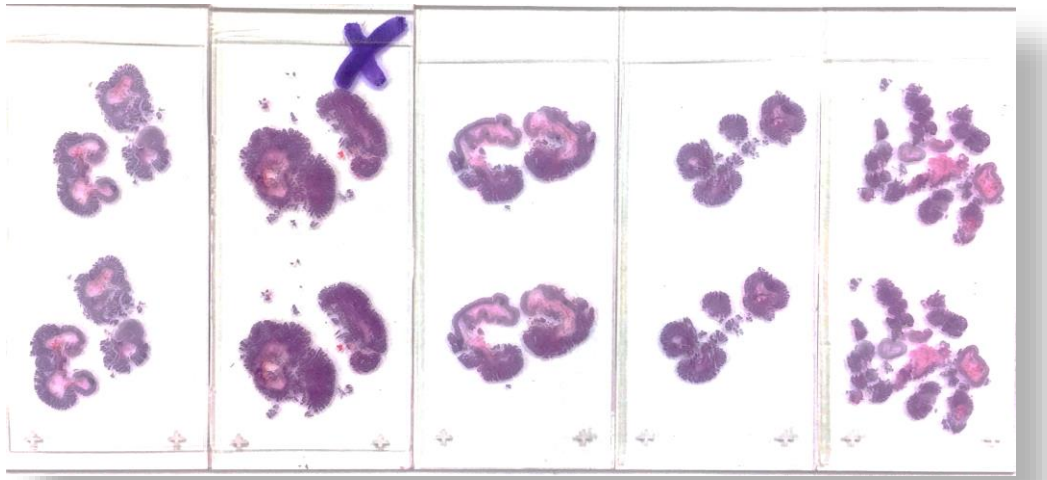




Early Rectal Cancer

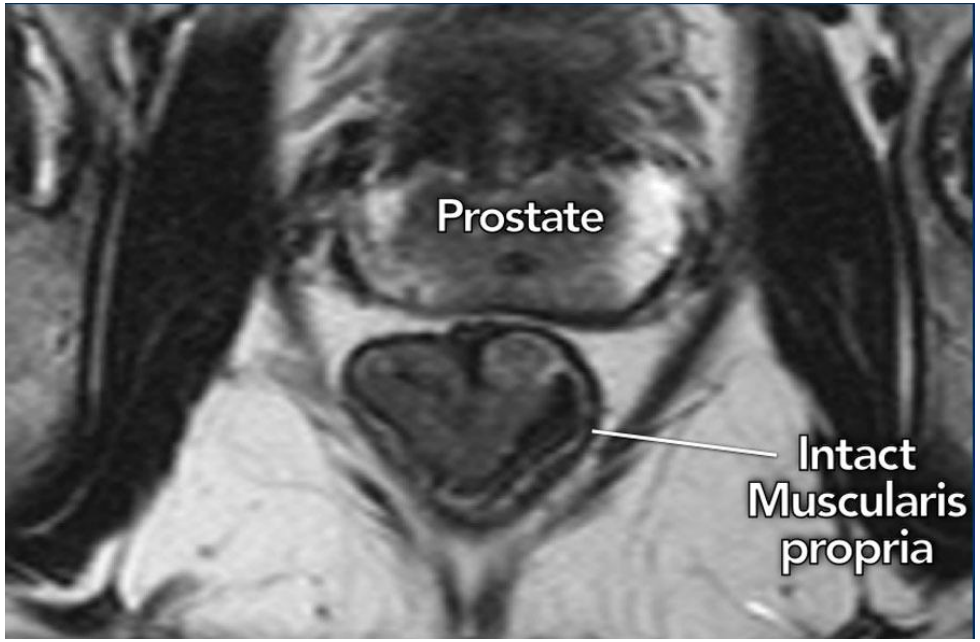
- Endoscopic/TES removal of suspicious lesions discouraged
- Flex sig re-evaluation for location/repeat biopsy
- Patients with cancer have options





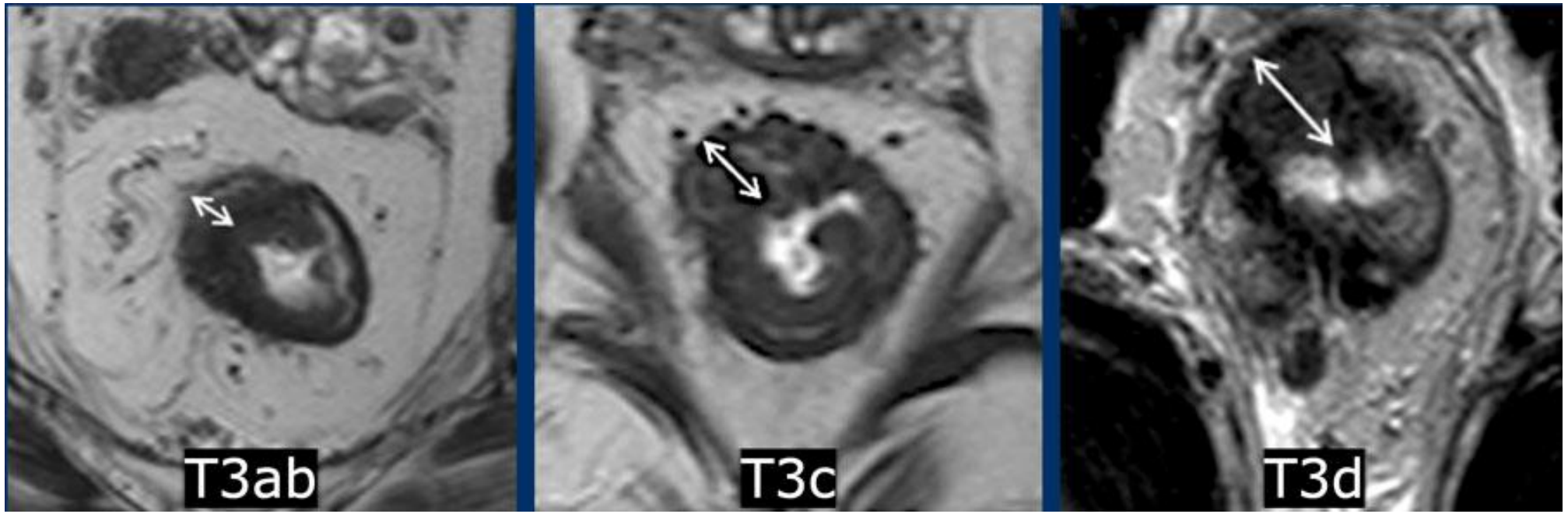
Staging Rectal Cancer – MRI Pelvis

- Best Tumour/Node Staging
  - T1/2/early3 tumours difficult to distinguish



Staging Rectal Cancer – MRI Pelvis

- Best Tumour/Node Staging
  - T3 is locally advanced disease, but not all T3 are the same



(*Ann Surg* 2011;253:711–719)

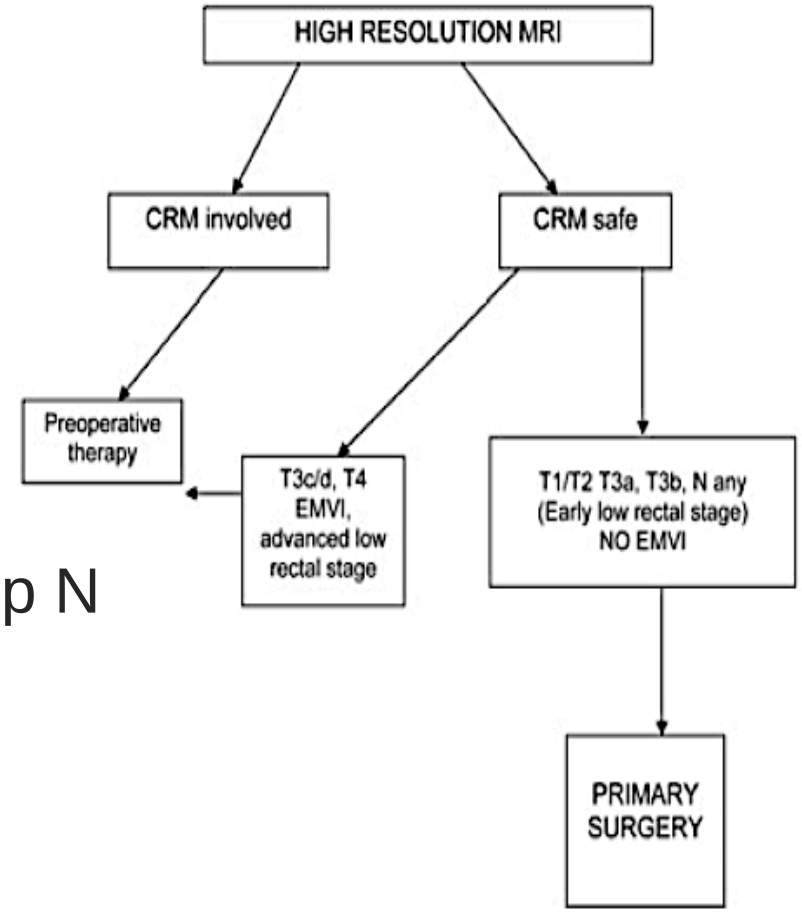
ORIGINAL ARTICLE

Preoperative High-resolution Magnetic Resonance Imaging Can Identify Good Prognosis Stage I, II, and III Rectal Cancer Best Managed by Surgery Alone

A Prospective, Multicenter, European Study

Fiona G.M Taylor, MBBS, FMRCS, Philip Quirke, PhD, BM, FRCPath†, Richard J Heald, MB, Bch, FRCS‡, Brendan Moran, MB, Bchir, FRCSI‡, Lennart Blomqvist, MD, PhD§, Ian Swift, MS, FRCS, FICS*, David J Sebag-Montefiore, FRCP, FRCR¶, Paris Tekkis, BMBS, MD, FRCS**, and Gina Brown, MBBS, MD, FRCR†† for the MERCURY study group*

MRI feature	Good prognosis	Poor prognosis
CRM	>1mm clear	<1mm involved
Low rectal <5cm	intersphincteric plane clear of tumor	intersphincteric plane involved by tumor
T stage	T1/T2, T3a<1mm, T3b, 1-5mm extramural spread	T3c>5mm extramural spread, T4
EMVI	negative	positive
N stage	any	any



- 11 hospital Swedish UK collaborative
- 122 patients w "Good" $T_{3ab}N_0$ Rectal CA on MRI
  - No pre- or postop radiation regardless of postop N
  - Median F/U of 61.8mo

(*Ann Surg* 2011;253:711–719)

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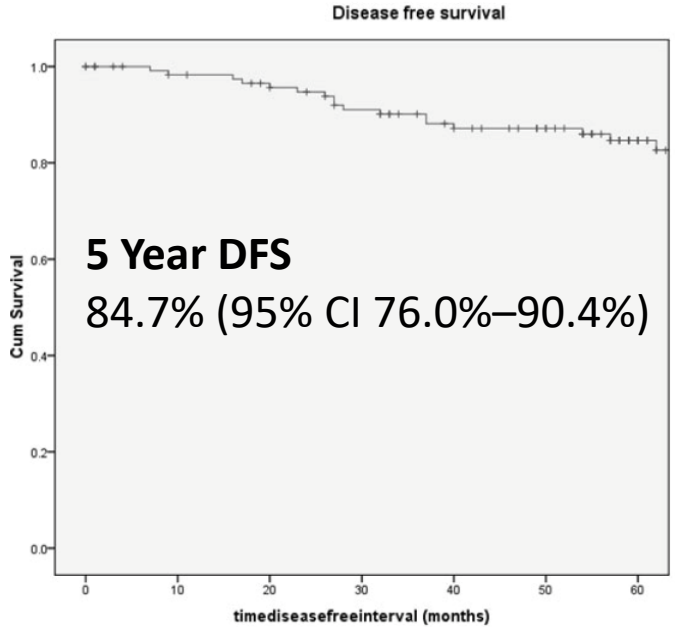
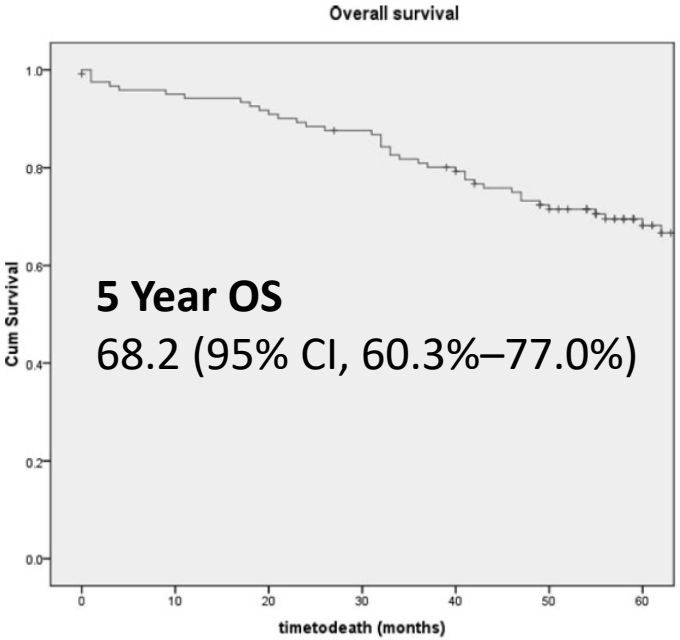


- Cancer survival similar to patients treated with neoadj CRT and TME
- First suggestion that MRI evaluation could deescalate therapeutic strategy



JAMA Oncology | Original Investigation

Safety and Feasibility of Using Magnetic Resonance Imaging Criteria to Identify Patients With "Good Prognosis" Rectal Cancer Eligible for Primary Surgery

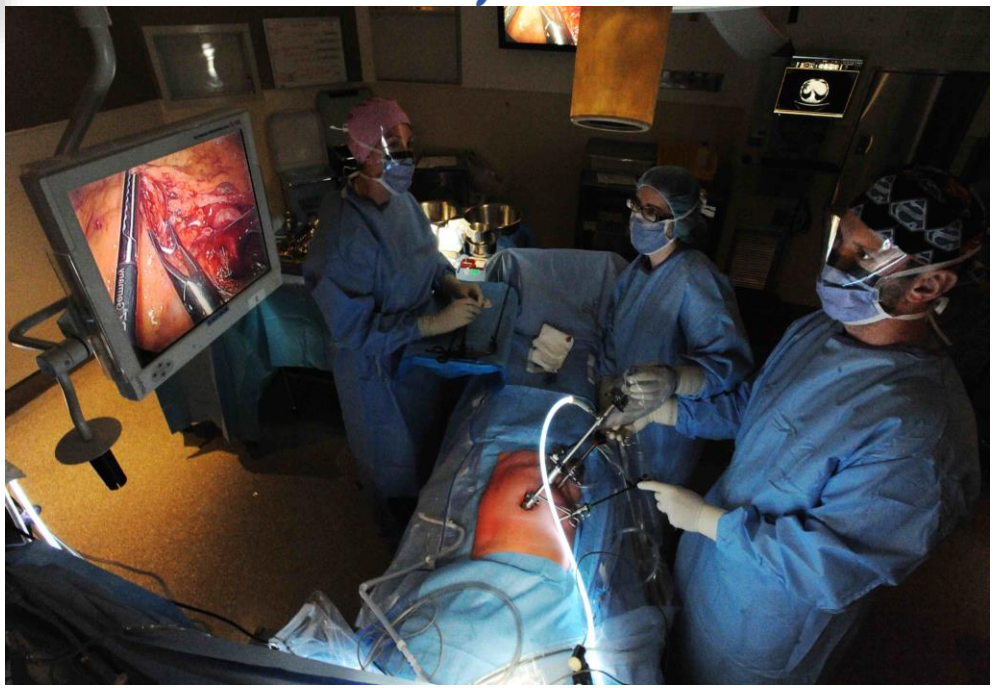
The Phase 2 Nonrandomized QuickSilver Clinical Trial

Erin D. Kennedy, MD, PhD; Marko Simunovic, MD, MPH; Kartik Jhaveri, MD; Richard Kirsch, MBChB, PhD; Jim Brierley, MS, MB; Sébastien Drolet, MD; Carl Brown, MD, MSc; Patrick M. Vos, MD; Wei Xiong, MD, PhD; Tony MacLean, MD; Selliah Kanthan, MBBS; Peter Stotland, MD; Simon Raphael, MD; Gil Chow, MD; Catherine A. O'Brien, MD, PhD; Charles Cho, MD, PhD; Cathy Streutker, MD, MSc; Raimond Wong, MD; Selina Schmocker, MSc; Sender Liberman, MDCM; Caroline Reinhold, MDCM; Neil Kopek, MD; Victoria Marcus, MD; Alexandre Bouchard, MD; Caroline Lavoie, MD; Stanislas Morin, MD; Martine Périgny, MD; Ann Wright; Katerina Neumann, MD, PhD; Sharon Clarke, MD; Nikhilesh G. Patil, MD, MBBS; Thomas Arnason, MD; Lara Williams, MD; Robin McLeod, MD; Gina Brown, MD, MBBS; Alex Mathieson, MD; Amandeep Pooni, MD; Nancy N. Baxter, MD, PhD

Calgary
Halifax
Montreal
Quebec City
Toronto
Vancouver
Winnipeg

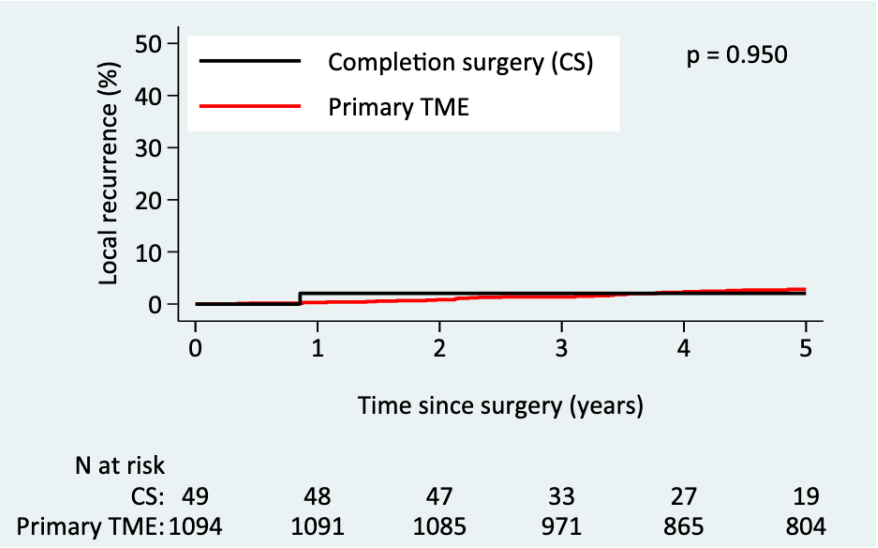
COLORECTAL SURGERY

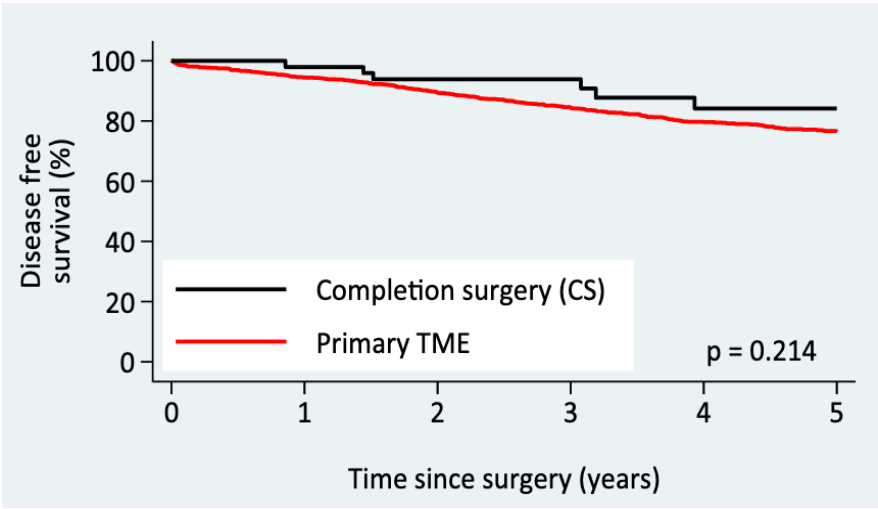
- Sept 2014 – Oct 2018, 12 Canadian Rectal CA Surgery Centres
  - 82 pts w $T_{1\text{-}3ab}N_0$ (MRI) Rectal CA
- Primary Outcome – CRM +ve
  - Anticipated 10% (based on sample size n=75, 95%CI +/- 6.7%
- Results
  - Actual CRM +ve 4.9% (4/82)



Primary TME Surgery for Stage I Cancer

- Norwegian pop-based study 2000-17
- pTME (n = 1094) vs cTME (n=49)
  - cTME = TME after TES
- Outcomes after radical resection
  - **5 yr local recurrence 2.4% (2.0-4.1%)**
  - **5 yr distant recurrence 9.1% (7.5-11.0%)**
  - Permanent stoma rate 32%





Lossius, Int J Col Dis, 2022

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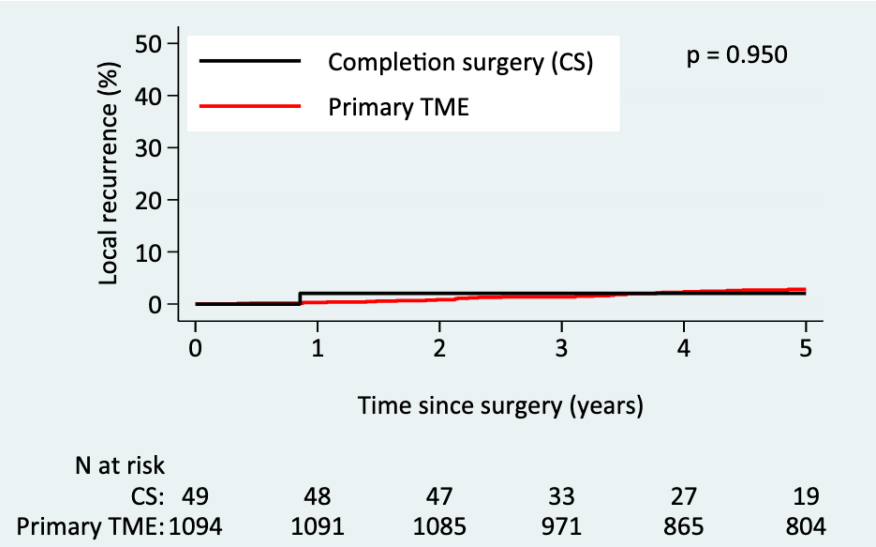
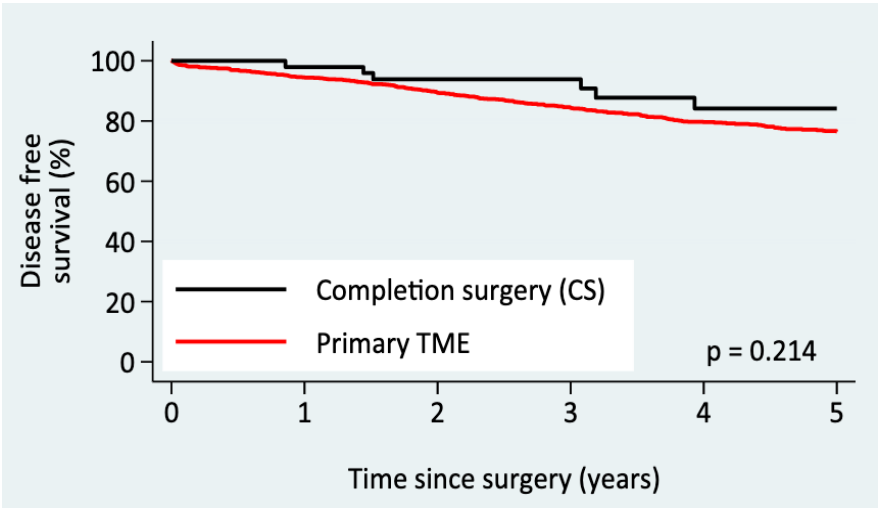




Lossius, Int J Col Dis, 2022

ORIGINAL ARTICLE

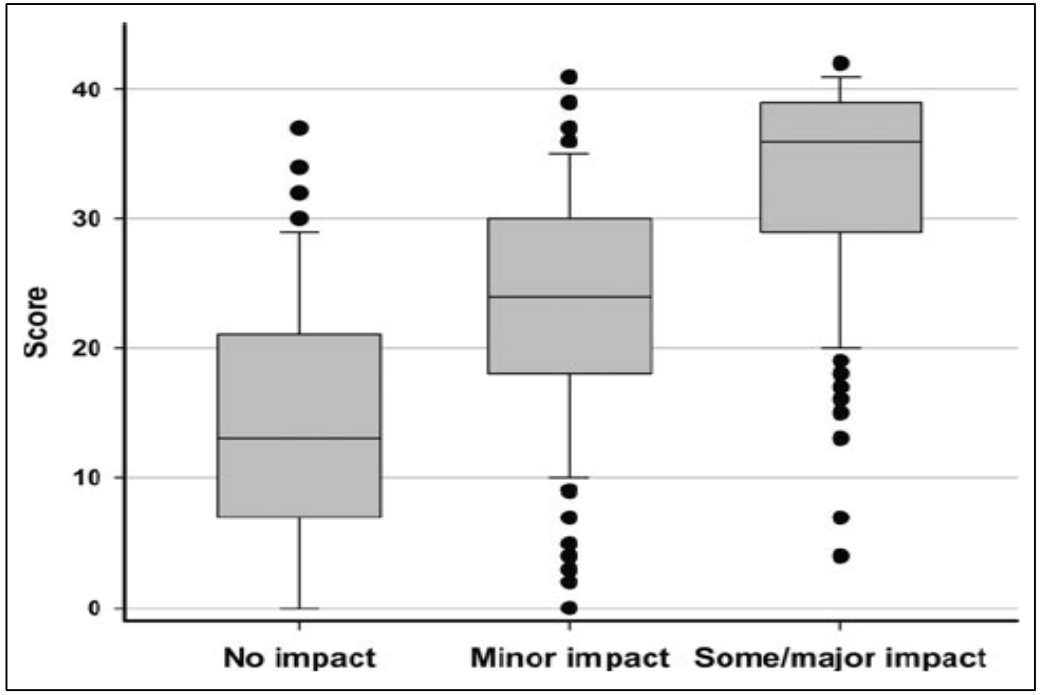
Low Anterior Resection Syndrome Score

Development and Validation of a Symptom-Based Scoring System for Bowel Dysfunction After Low Anterior Resection for Rectal Cancer

Katrine J. Emmertsen, MD,† and Søren Laurberg, MD**

Ann Surg 2012

	No LARS	Minor LARS	Major LARS	Total
No impact on QoL	92	21	8	121
Little impact on QoL	57	65	42	164
Some/major impact on QoL	20	33	140	193
Total	169	119	190	478



Low Anterior Resection Syndrome (LARS) – General Population

Questionnaire distributed to n=1,259 patients in general Dutch population (i.e. non-surgical):

Results:

Minor LARS in 24.3%

Major LARS in 12.2%

Associated with:

Interpretation:

LARS score requires baseline (preop) measurement to reliably interpret (postop) dysfunction

Al-Saidi AMA et al. *Dis Colon Rectum* 2020;63(4):520-6

DISEASES OF THE COLON & RECTUM

The Incidence of Low Anterior Resection Syndrome as Assessed in an International Randomized Controlled Trial (MRC/NIHR ROLARR)

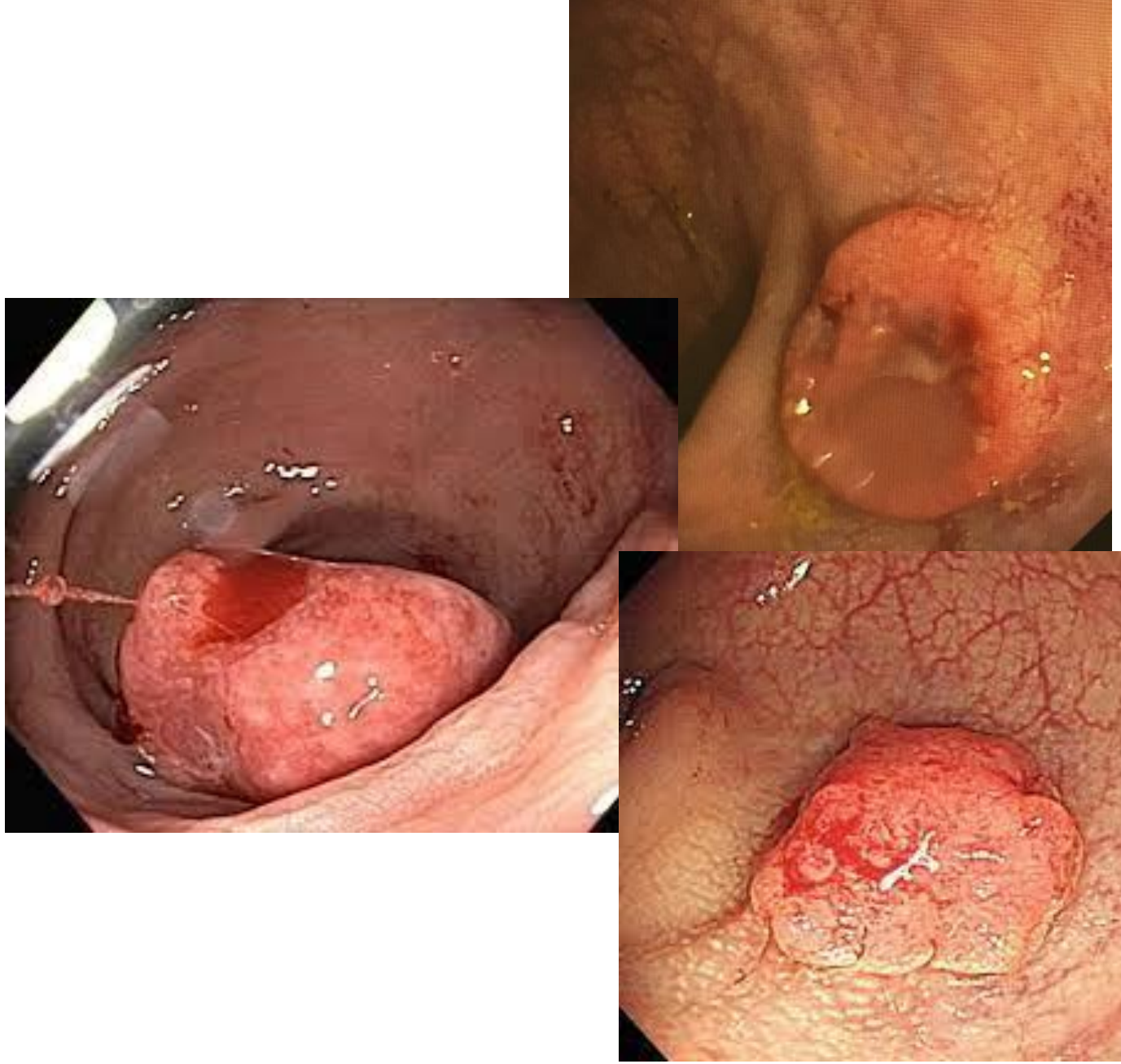
William S. Bolton, MBChB,✉ Stephen J. Chapman, MRCS,* Neil Corrigan, MSc,† Julie Croft, BSc,† Fiona Collinson, MD,† Julia M. Brown, MSc,† and David G. Jayne, MD**

Variable	Laparoscopic Surgery (n = 63)	Robotic Surgery (n = 69)
Time from operation to LARS score assessment (days) (range)		
Mean (SD)	981.3 (304.59)	996.7 (313.74)
Median (range)	973.0 (333.0, 1655.0)	1083.0 (174.0, 1652.0)
LARS		
No LARS	7 (11.1%)	15 (21.7%)
All LARS	56 (88.9%)	53 (76.8%)
Minor LARS	15 (23.8%)	11 (15.9%)
Major LARS	41 (65.1%)	42 (60.9%)
Missing	0 (0.0%)	1 (1.4%)

Organ Preservation Strategies

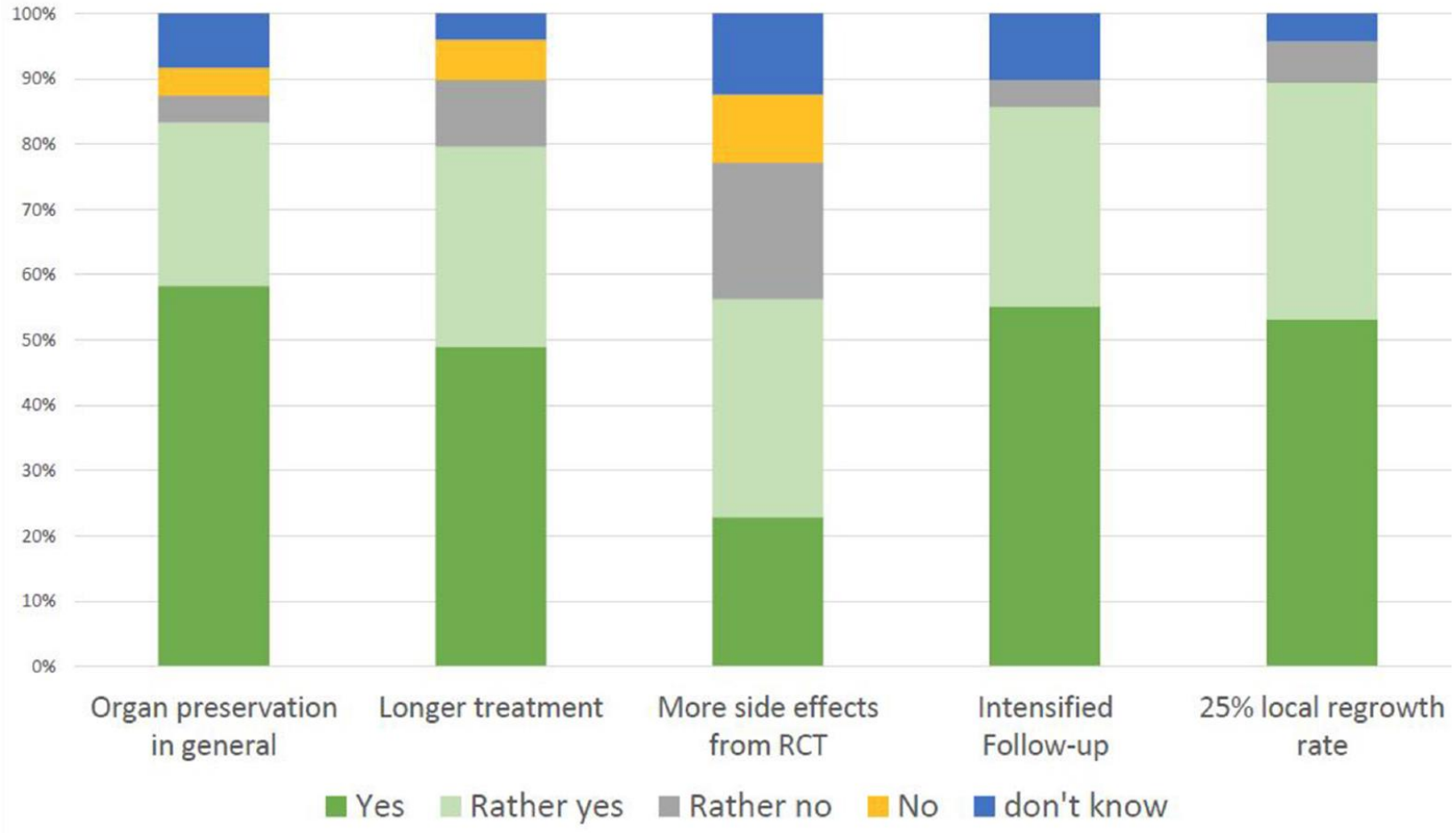
Early Rectal Cancer

- T1-T3$_{ab}$N0M0 that are locally excisable by Transanal Endoscopic Surgery (TES)
- What do patients want?
- What are the options?



What Do Patients Want? Risk Tolerance?

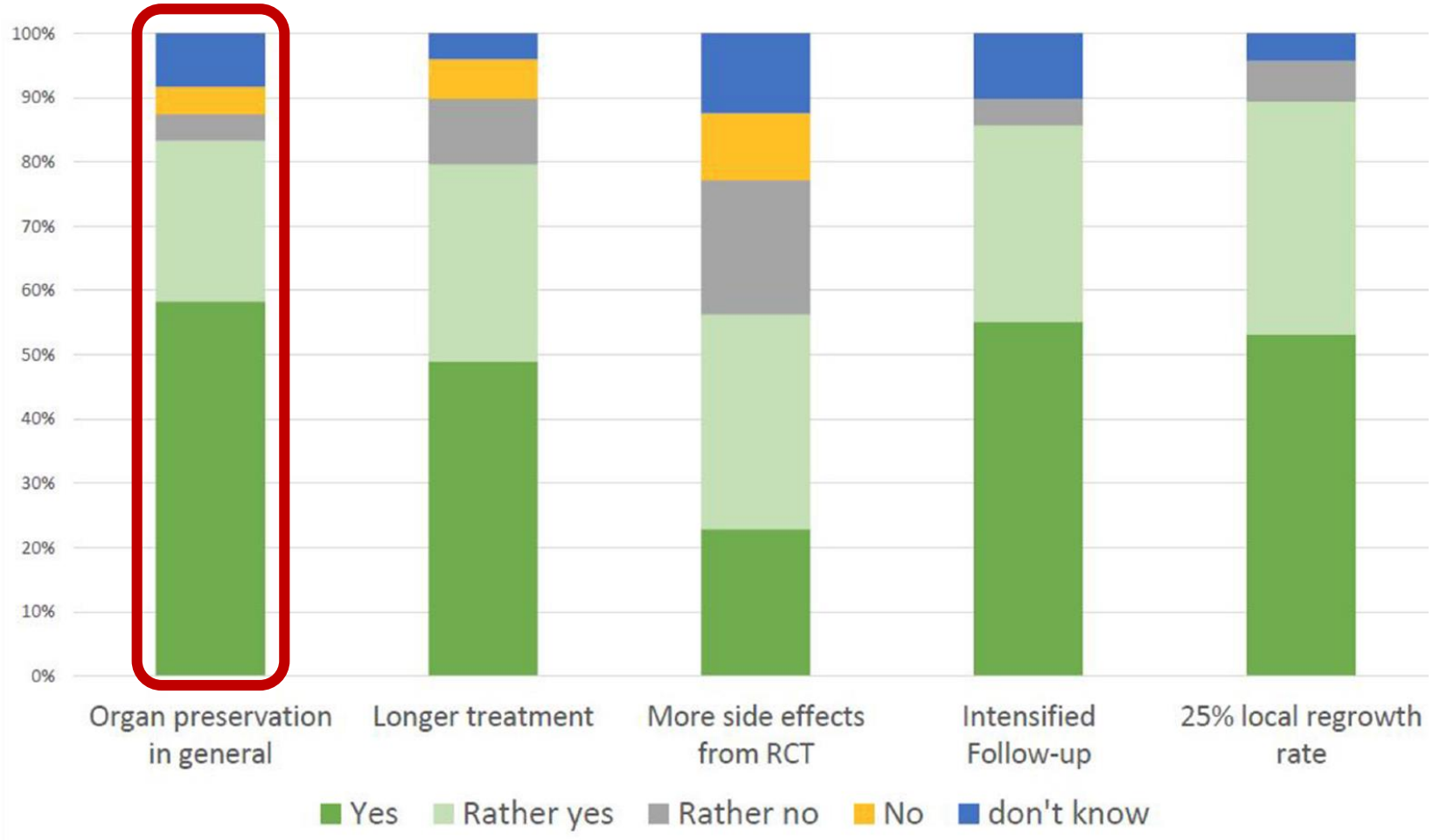
- Survey of 49 pts with locally advanced rectal cancer



Gani, Front Onc, 2019

What Do Patients Want? Risk Tolerance?

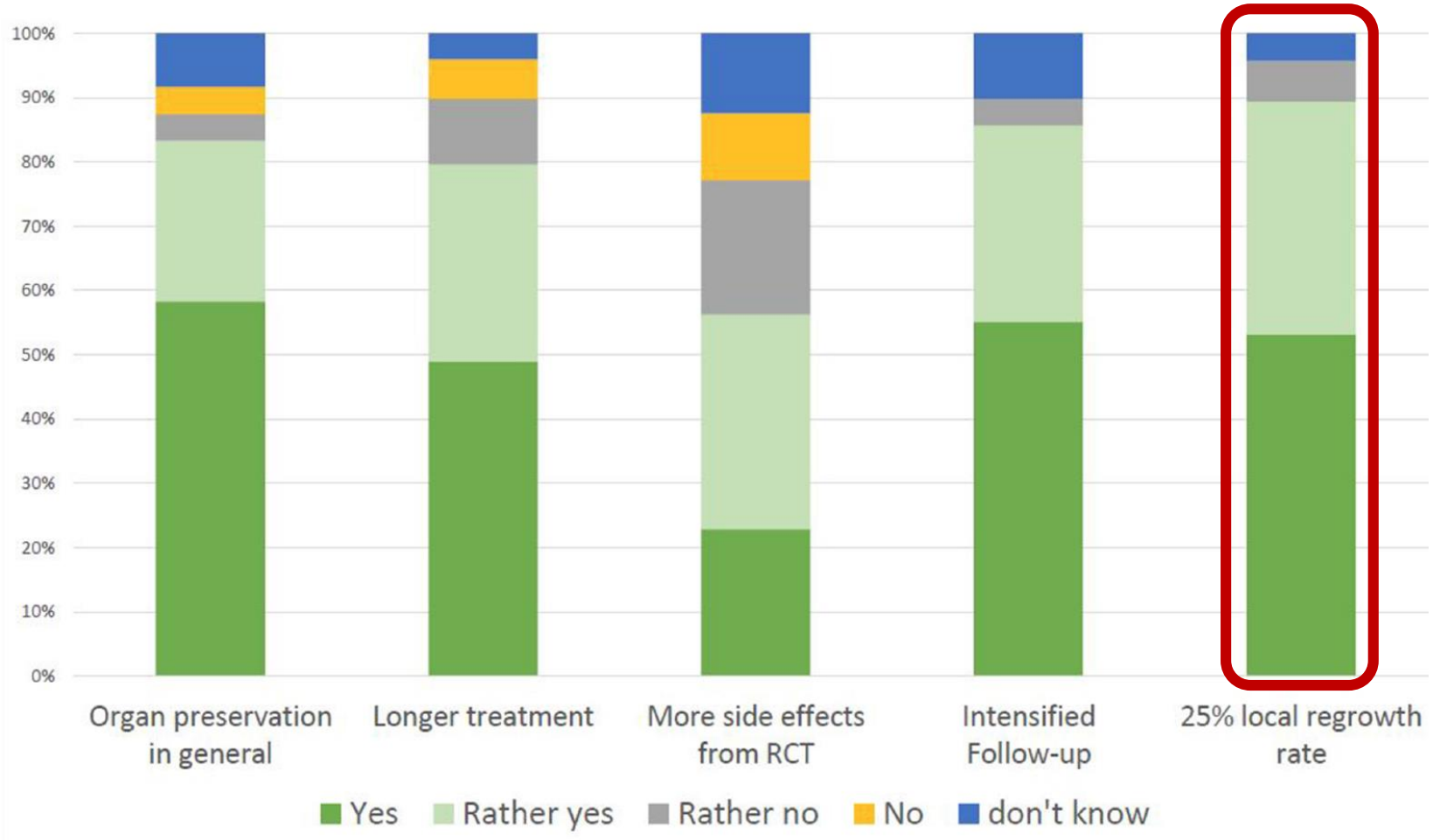
- Survey of 49 pts with locally advanced rectal cancer
- 83% interested in organ preservation



Gani, Front Onc, 2019

What Do Patients Want? Risk Tolerance?

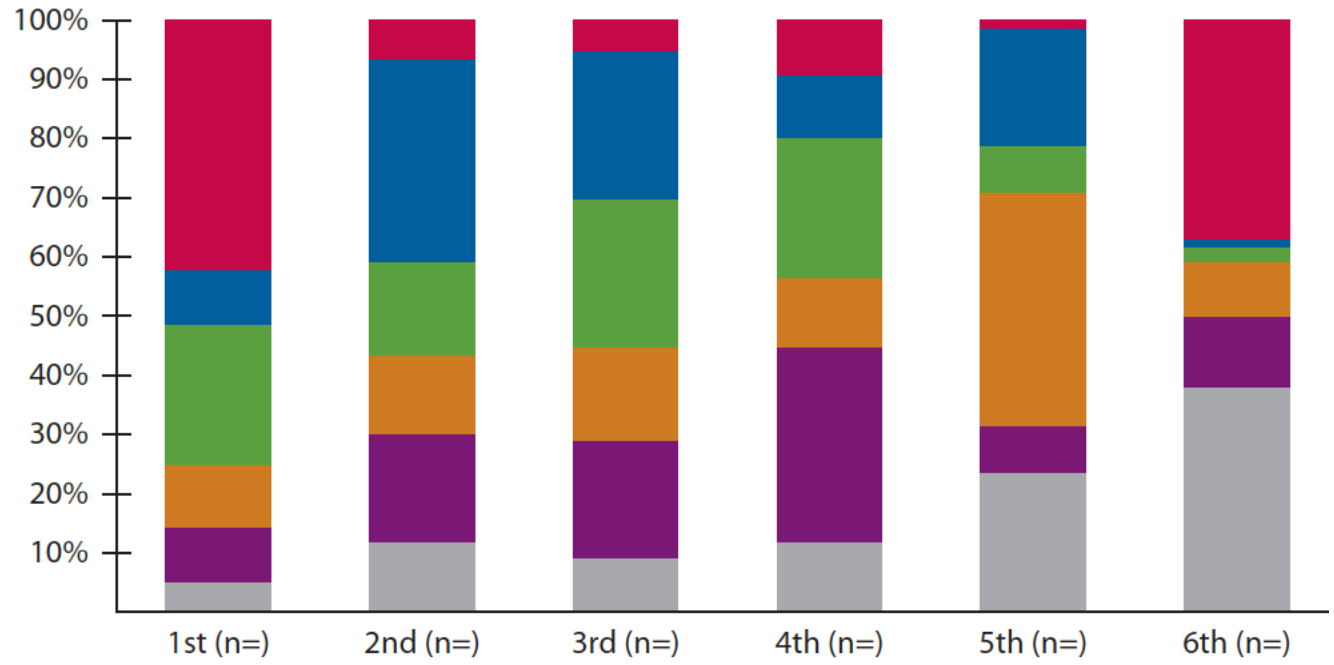
- Survey of 49 pts with locally advanced rectal cancer
- 83% interested in organ preservation
- Only 6.4% consider 25% regrowth rate “unacceptable”



Gani, Front Onc, 2019

What Do Patients Want? Risk Tolerance?

- Survey of 95 people (57 rectal CA pts, 38 healthy volunteers) 83% interested in organ preservation

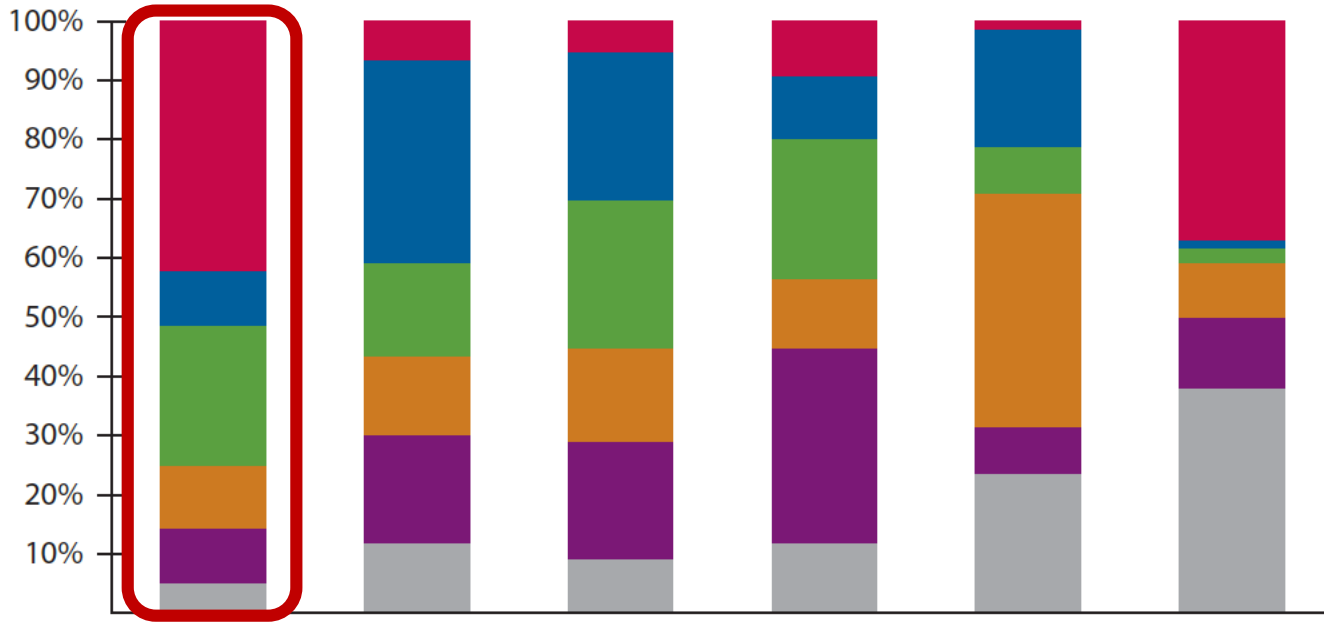


	1st (n=)	2nd (n=)	3rd (n=)	4th (n=)	5th (n=)	6th (n=)
Wait-and-see	32	5	4	7	1	28
Local excision	7	26	19	8	15	1
SCRT-LAR	18	12	19	18	6	2
SCRT-APR	8	10	12	9	30	7
CRT-LAR	7	14	15	25	6	9
CRT-APR	4	9	7	9	18	29

Couwenberg, DCR, 2018

What Do Patients Want? Risk Tolerance?

- Survey of 95 people (57 rectal CA pts, 38 healthy volunteers) 83% interested in organ preservation
- 51% selected NOM or CRT + local excision as 1st choice



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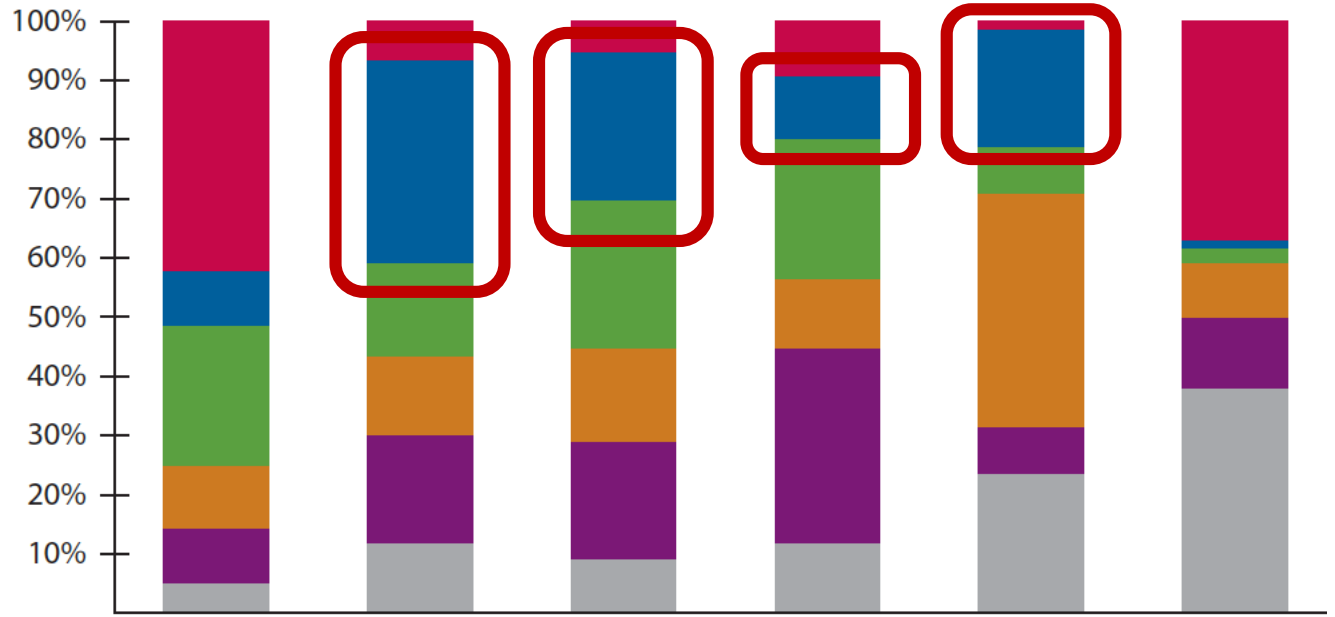
What Do Patients Want? Risk Tolerance?

- Survey of 95 people (57 rectal CA pts, 38 healthy volunteers) 83% interested in organ preservation
- 51% selected NOM or CRT + local excision as 1st choice
- Combined modality TES favoured by many



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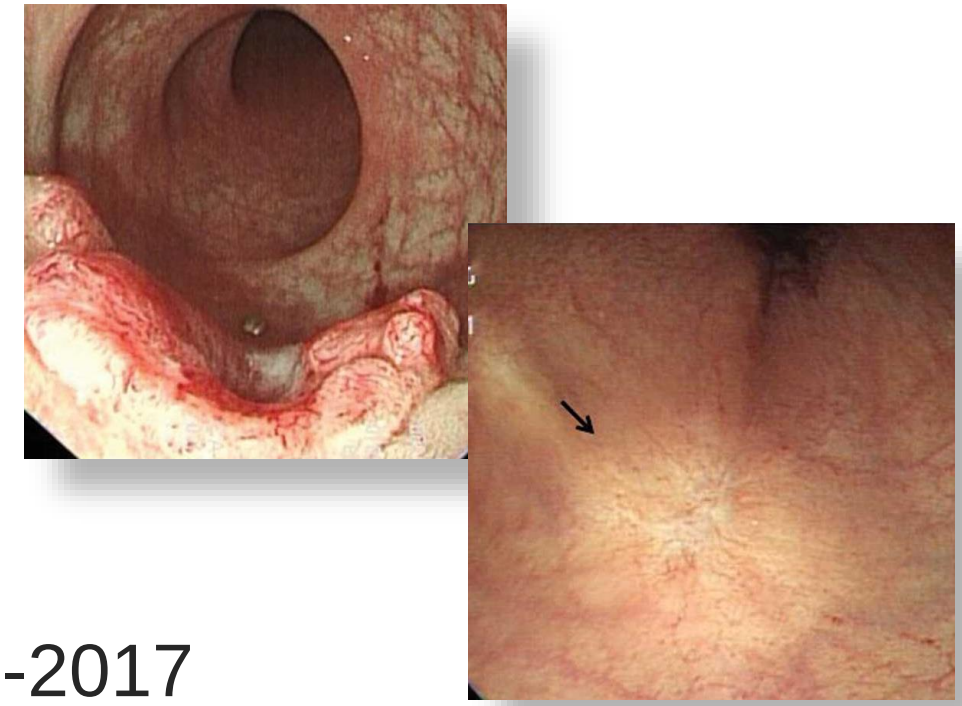
Couwenberg, DCR, 2018

Factors affecting local regrowth after watch and wait for patients with a clinical complete response following chemoradiotherapy in rectal cancer (InterCoRe consortium): an individual participant data meta-analysis

Lancet Gastroenterol Hepatol 2018

Sami A Chadi, Lee Malcomson, Joie Ensor, Richard D Riley, Carlos A Vaccaro, Gustavo L Rossi, Ian R Daniels, Neil J Smart, Melanie E Osborne, Geerard L Beets, Monique Maas, Danielle S Bitterman, Kevin Du, Simon Gollins, Arthur Sun Myint, Fraser M Smith, Mark P Saunders, Nigel Scott, Sarah T O'Dwyer, Rodrigo Otavio de Castro Araujo, Marcus Valadao, Alberto Lopes, Cheng-Wen Hsiao, Chien-Liang Lai, Radhika K Smith, Emily Carter Paulson, Ane Appelt, Anders Jakobsen, Steven D Wexner, Angelita Habr-Gama, Guilherme Sao Julião, Rodiguo Perez, Andrew G Renehan

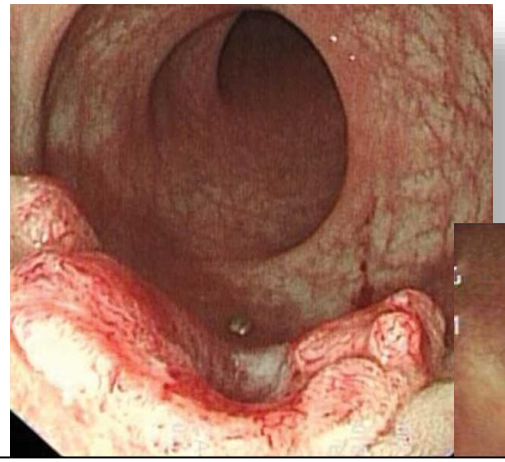


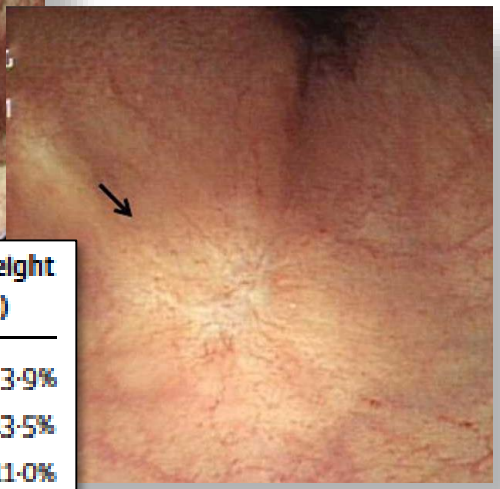
- Pooled (individual patient) metanalysis 1990-2017
  - 11 Studies – 602 patients
  - Med follow up 37.6 months

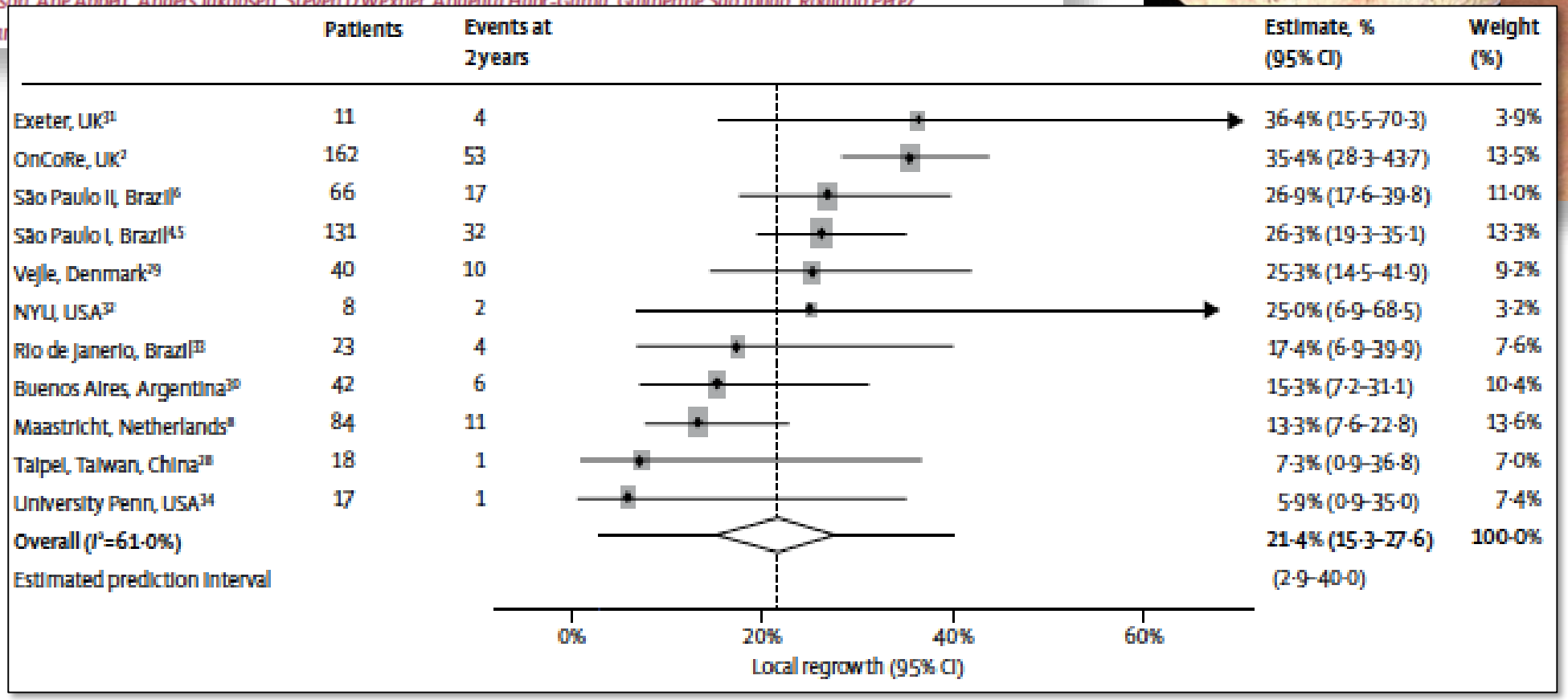
Factors affecting local regrowth after watch and wait for patients with a clinical complete response following chemoradiotherapy in rectal cancer (InterCoRe consortium): an individual participant data meta-analysis

Lancet Gastroenterol Hepatol 2018

Sami A Chadi, Lee Malcomson, Joie Ensor, Richard D Riley, Carlos A Vaccaro, Gustavo L Rossi, Ian R Daniels, Neil J Smart, Melanie E Osborne, Geerard L Beets, Monique Maas, Danielle S Bitterman, Kevin Du, Simon Gollins, Arthur Sun Myint, Fraser M Smith, Mark P Saunders, Nigel Scott, Sarah T O'Dwyer, Rodrigo Otavio de Castro Araujo, Marcus Valadao, Alberto Lopes, Cheng-Wen Hsiao, Chien-Liang Lai, Radhika K Smith, Emily Carter Paulson, Ane Appelt, Anders Jakobsen, Steven D Wexner, Angelita Habr-Gama, Guilherme Sao Julião, Rodiguo Perez, Andrew G Renehan







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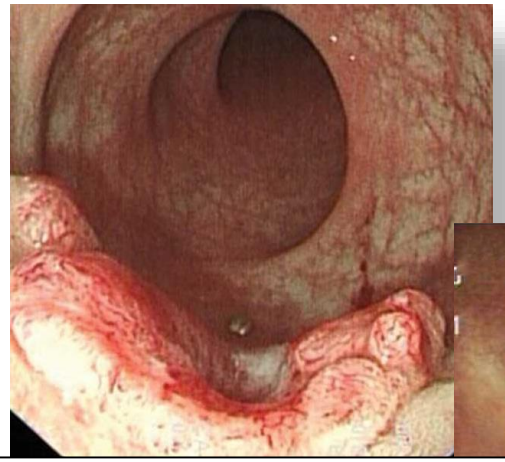

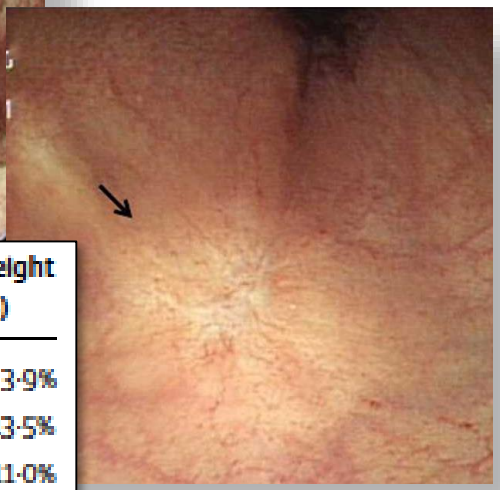

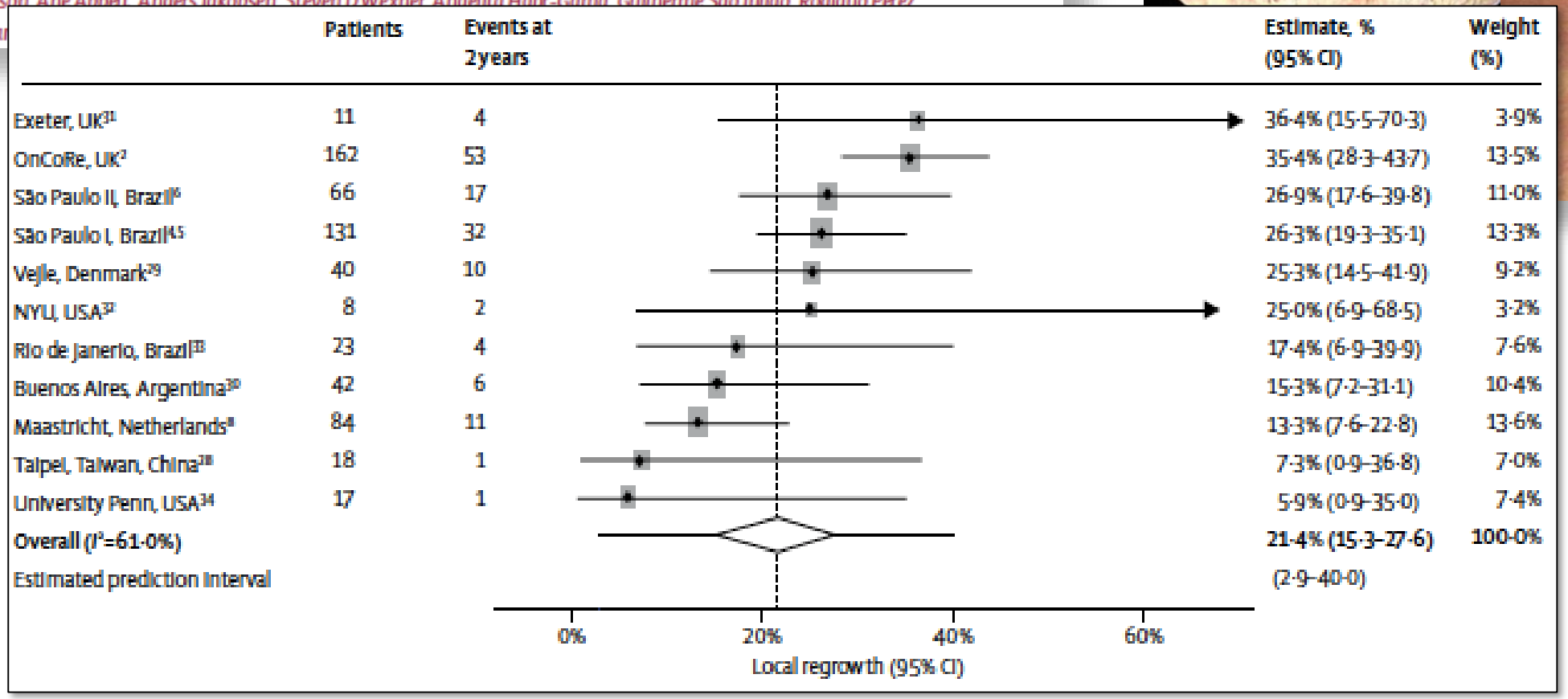

T1/2 Subgroup – 19% (95%CI 13-25%)

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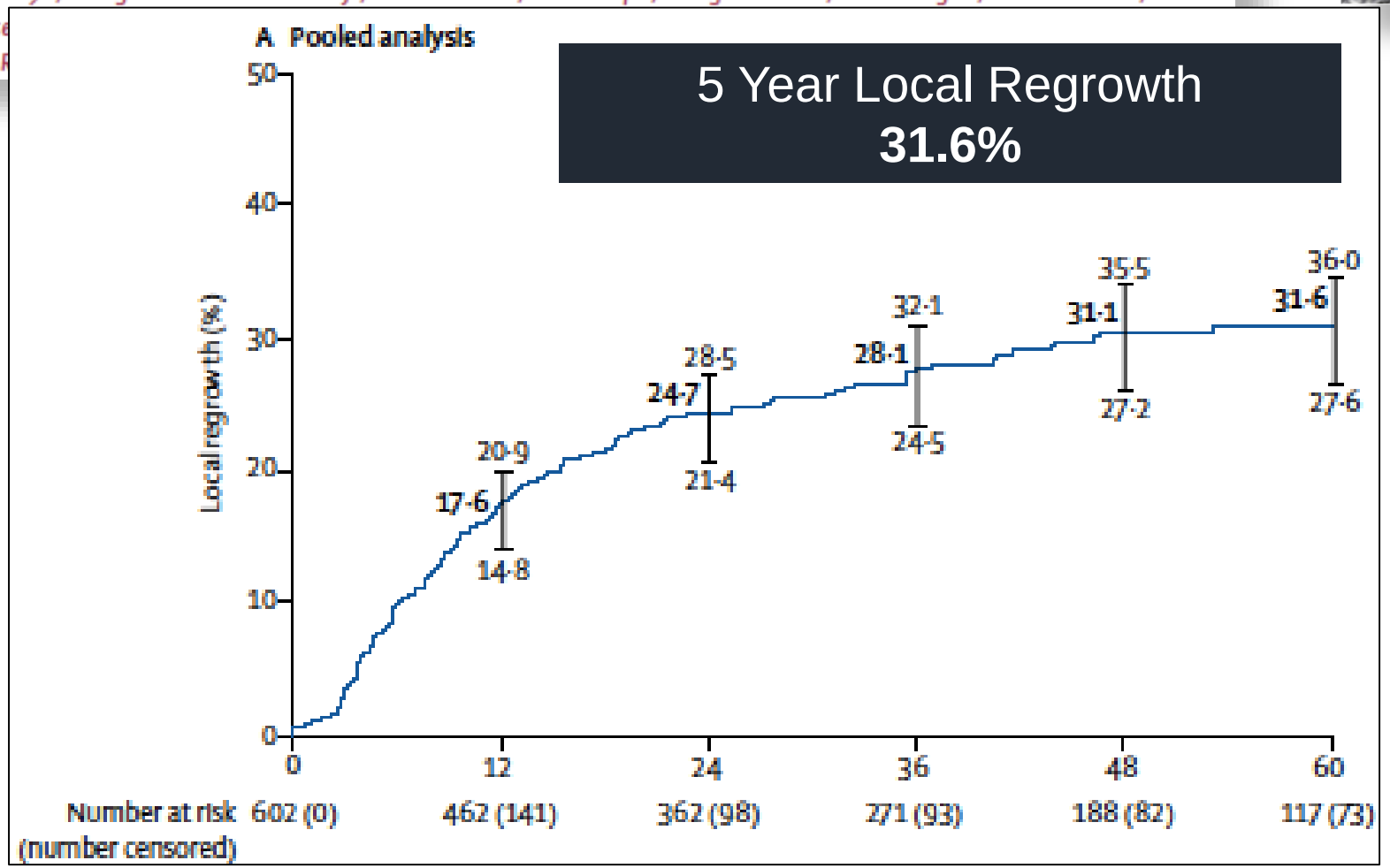
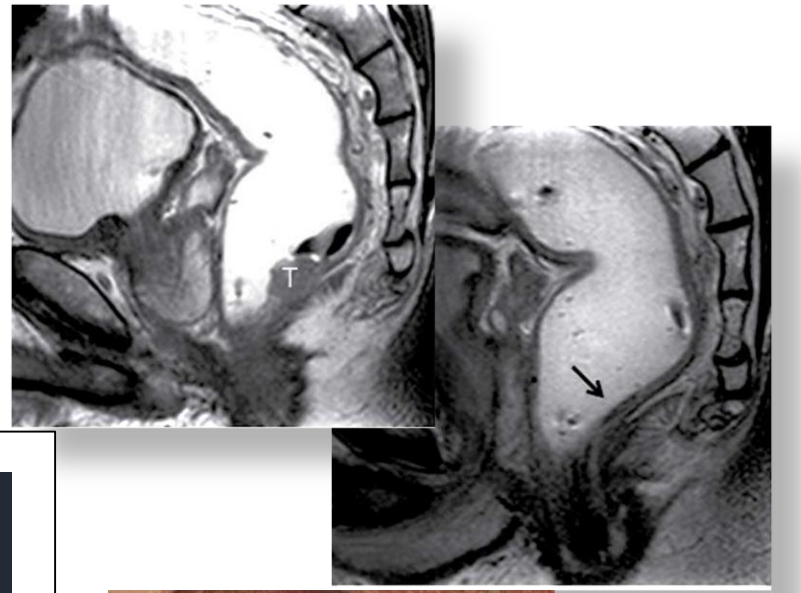
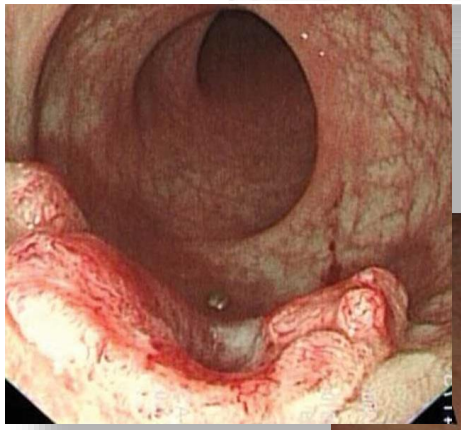
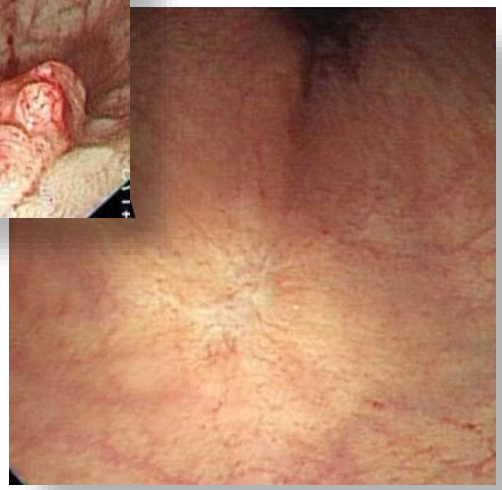
Andrew G R



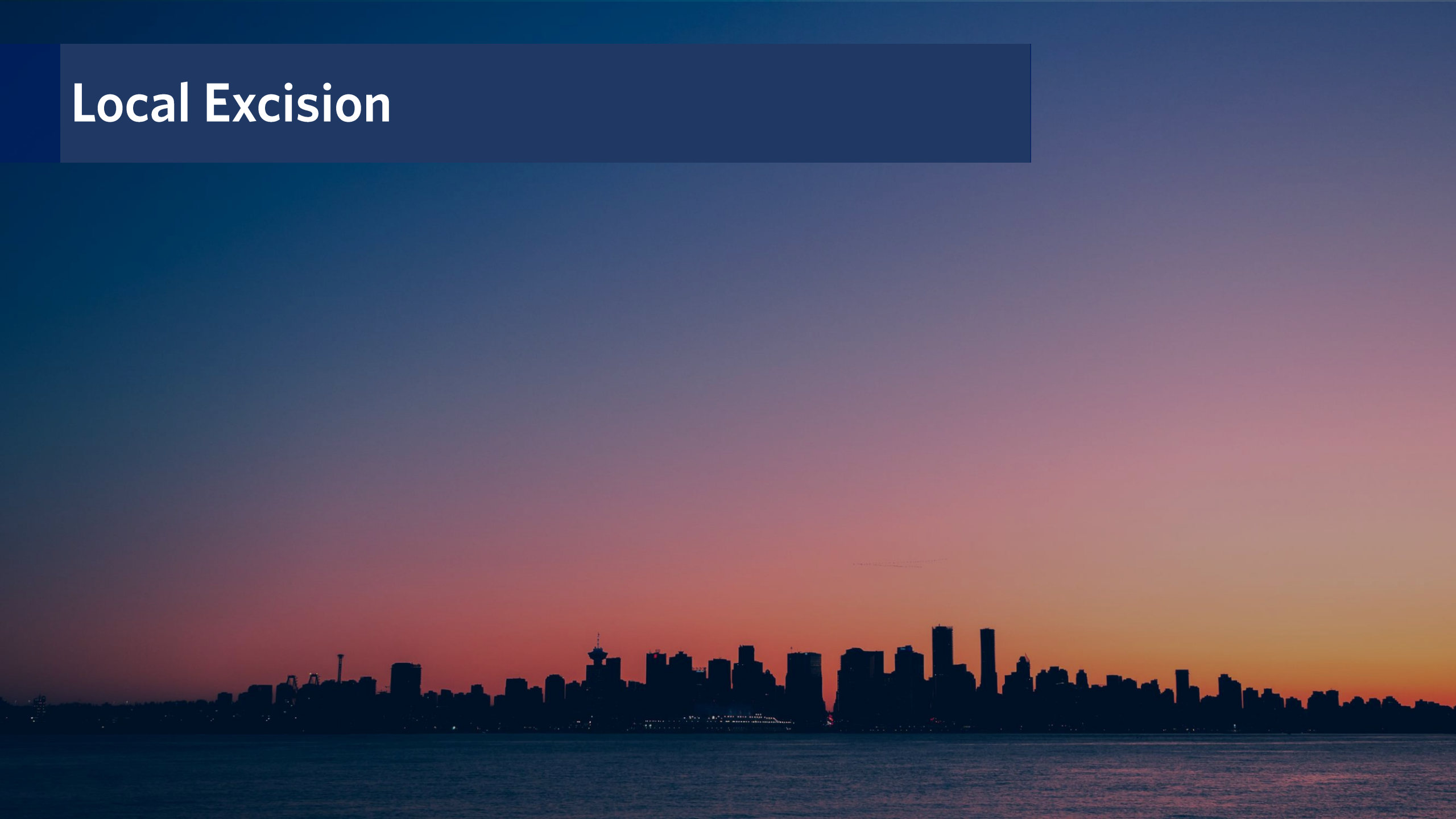
5 Year Local Regrowth
31.6%





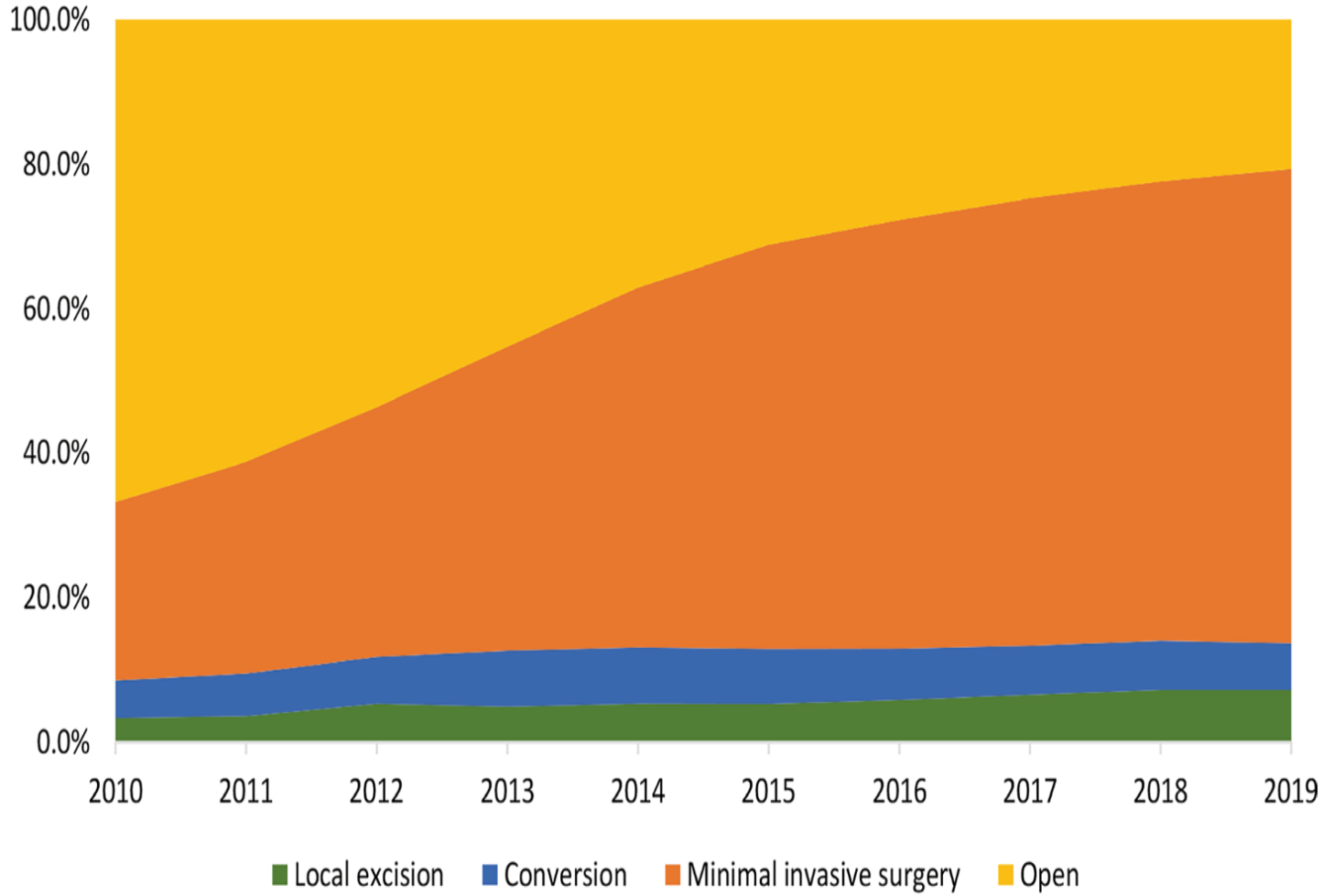


Local Excision



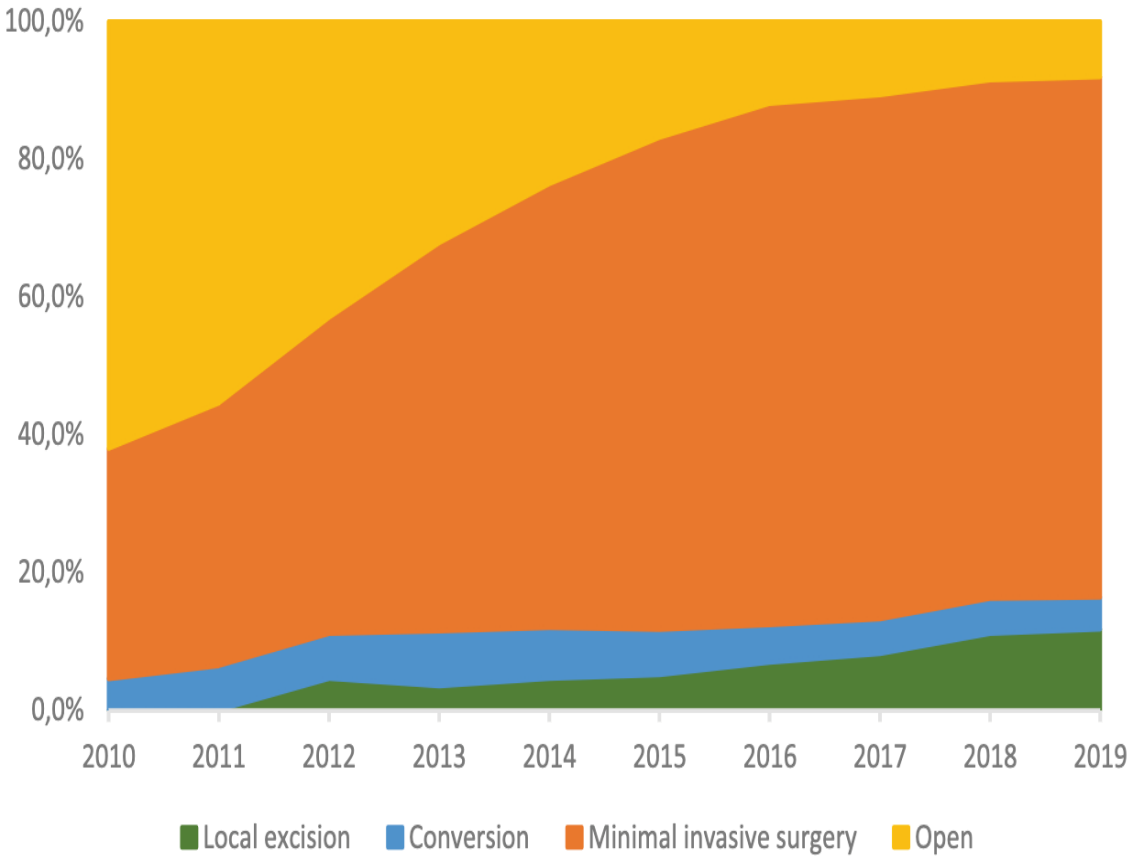
“Excisable” Early Rectal Cancer Uncommon

- Population based study of 99,597 pts w rectal cancer 2010-19
- Netherlands, Sweden, England and Australia



Sijmons, Int J Col Dis, 2024

“Excisable” Early Rectal Cancer - Netherlands



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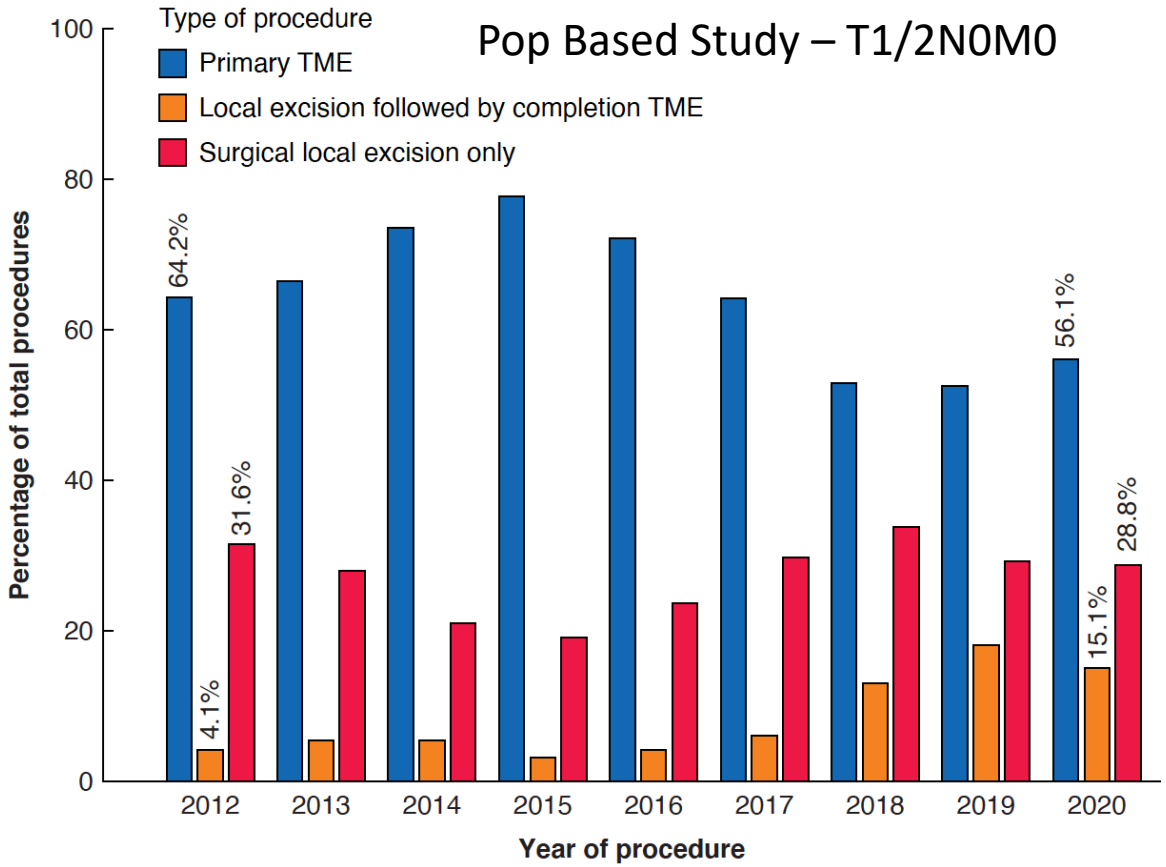


van Lieshout, BJS Open, 2024

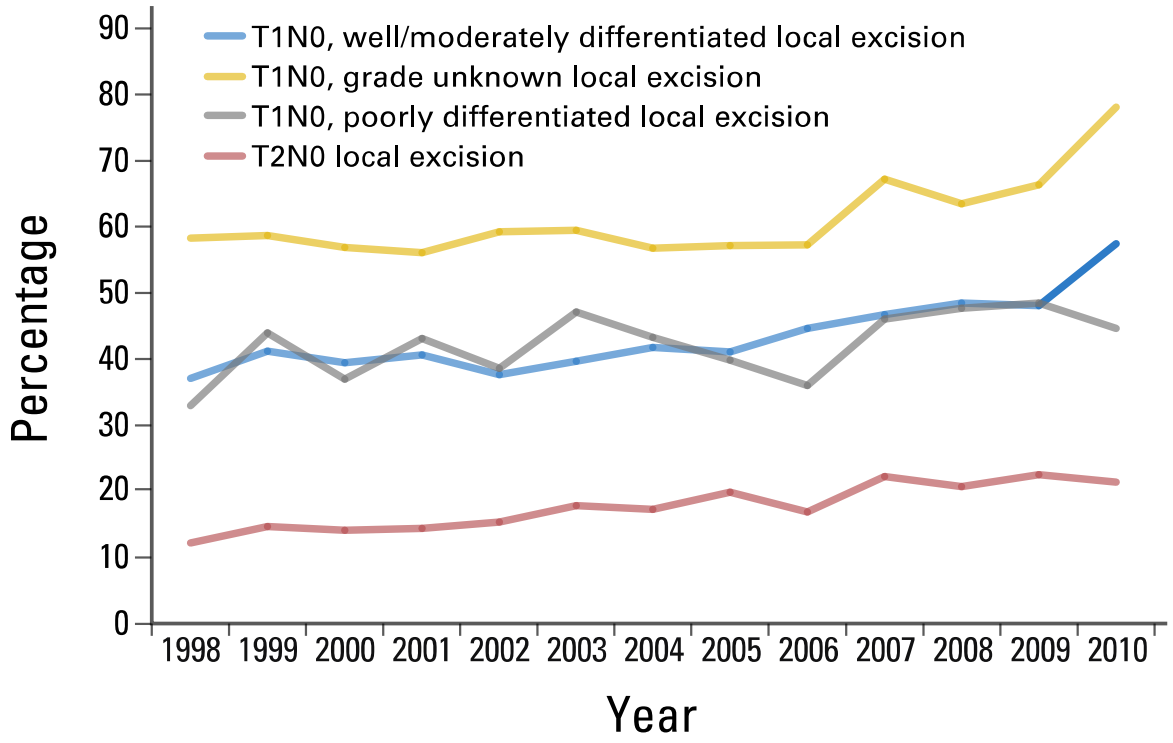
VOLUME 31 · NUMBER 34 · DECEMBER 1 2013

JOURNAL OF CLINICAL ONCOLOGY

Practice Patterns and Long-Term Survival for Early-Stage Rectal Cancer

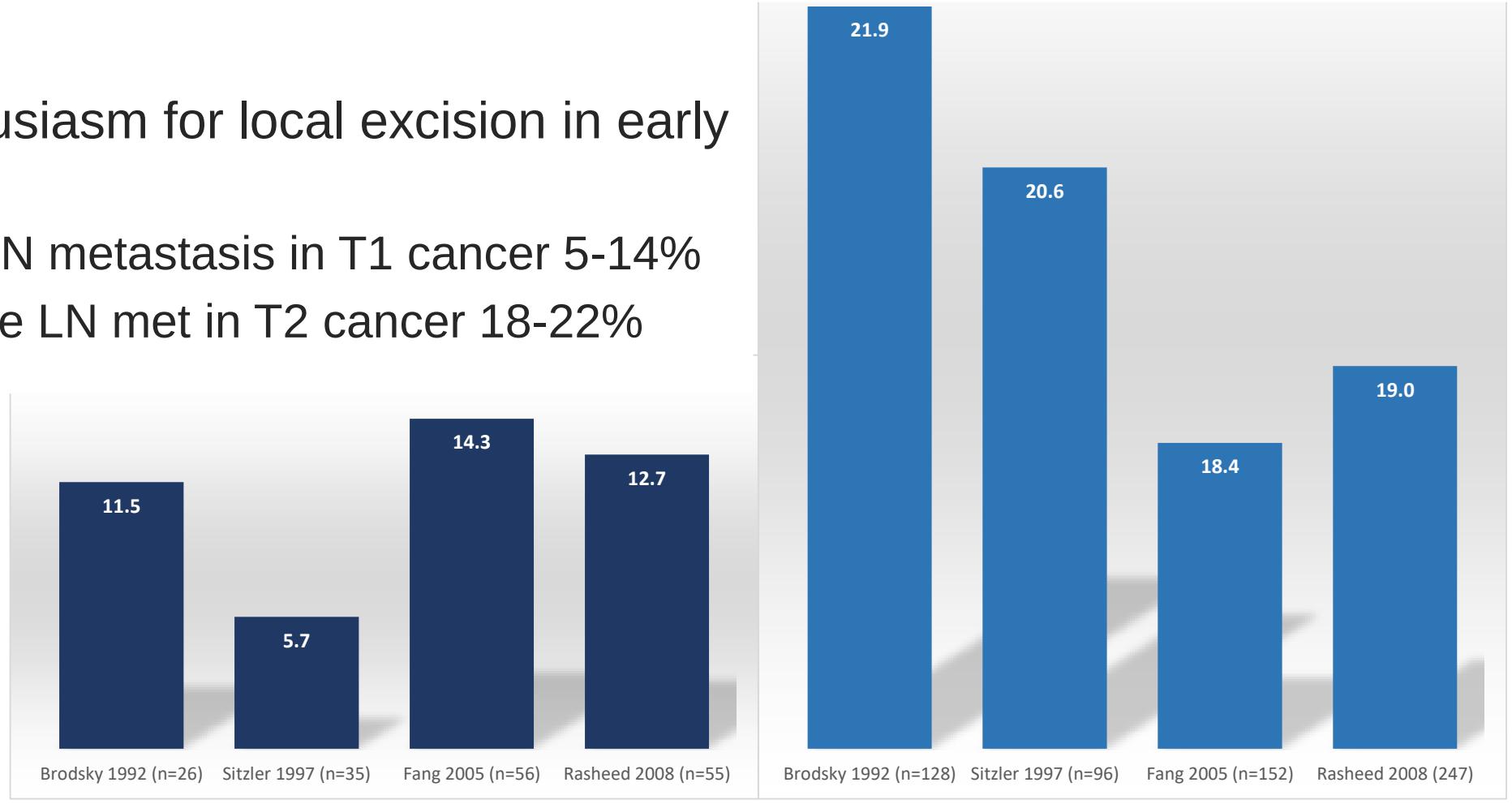
Karyn B. Stitzenberg, Hanna K. Sanoff, Dolly C. Penn, Michael O. Meyers, and Joel E. Tepper

- 2013 National Cancer Data Base study of Stage I Rectal Cancer
  - >1500 hospitals
  - 70% of all newly diagnosed cancer
  - N=35,000 local excision
  - N=77,000 radical resection



Local Excision Rationale - LN Positivity

- Late 90s, enthusiasm for local excision in early rectal cancer
  - Low risk of LN metastasis in T1 cancer 5-14%
  - Unacceptable LN met in T2 cancer 18-22%
- Low risk T1 expected LR less than 10% based on LN +ve in radical resection



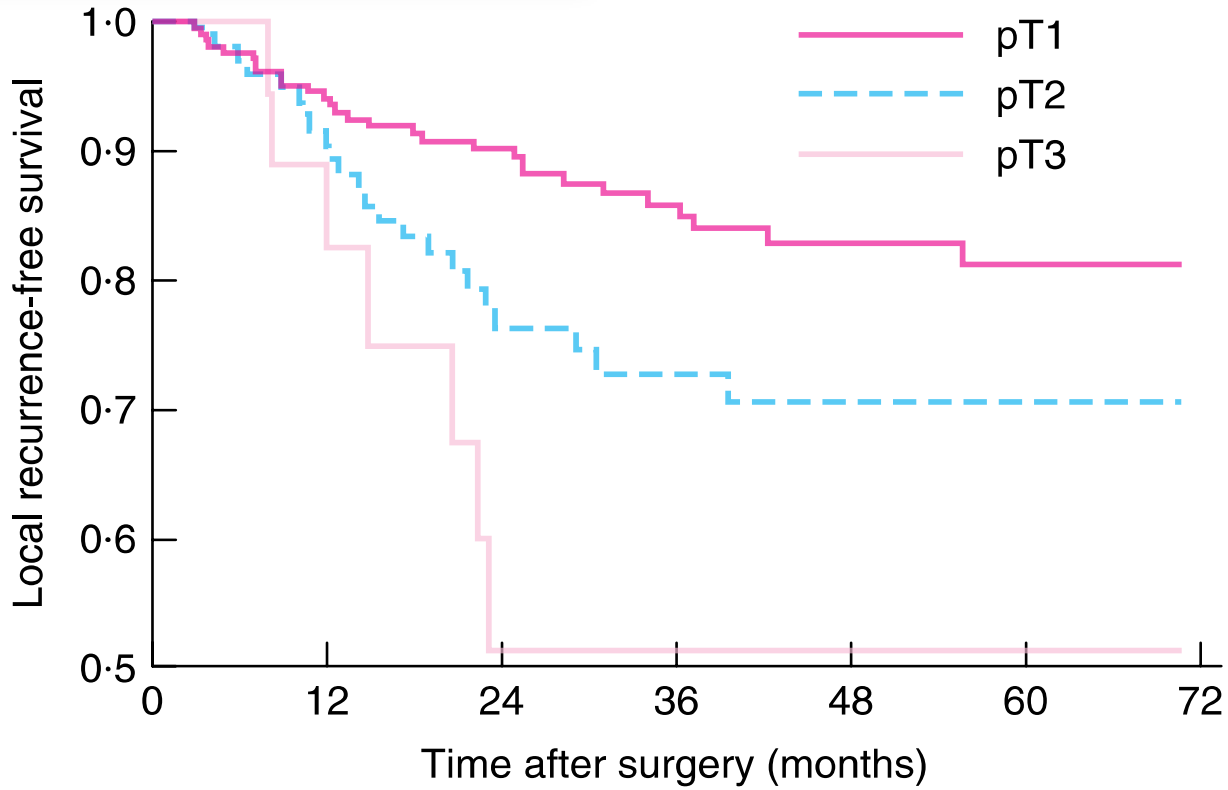
A predictive model for local recurrence after transanal endoscopic microsurgery for rectal cancer

S. P. Bach[1], J. Hill[2], J. R. T. Monson[3], J. N. L. Simson[4], L. Lane[5], A. Merrie[7], B. Warren[6] and N. J. McC. Mortensen[5], on behalf of the Association of Coloproctology of Great Britain and Ireland Transanal Endoscopic Microsurgery (TEM) Collaboration

British Journal of Surgery 2009; **96**: 280–290

487 TEM (253 T1)

- 49 local recurrences
- 11 local + distant
- 6 distant
- Median time to recurrence 13 months (3-55)



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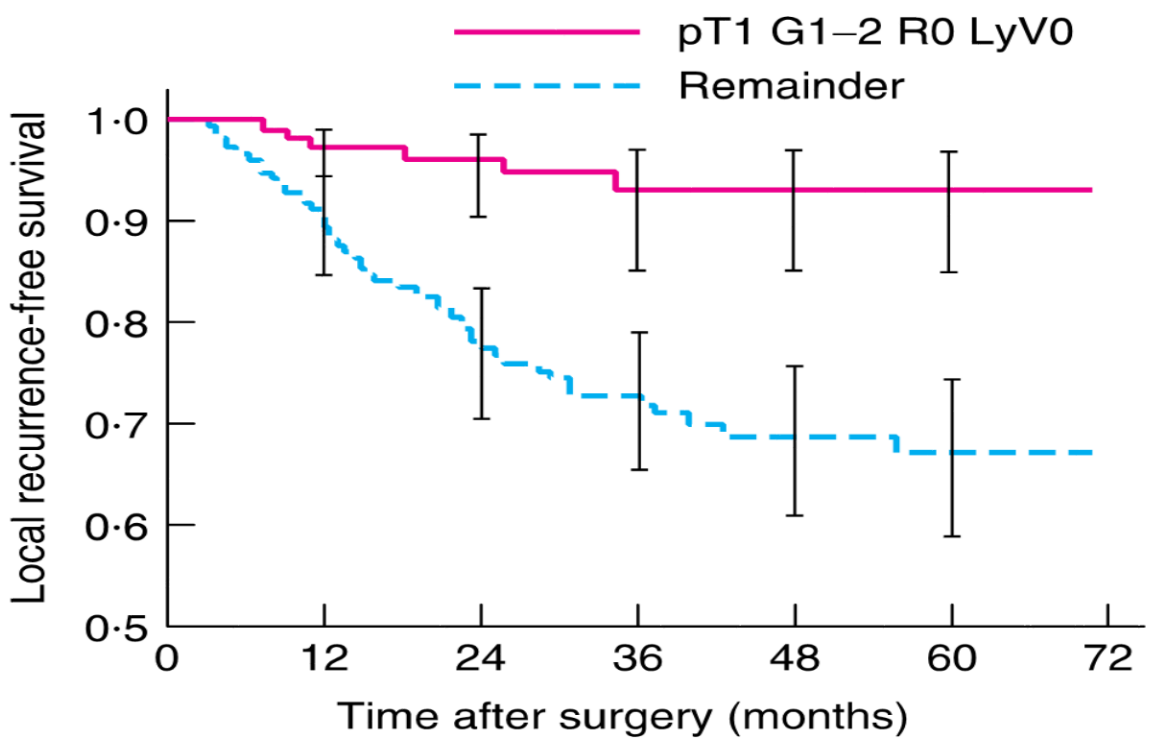


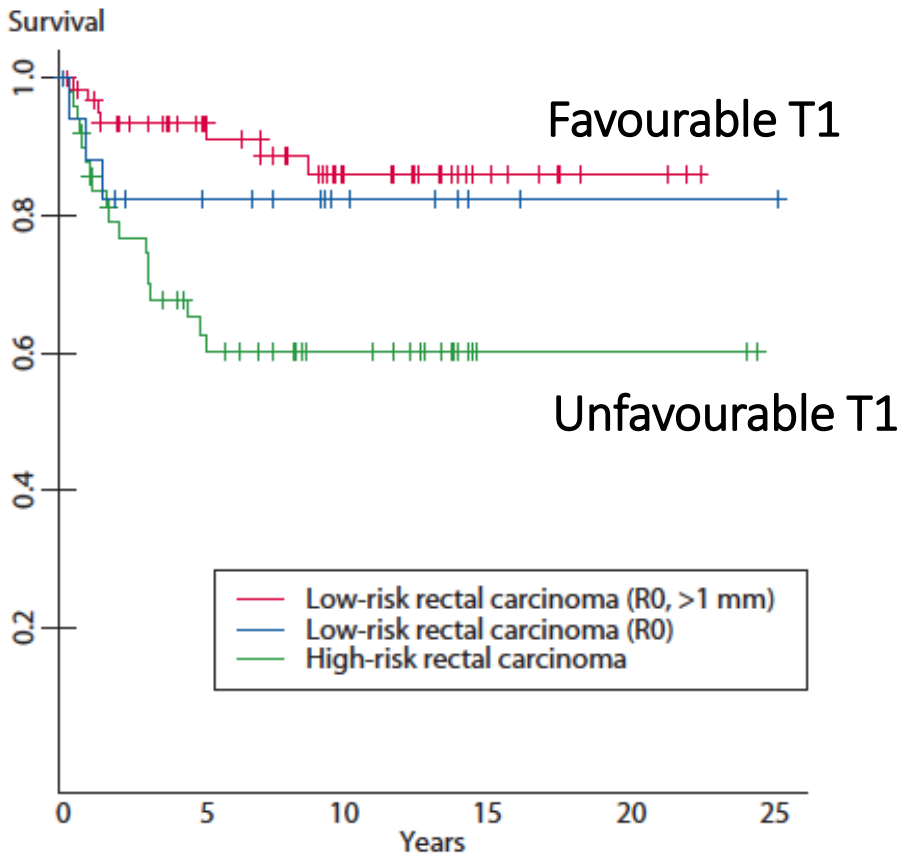
Favourable T1

Unfavourable T1

Low Risk T1 – TES acceptable

Risk Factors

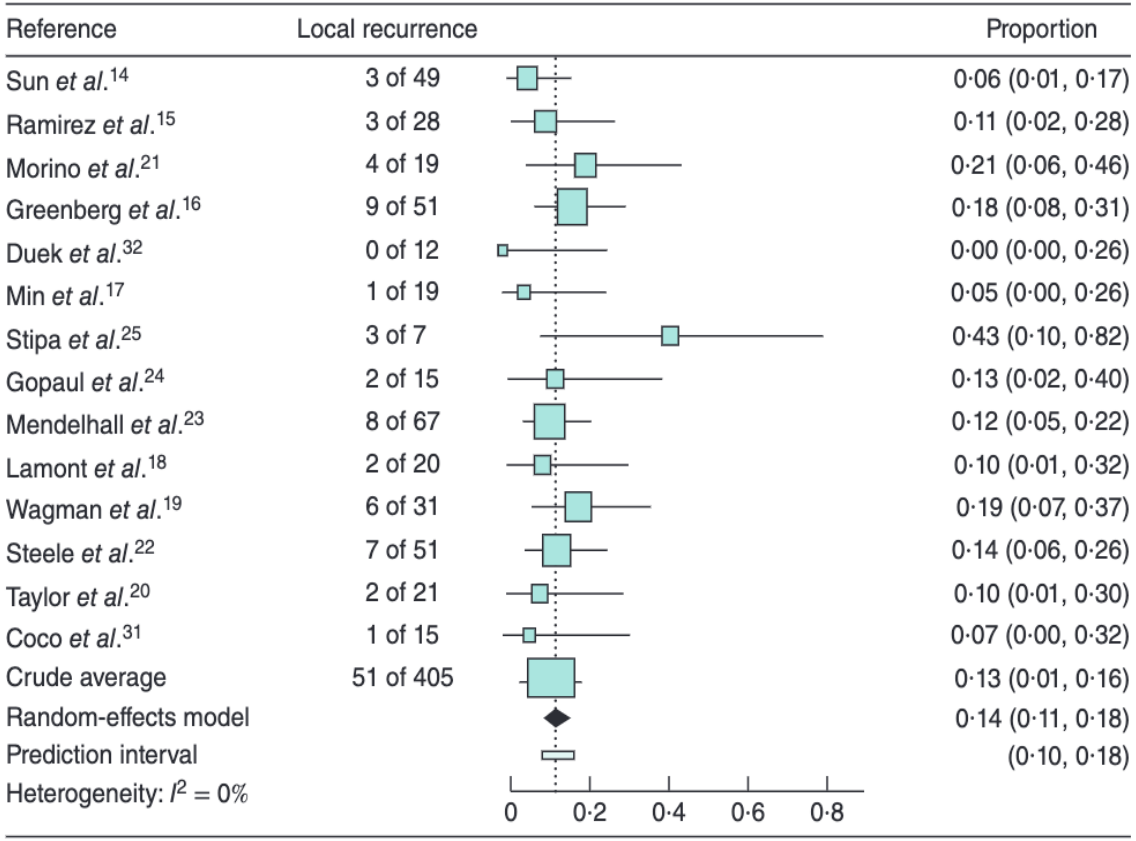
- Margin >1mm
- Depth of submucosal invasion (SM1 vs <1mm)
- Tumour Grade, Features (signet, mucinous)
- Lymphovascular/Perineural Invasion
- Width of invasion
- Tumour budding



Junginger, DCR, 2016

Why not excise and hope for $T1_{fav}$?

- If $T1_{unfav}$ or T2/3, no chance for neoadj therapy
  - Adjuvant CRT possible
  - LR 14% (95%CI 11-18%)



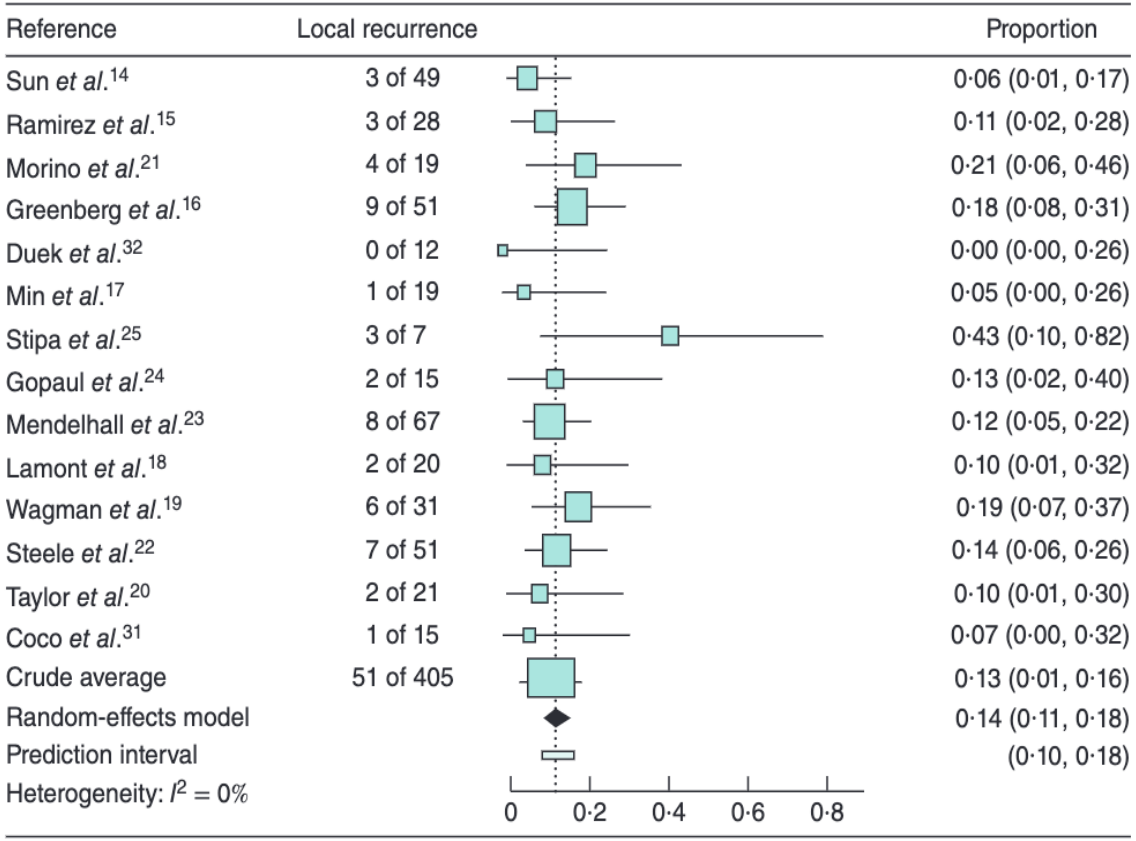
Reference	Local recurrence	Proportion
Sun *et al.*[14]	3 of 49	0·06 (0·01, 0·17)
Ramirez *et al.*[15]	3 of 28	0·11 (0·02, 0·28)
Morino *et al.*[21]	4 of 19	0·21 (0·06, 0·46)
Greenberg *et al.*[16]	9 of 51	0·18 (0·08, 0·31)
Duek *et al.*[32]	0 of 12	0·00 (0·00, 0·26)
Min *et al.*[17]	1 of 19	0·05 (0·00, 0·26)
Stipa *et al.*[25]	3 of 7	0·43 (0·10, 0·82)
Gopaul *et al.*[24]	2 of 15	0·13 (0·02, 0·40)
Mendelhall *et al.*[23]	8 of 67	0·12 (0·05, 0·22)
Lamont *et al.*[18]	2 of 20	0·10 (0·01, 0·32)
Wagman *et al.*[19]	6 of 31	0·19 (0·07, 0·37)
Steele *et al.*[22]	7 of 51	0·14 (0·06, 0·26)
Taylor *et al.*[20]	2 of 21	0·10 (0·01, 0·30)
Coco *et al.*[31]	1 of 15	0·07 (0·00, 0·32)
Crude average	51 of 405	0·13 (0·01, 0·16)
Random-effects model		0·14 (0·11, 0·18)
Prediction interval		(0·10, 0·18)
Heterogeneity: $I^2 = 0\%$		

0 0·2 0·4 0·6 0·8

Borstlap, BJS, 2016

Why not excise and hope for $T1_{fav}$?

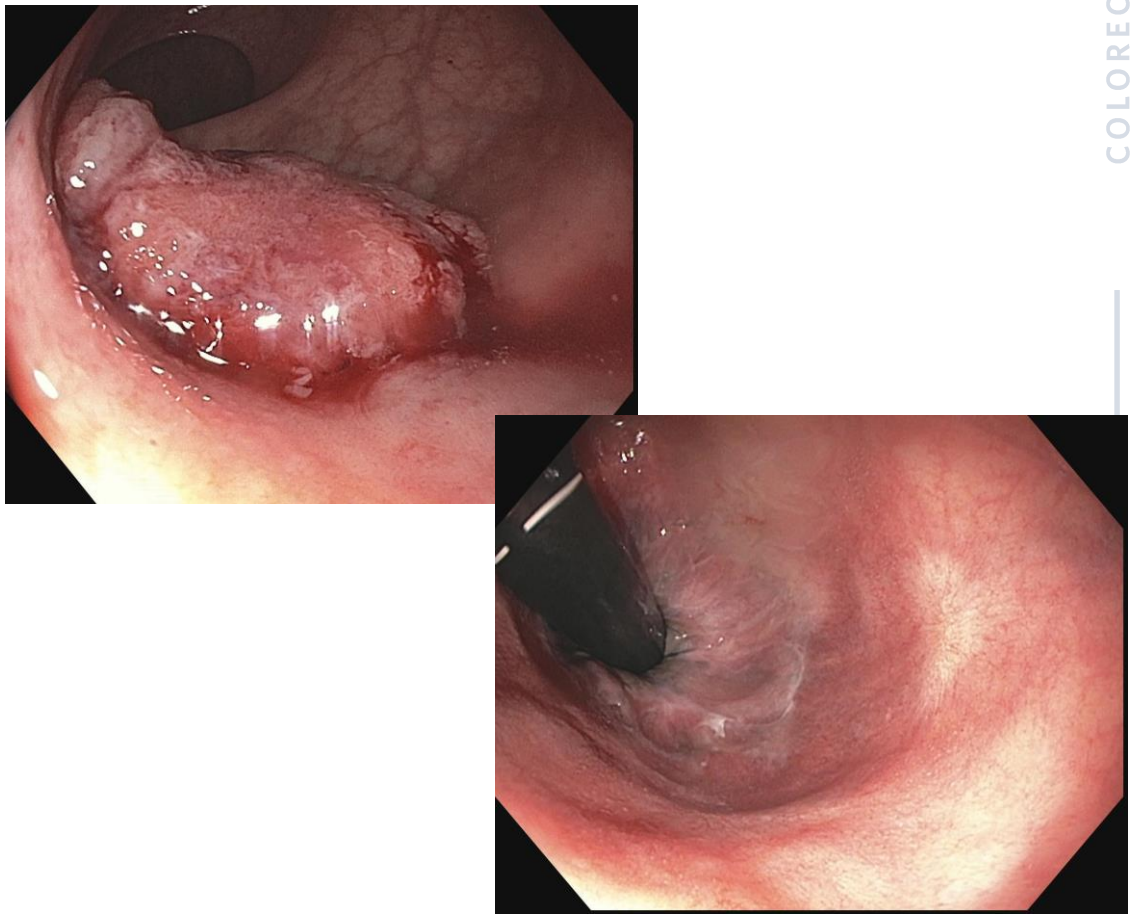
- If $T1_{unfav}$ or T2/3, no chance for neoadj therapy
  - Adjuvant CRT possible
  - LR 14% (95%CI 11-18%)
- Potential Benefit of Neoadj CRT
  - Tumour response can select good outcome
  - Neoadj CRT better than Adj CRT in LARC



Borstlap, BJS, 2016

Neoadjuvant Chemoradiotherapy followed by LE

- Best studied organ preservation strategy for early rectal cancer
- Consistent with neoadjuvant treatment advantage seen in LARC trials



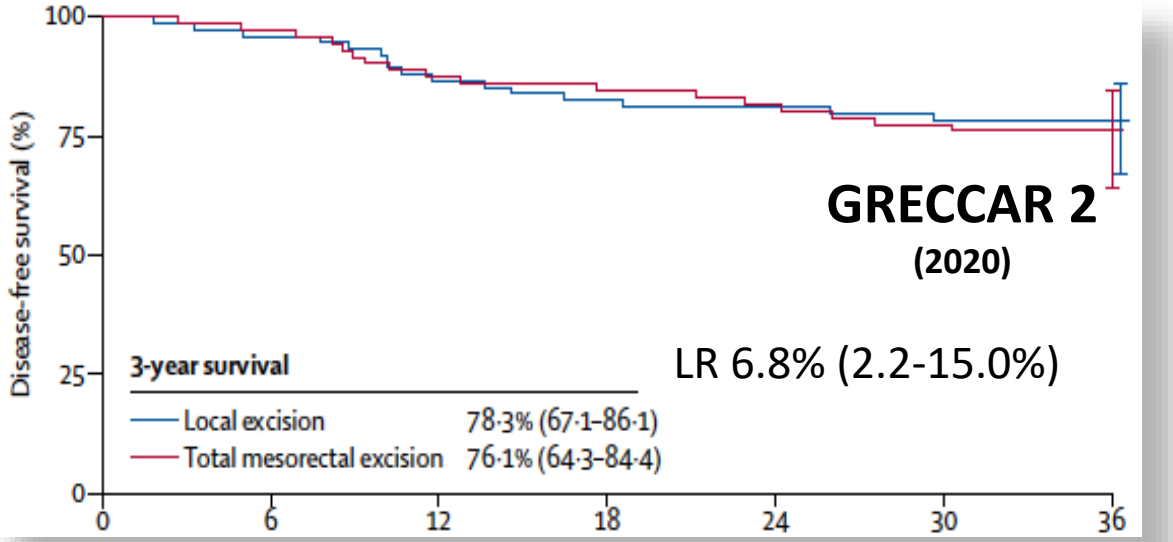
Neoadjuvant Chemoradiotherapy followed by LE

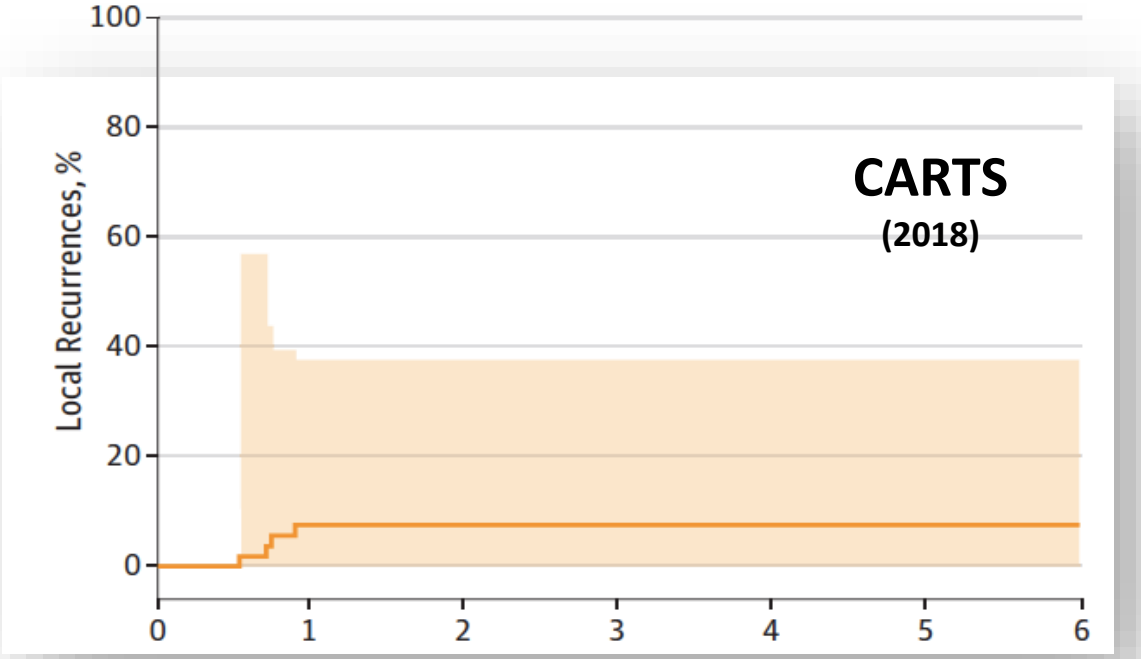
Study	Population	N	ypT0/1N0	Organ Sparing Rate (OSR)
CARTS[1,5]	cT1-3bN0, Low Rectal	55	55%	65%
Garcia-Aguilar[3]	T2N0	77	64%	91%
Lezoche[4]	T2N0	50	52%	100%
GRECCAR[6]	T2T3 N0/1, <4cm	74	54%	65%

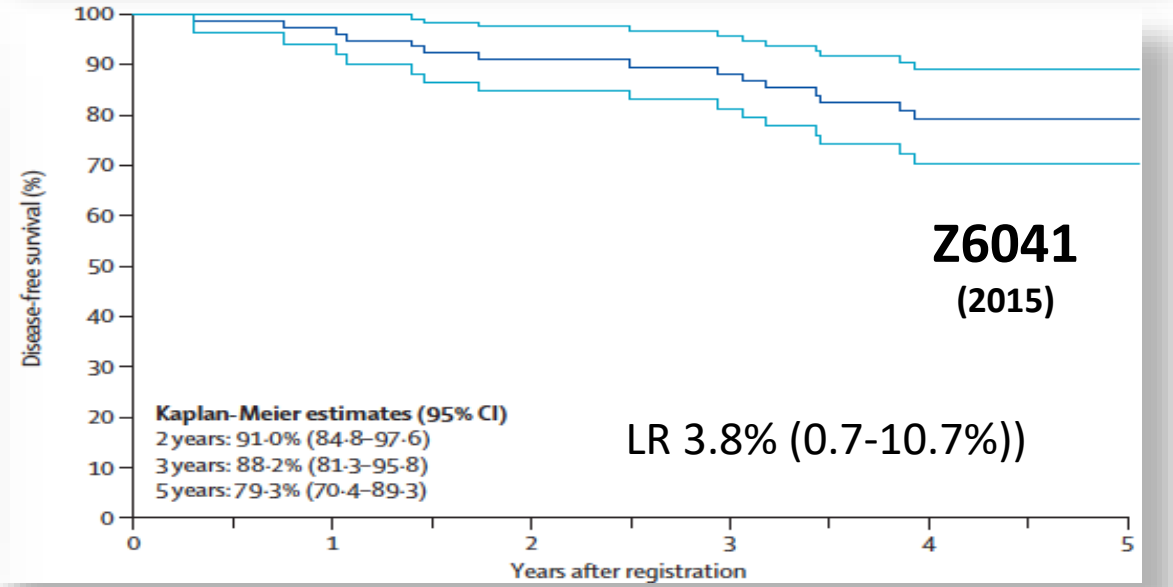
(1)Verseveld BJS 2015 (2) Puccairelli Dis Colon Rectum 2013 (3)Garcia-Aguilar Ann Surg Oncol 2012 (4)Lezoche BJS 2012 (5) Stijns JAMA 2019 (6) Rullier Lancet GI 2020

Local Recurrence and Disease Free Survival

- Chemoradiotherapy followed by TES achieves good cancer outcomes with organ preservation







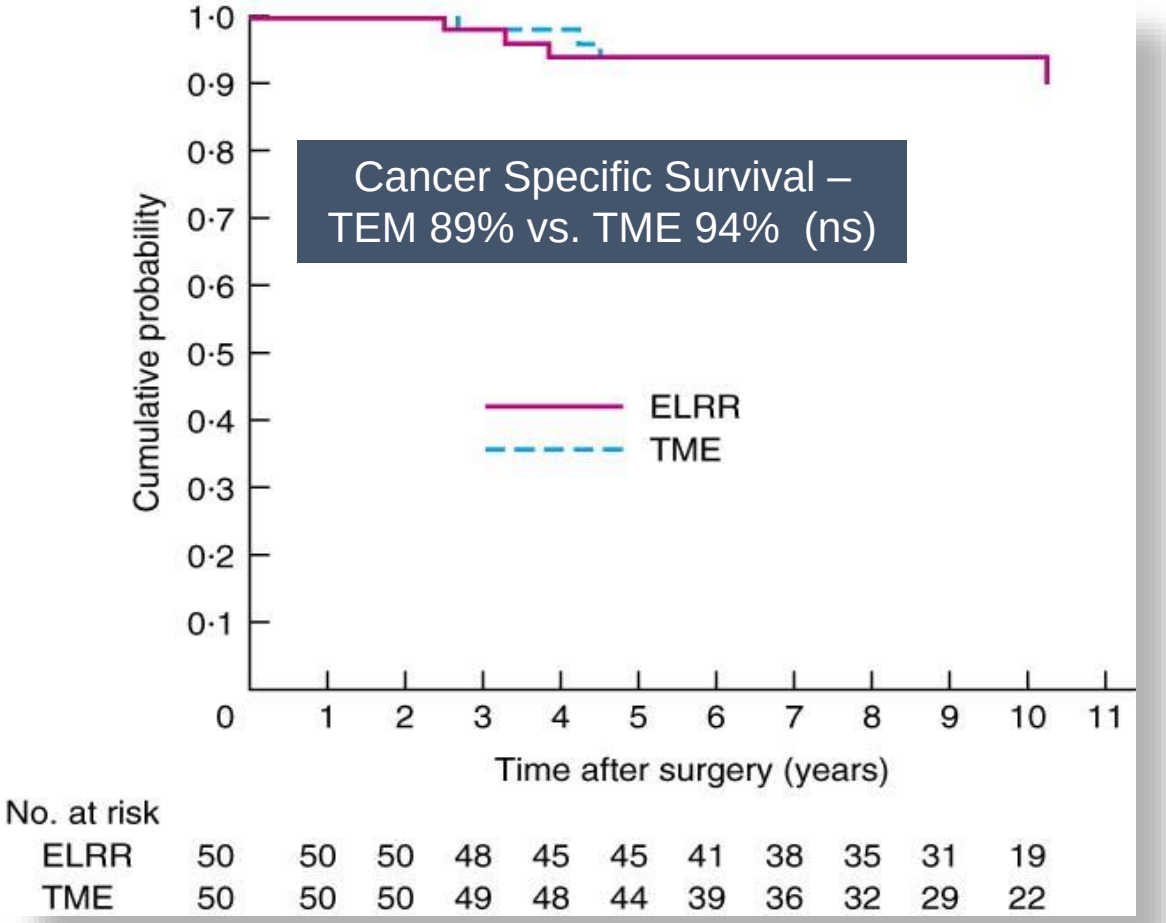
CRT + TES vs Radical Resection - RCT

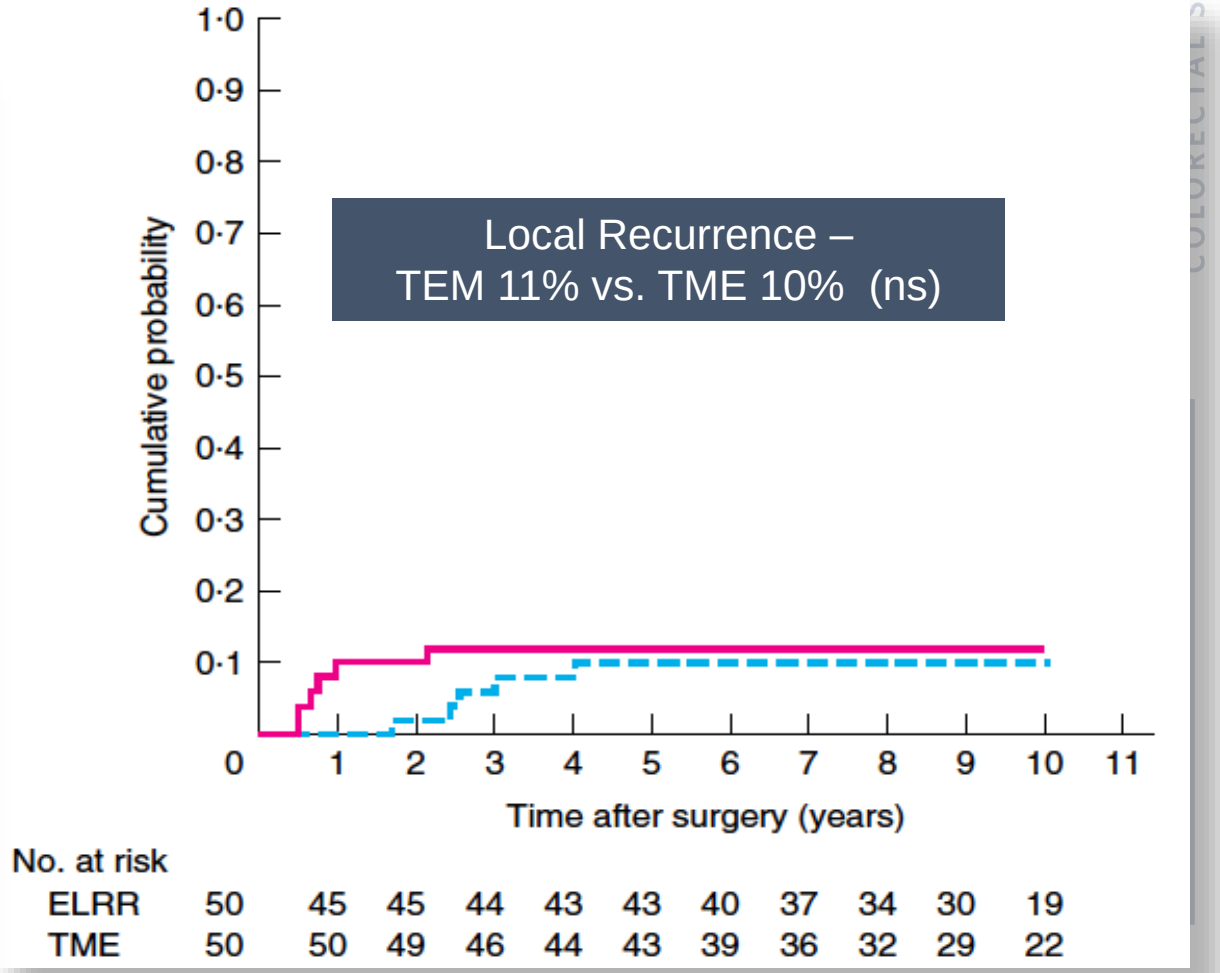
- Lezoche et al, Br J Surg 2012
  - April 1997 – April 2004, 2 Hospitals in Italy
  - Low rectal tumours limited to T2N0M0
  - All received neoadjuvant long-course chemo (5-FU) and radiotherapy (four-field, 50.4Gy over 5 weeks)
  - Restaged post-chemoradiation
  - Randomized to TEM vs laparoscopic TME

	ELRR ($n = 50$)	TME ($n = 50$)	P†
Intraoperative programme change	0 (0)	6 (12)	0·013‡
Conversion to open surgery	0 (0)	5 (10)	0·028‡
Stoma			
Temporary	0 (0)	11 (22)	< 0·001
Definitive	0 (0)	12 (24)	< 0·001
Duration of operation (min)*	90 (90–100)	174 (160–190)	< 0·001§
Blood loss (ml)*	45 (45–45)	200 (100–350)	< 0·001§
No. of patients receiving transfusion	0 (0)	10 (20)	< 0·001
No. of patients receiving analgesia	7 (14)	50 (100)	< 0·001
Hospital stay (days)*	3 (3–4)	6 (5–7)	< 0·001§
Postoperative complications			
Minor	6 (12)	7 (14)	0·766
Major	1 (2)	3 (6)	0·250‡

Lezoche, BJS, 2012

TES + CRT vs Radical Resection - RCT





Lezoche, BJS, 2012

ORIGINAL CONTRIBUTION

Transanal Endoscopic Microsurgery for Residual Rectal Cancer After Neoadjuvant Chemoradiation Therapy Is Associated With Significant Immediate Pain and Hospital Readmission Rates

Rodrigo Oliva Perez, M.D., Ph.D.[1,2] • Angelita Habr-Gama, M.D., Ph.D.[1]
Guilherme Pagin São Julião, M.D.[1,3] • Igor Proscurshim, M.D.[1,3]
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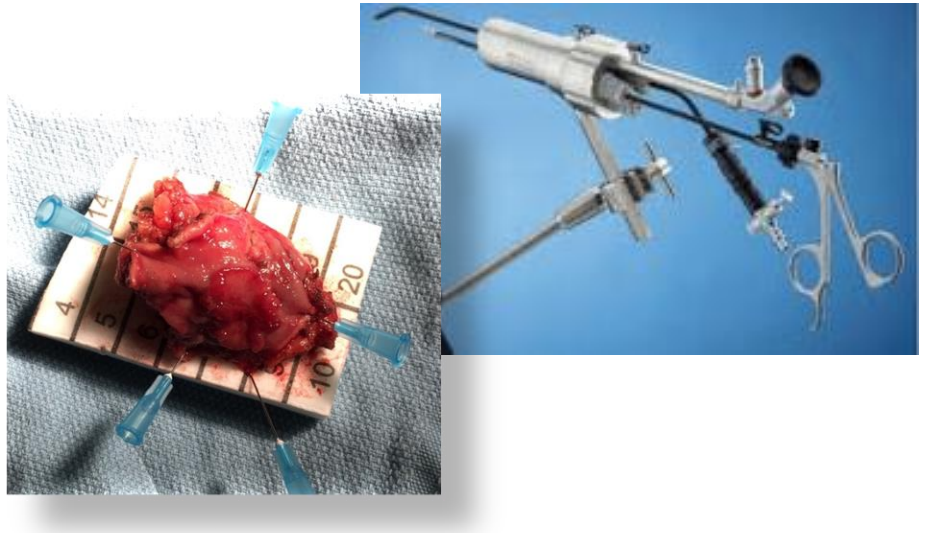

- 36 consecutive TEM procedures for early rectal cancer
  - Neoadj CRT (n=23) vs Surgery Alone (n=13)
- Periop care
  - Defect closed in all patients
  - Postop abx x 7days
- Follow up 30 days, including endoscopic evaluation

	Study group (neoadjuvant CRT)	*Control group (no CRT)*	*P*
n	23	13	
Age, y	59.3 ± 11.6	61.1 ± 19.7	
Sex (M:F)	12:11 (52.2:47.8)	7:6 (53.8:46.2)	.92
Distance from anal verge, cm	3.5 ± 1.9	4.8 ± 2.3	.08
Pathology[a]			
T0	3	4	
T1	5	5	
T2	12	1	
T3	3	0	.06
Final tumor size, cm	1.9 ± 1.3	3.3 ± 2.8	.10

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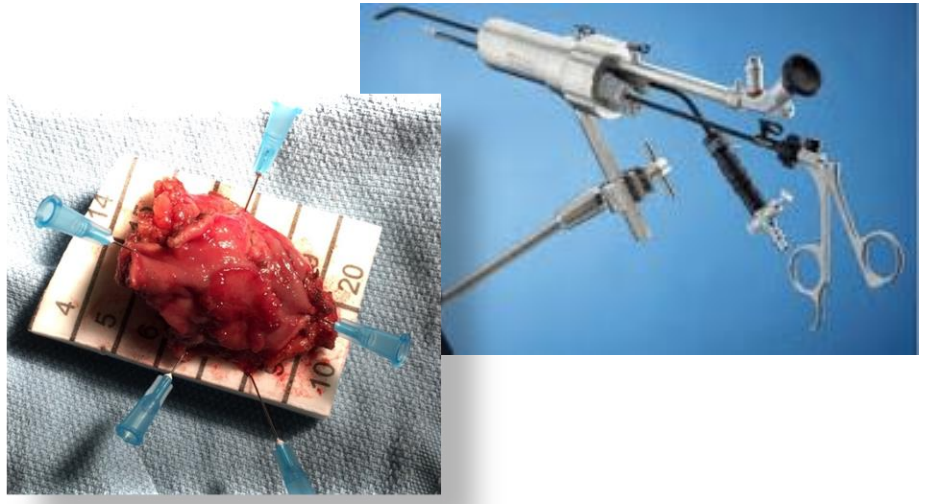

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- Periop care
  - Defect closed in all patients
  - Postop abx x 7days
- Follow up 30 days, including endoscopic evaluation

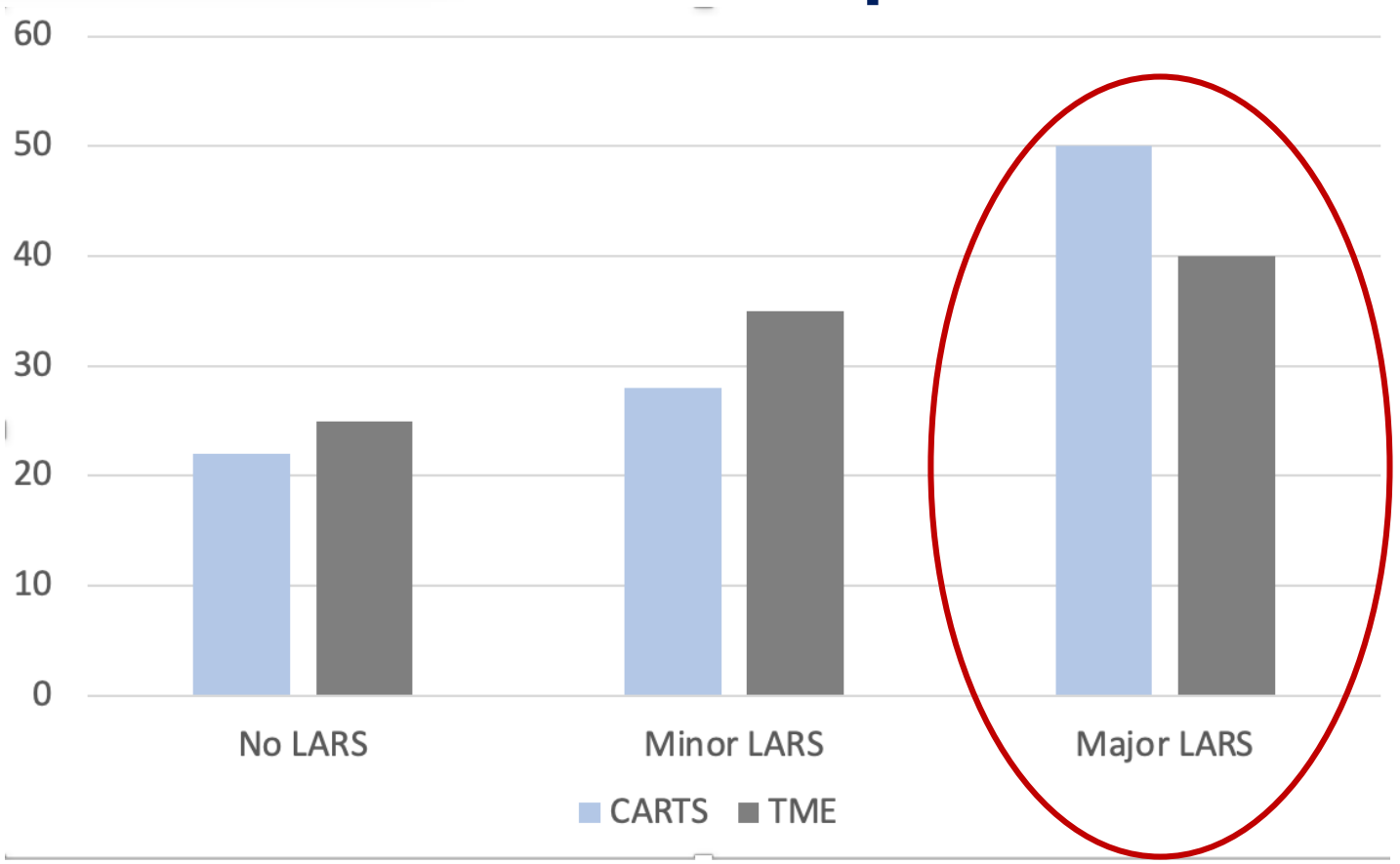
	Study group (neoadjuvant CRT), n (%)	*Control group (no CRT), n (%)*	*P*
n	23	13	
Immediate grade I complication	12 (52)	2 (15)	.030
Immediate grade II/III complication	13 (56.5)	3 (23.1)	.054
Wound dehiscence	14 (60.9)	3 (23.1)	.032
Hospital readmission	10 (43.5)	1 (7)	.025
Late complication	1 (4)	2 (15)	.25

Chemoradiation therapy for rectal cancer in the distal rectum followed by organ-sparing transanal endoscopic microsurgery (CARTS study)

M. Verseveld[1,2], E. J. R. de Graaf[1], C. Verhoef[2], E. van Meerten[3], C. J. A. Punt[5], I. H. J. T. de Hingh[6], I. D. Nagtegaal[7], J. J. M. E. Nuyttens[4], C. A. M. Marijnen[9] and J. H. W. de Wilt[8], on behalf of the CARTS study group*

- Multicentre phase II trial of neoCRT + TEM for T1-3N0M0 lesions
- Feb 2011 - Sept 2012
- 55 pts enrolled
  - 43 pts ypT0/1N0 post TEM
  - Surveillance

LARS 1 year Postop



Chemotherapy Alone + TES

Chemotherapy and Early Rectal Cancer?

- In Stage IV rectal CA, chemo alone causes tumour regression in many
- In 2013, BC Cancer was a recruitment site for PROSPECT
  - Observed good local response to chemo
- Developed NEO trial with Dr. Hagen Kennecke (medical oncology)

ORIGINAL ARTICLE

Preoperative Treatment of Locally Advanc
Rectal Cancer

Deborah Schrag, M.D., M.P.H., Qian Shi, Ph.D., Martin R. Weiser, M.D.,
Marc J. Gollub, M.D., Leonard B. Saltz, M.D., Benjamin L. Musher, M.D.,
Joel Goldberg, M.D., Tareq Al Baghdadi, M.D., Karyn A. Goodman, M.D.,
Robert R. McWilliams, M.D., Jeffrey M. Farma, M.D., Thomas J. George, M.
Hagen F. Kennecke, M.D., Ardaman Shergill, M.D., Michael Montemurro, M
Garth D. Nelson, M.S., Brian Colgrove, B.S., Vallerie Gordon, M.D.,
Alan P. Venook, M.D., Eileen M. O'Reilly, M.D., Jeffrey A. Meyerhardt, M.D., M.P.H.,
Amylou C. Dueck, Ph.D., Ethan Basch, M.D., George J. Chang, M.D.,
and Harvey J. Mamon, M.D., Ph.D.

ABSTRACT

BACKGROUND

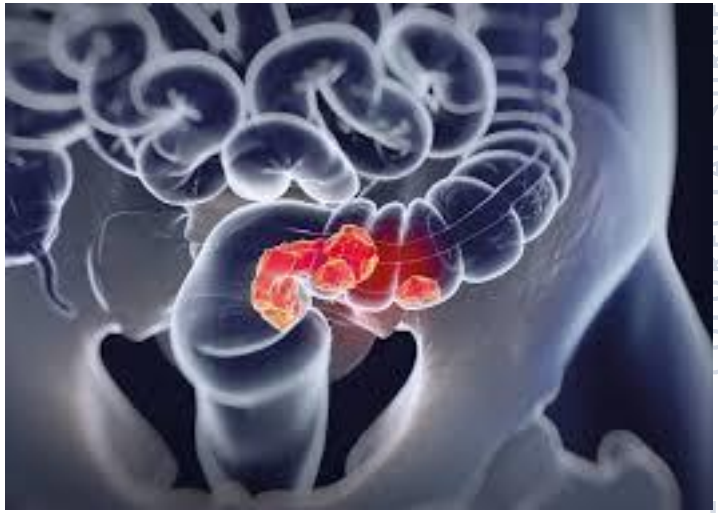
Pelvic radiation plus
diotherapy) before
North America. Wh
and oxaliplatin (FO

METHODS

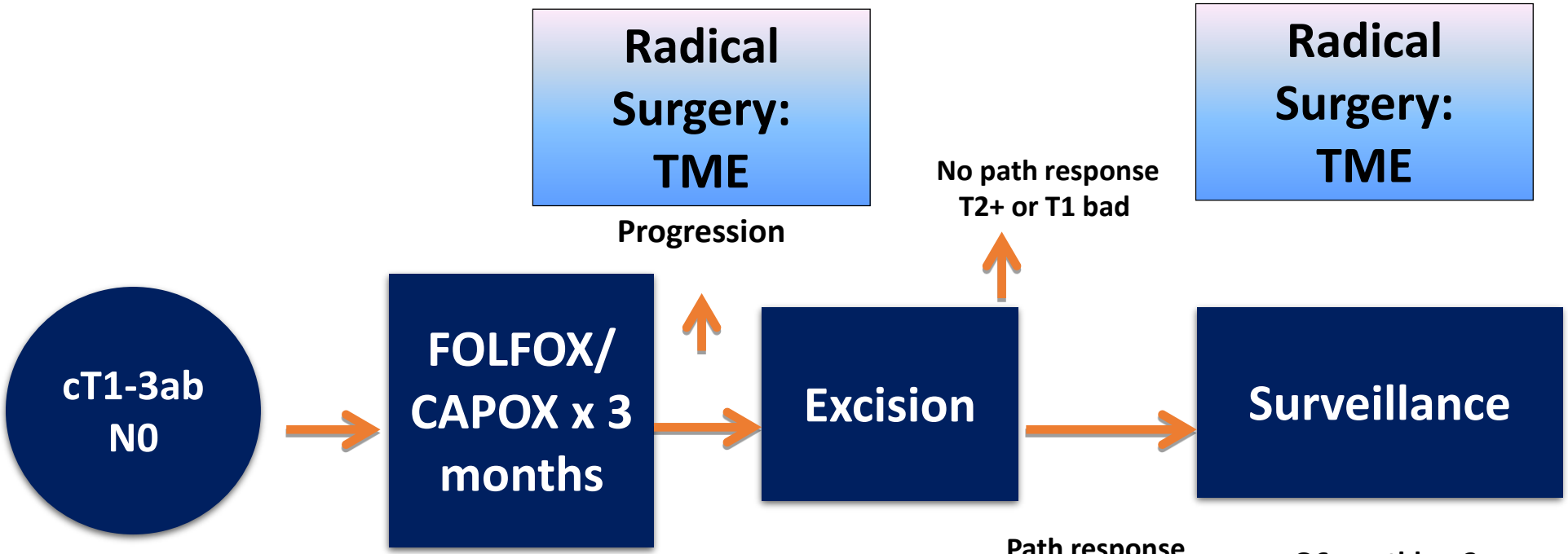
We conducted a mu
juvant FOLFOX (wi
creased in size by <
compared with che
cally staged as T2

Main Inclusion

- MRI T1-T3b N0
- Tumor excisable by transanal endoscopic surgery (TES)
- Well-mod differentiated adenocarcinoma
- No pathologic high-risk features:
    - non-mucinous
    - no lymphovascular/perineural invasion



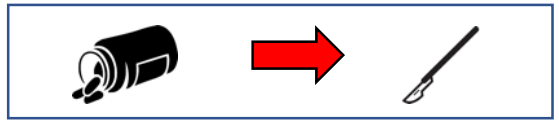
Neoadjuvant Chemotherapy, Excision and Observation



N= 58

1^{o} Endpoint= Rate of pT0/T1N0

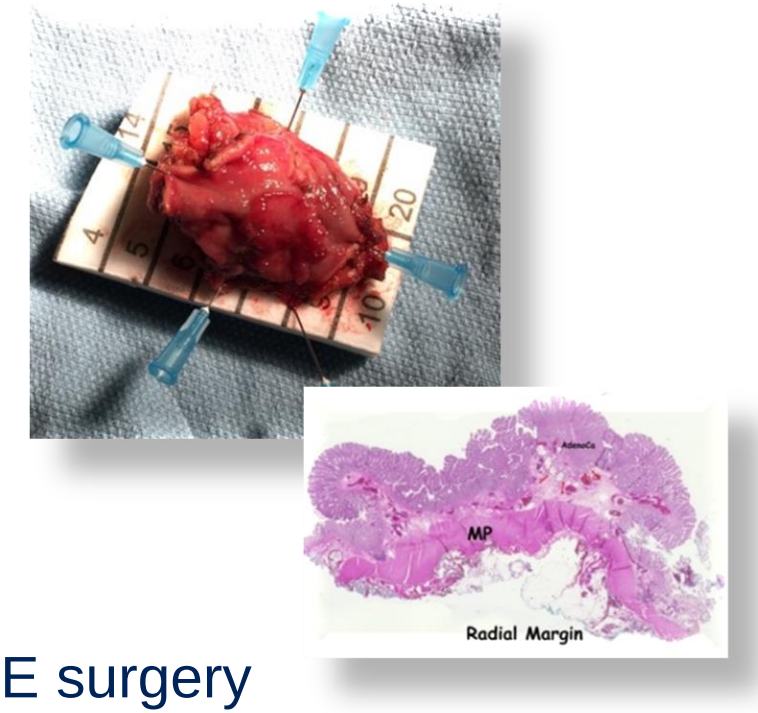
Goal= >65% are managed without radical surgery



Primary study endpoint:

(protocol specified) Organ Preservation Rate, psOPR:

ypT0-T1 cN0, no path ⬆ risk on TES



Secondary study endpoints:

actual Organ Preservation Rate, aOPR:

ypT0-T1,cN0 on TES specimen *plus*

Higher stage patients who declined recommended TME surgery

NOTE: Endpoint created to accommodate patient preference

3-year Locoregional Relapse Rate (LRR), DRR, DFS, QOL, LARS

Sample size and statistics:

H1: the study would be considered positive if a psOPR $\geq 65\%$

H0: the study is negative if the psOPR is $\leq 50\%$

The type I error 0.1, power 0.8

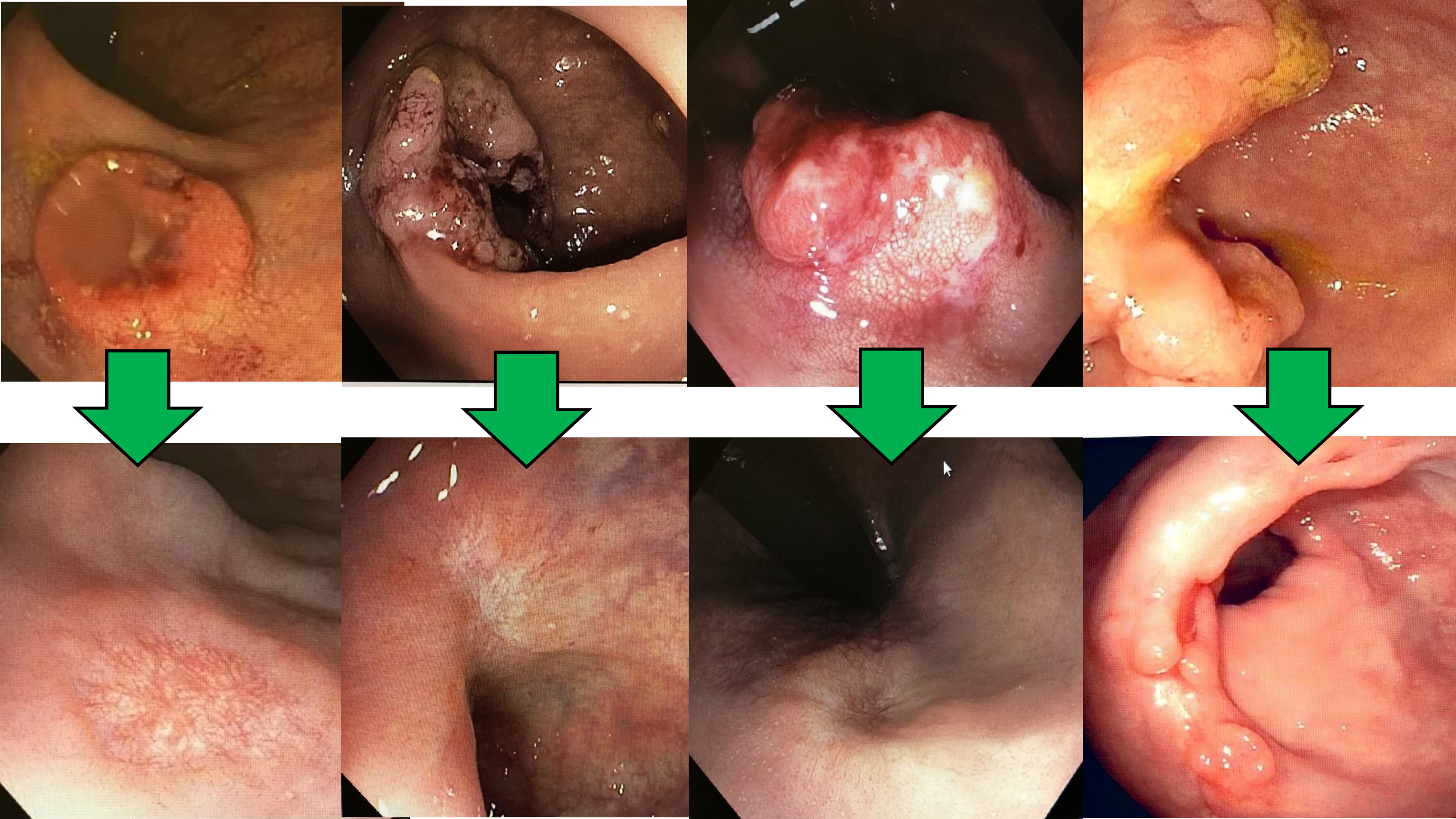
Final Analysis – Minimum 3 year Follow up

- Recruitment: August 2017 – May 2020
- Final accrual: 58 patients in 8 Canadian and 1 US centers
- Current database lock: April 2024
- Median follow-up: 4.3 years (Range 3.3-5.6 years)
- Quality control: All participating surgeons required to submit a video of a TEMS/TAMIS procedure prior to performing the initial TES
- Intent to treat (ITT) analysis: All 58 patients enrolled
- Primary Analysis Presentation: ASCO Annual Meeting 2021
- Secondary Analysis Presentation: ESMO Congress 2024

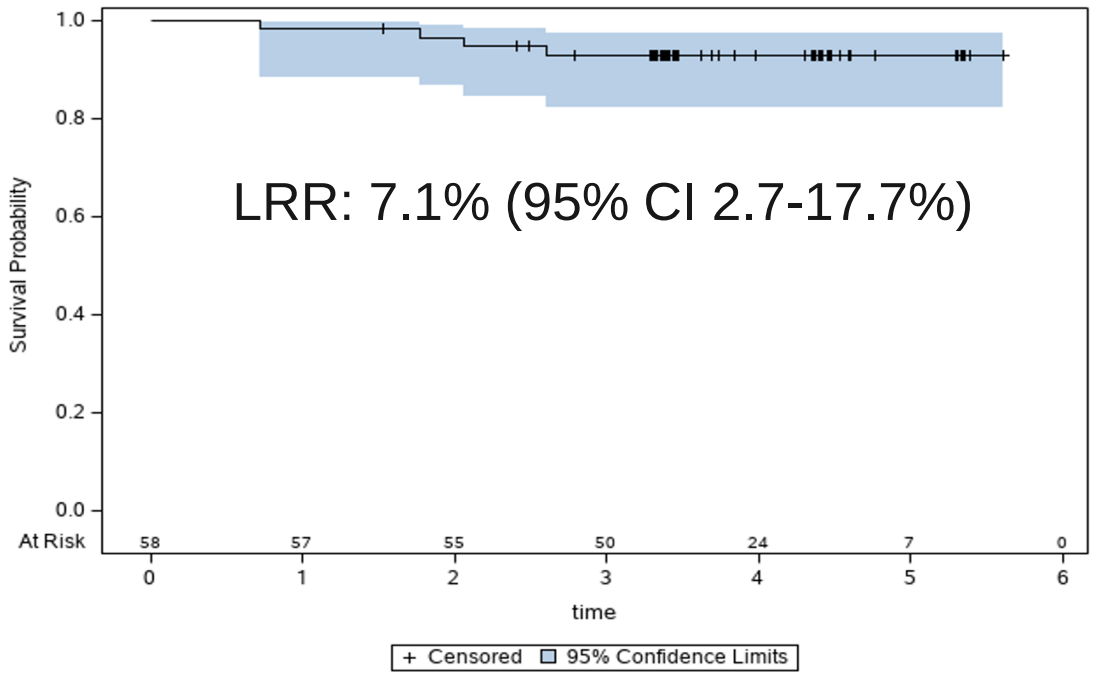
Primary Outcome – PS OPR

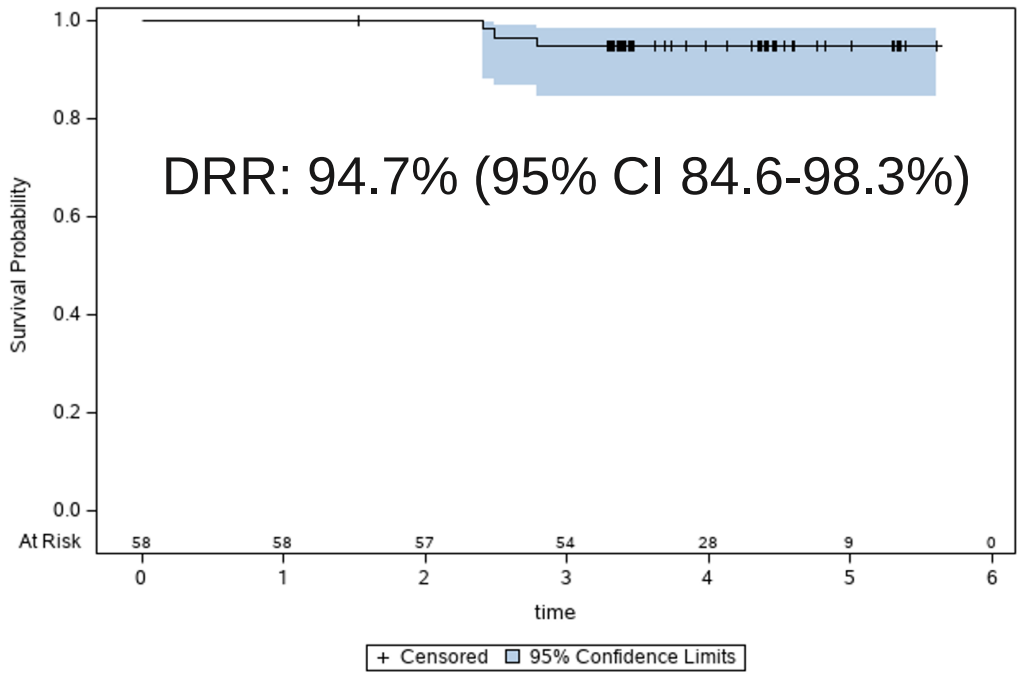
cT stage	Commenced FOLFOX/ CAPOX	Received TES	TES ypstage* *all cases N0/NX and no path high risk				psOPR
			T0	T1	T2	T3	
T1 (n=8)	8	7	3	2	1	1	5/8 (63%)
T2 (n=37)	37	36	10	10	16	0	20/37 (54%)
T3a/b (n=13)	13	13	7	1	3	1	8/13 (62%)
ITT pop'n	**58**	**56**	**33**				**33/58 (57%)** 90% CI 45-68%

- 10/23 had protocol recommended TME after TES, 7/10 no residual disease
- 13/23 declined protocol recommended TME → **aOPR 46/58 (79%)**

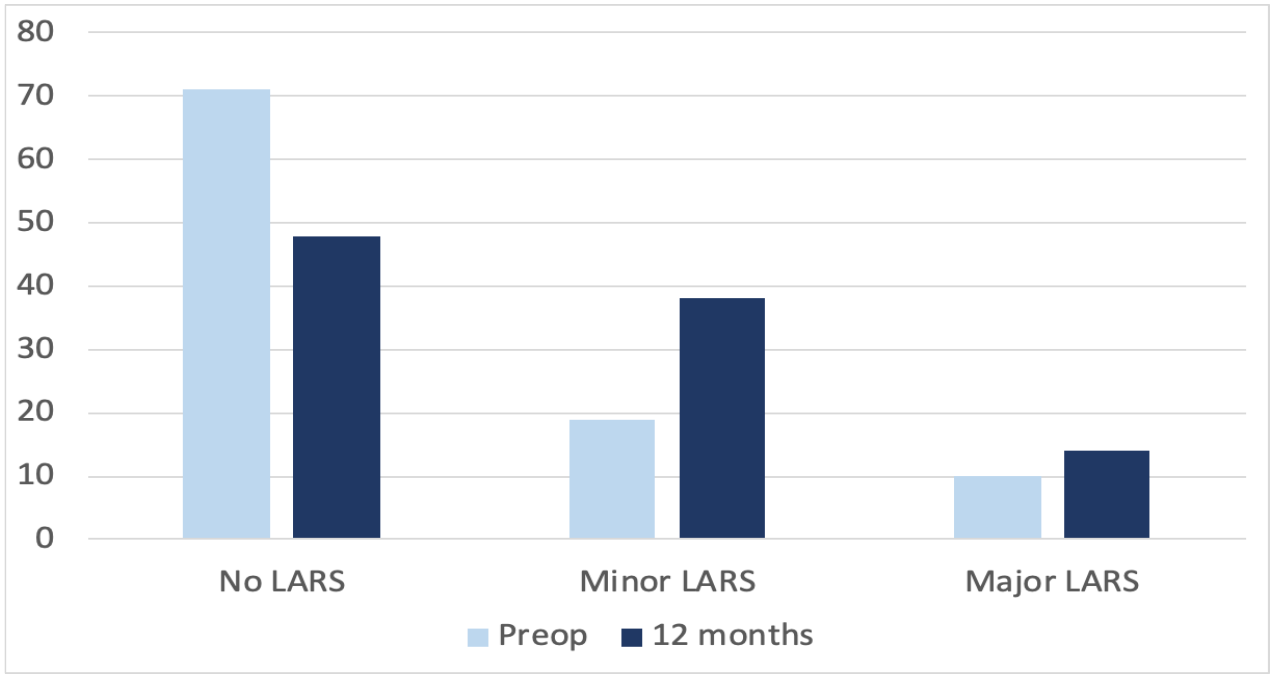


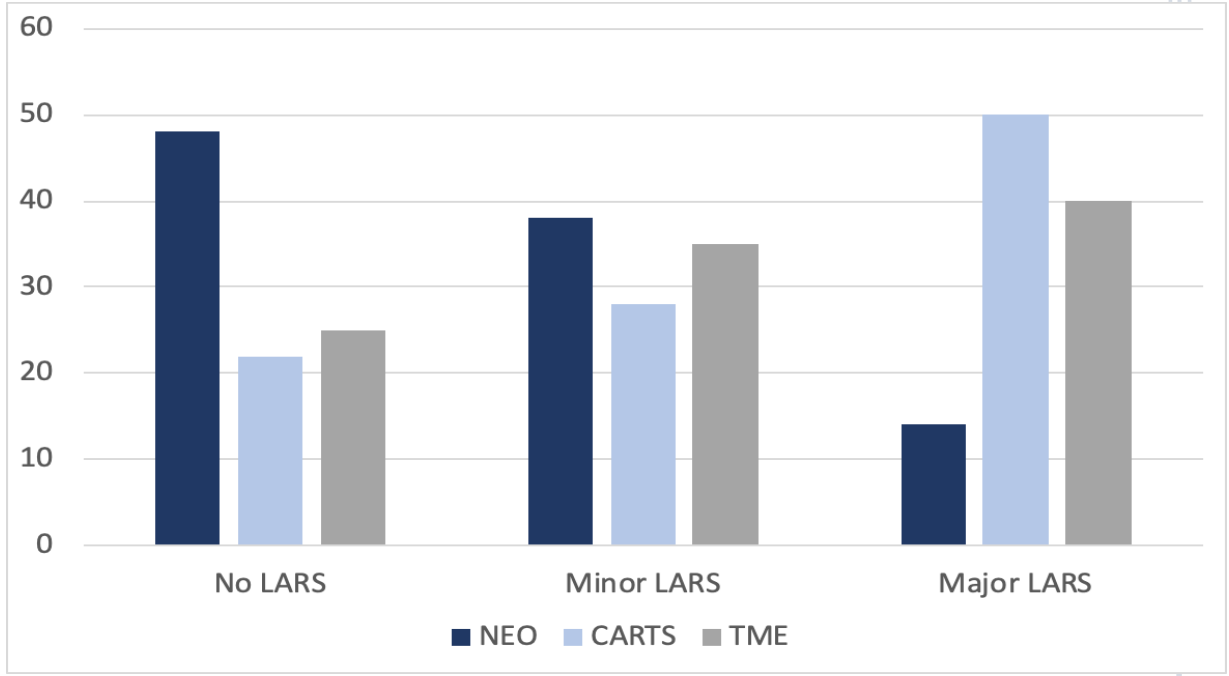
Oncologic Outcomes – Min 3 Years Postop





Functional Outcome 1 year Postop





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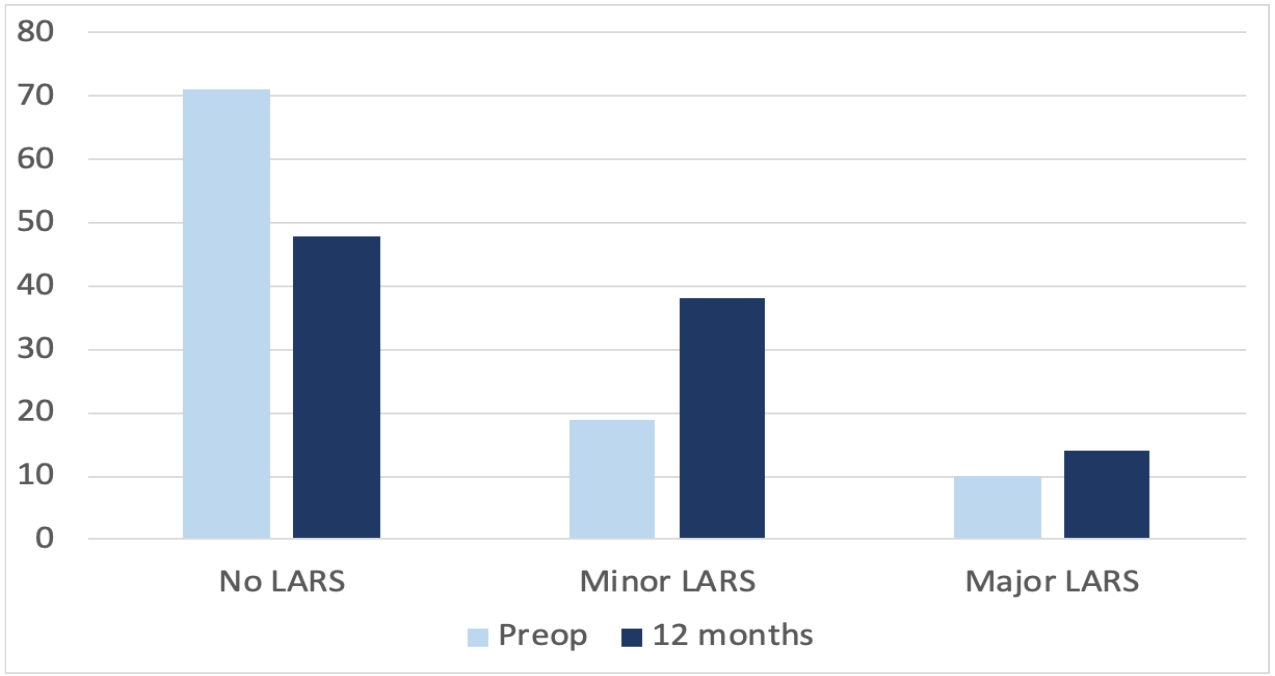
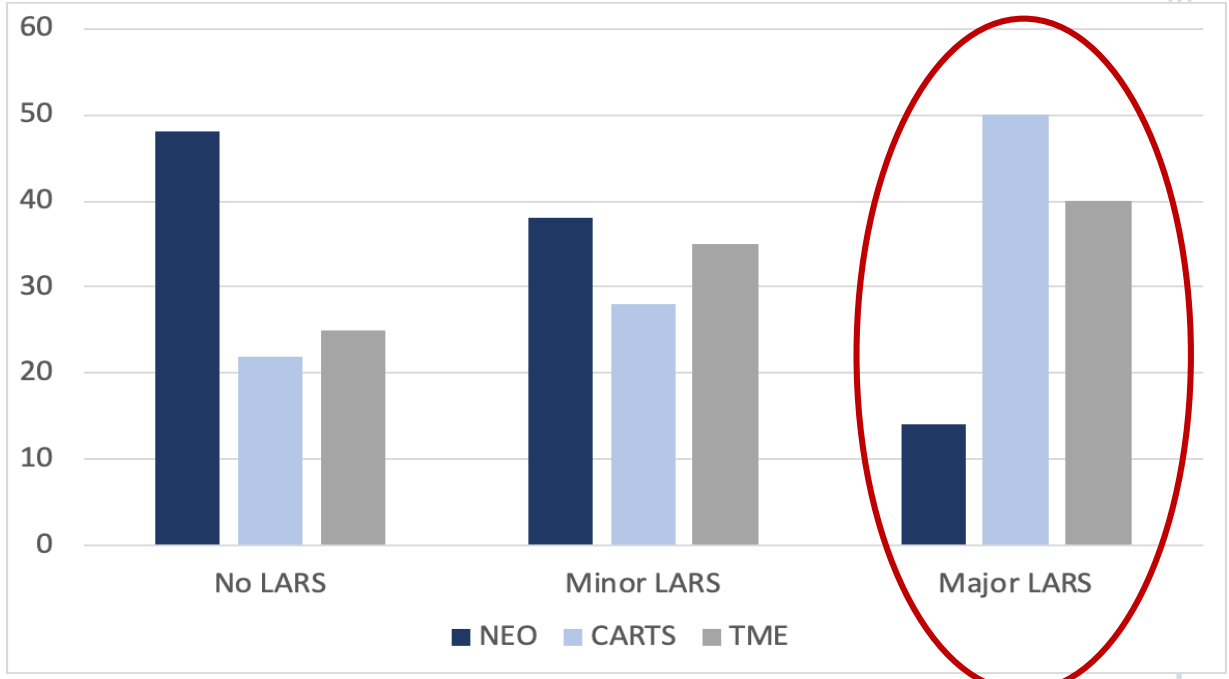
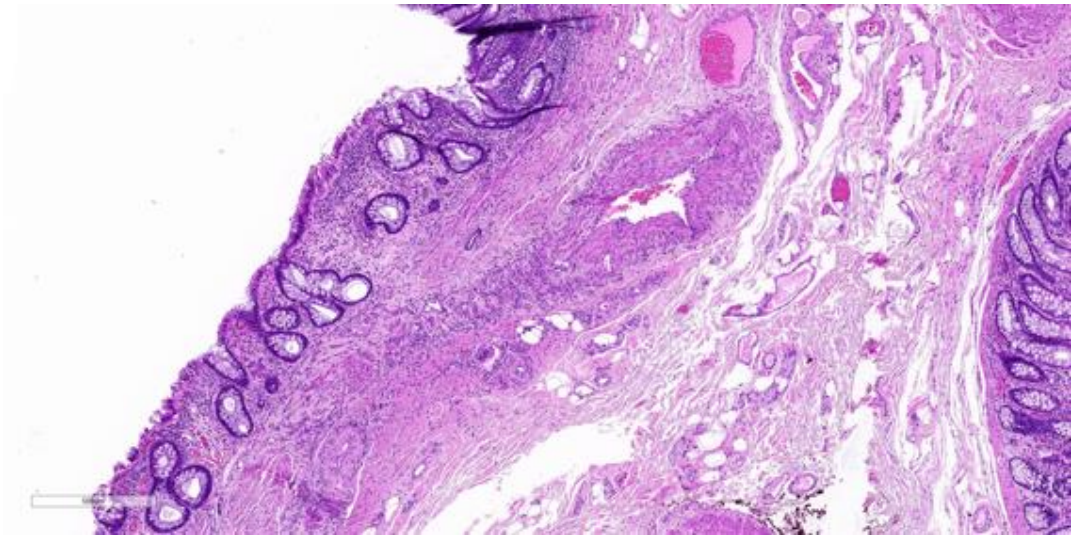
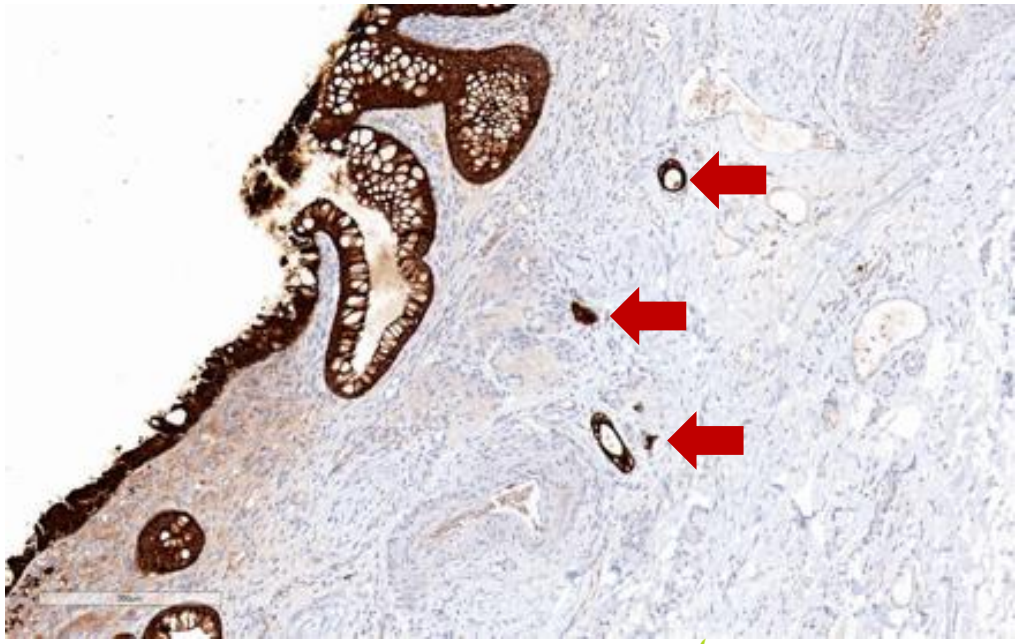


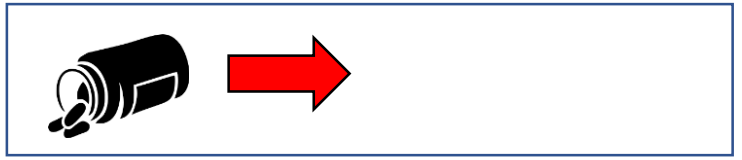


Residual Disease?

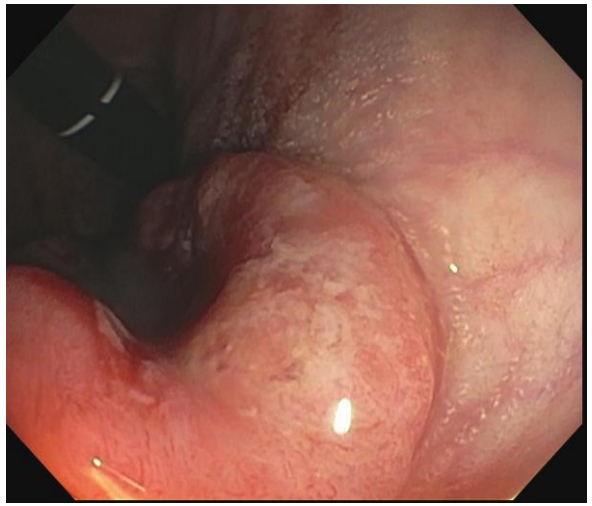




Tumour Sensitivity – Chemo vs RT



- 65 yo woman diagnosed early rectal CA
  - Small lesion in distal rectum
  - Biopsy confirmed adenoCA



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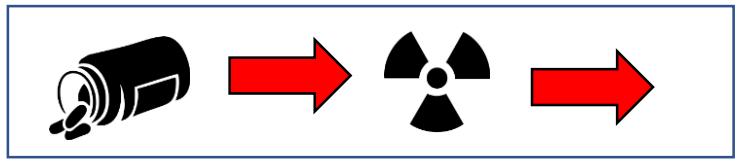

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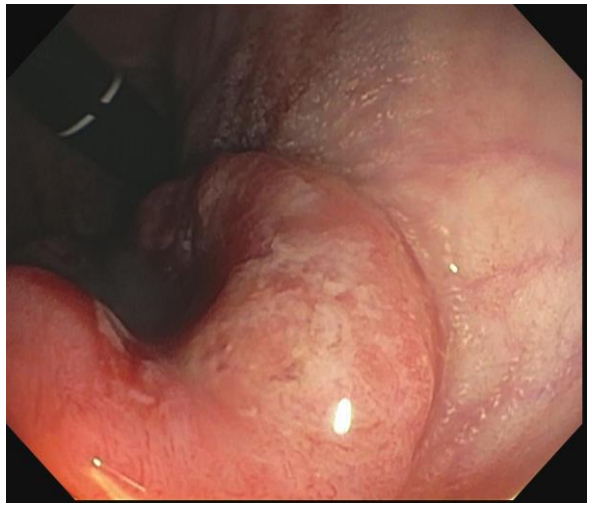
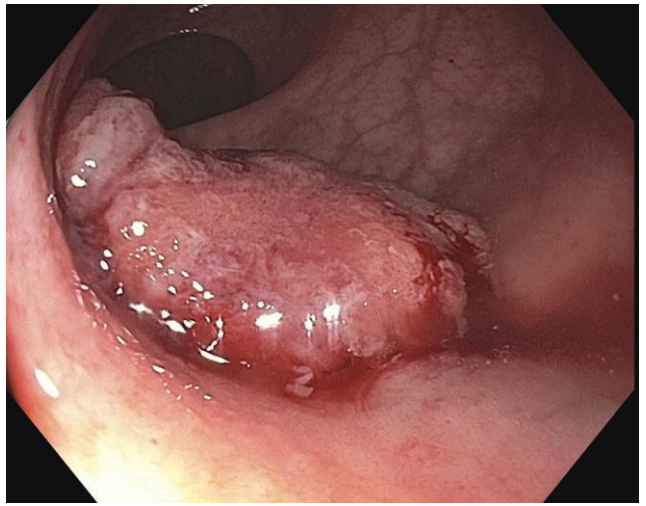


4 cycles
CAPOX

NEO Trial



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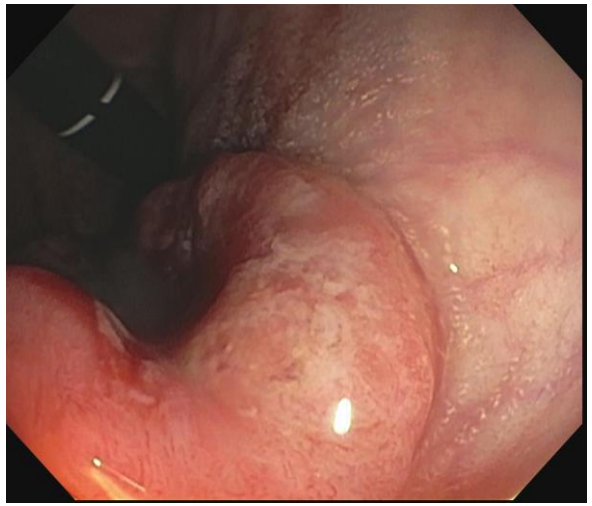

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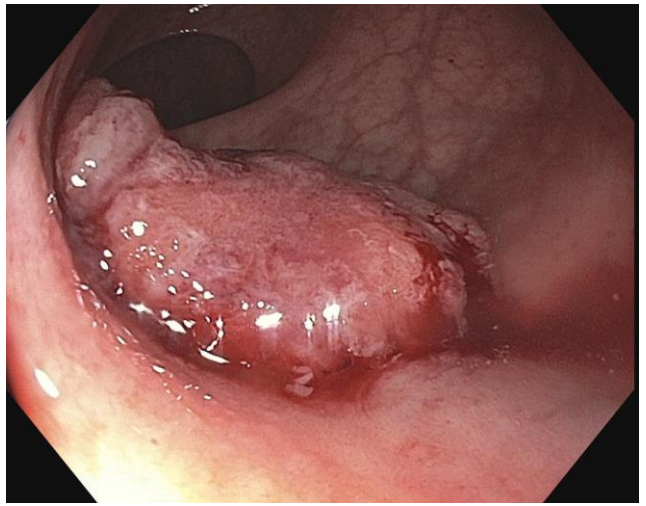
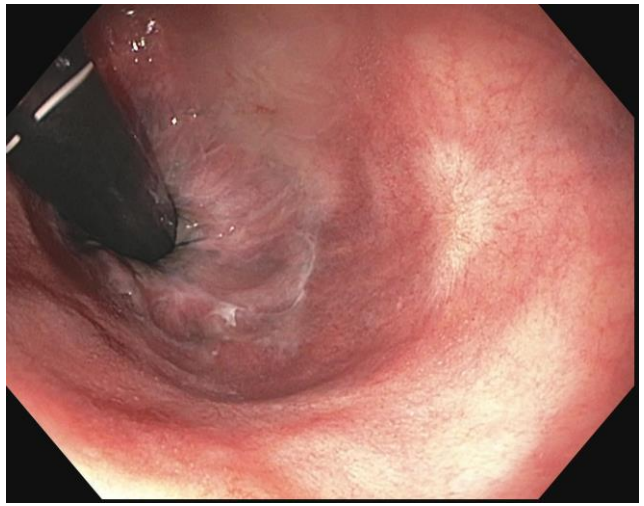


Long Course
CRT



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CCTG CO 32, NEO-RT:

Randomized Non-Inferiority Trial of Neoadjuvant chemotherapy, Excision and Observation vs chemoRT and Excision for Early Rectal Cancer.

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Co-PI

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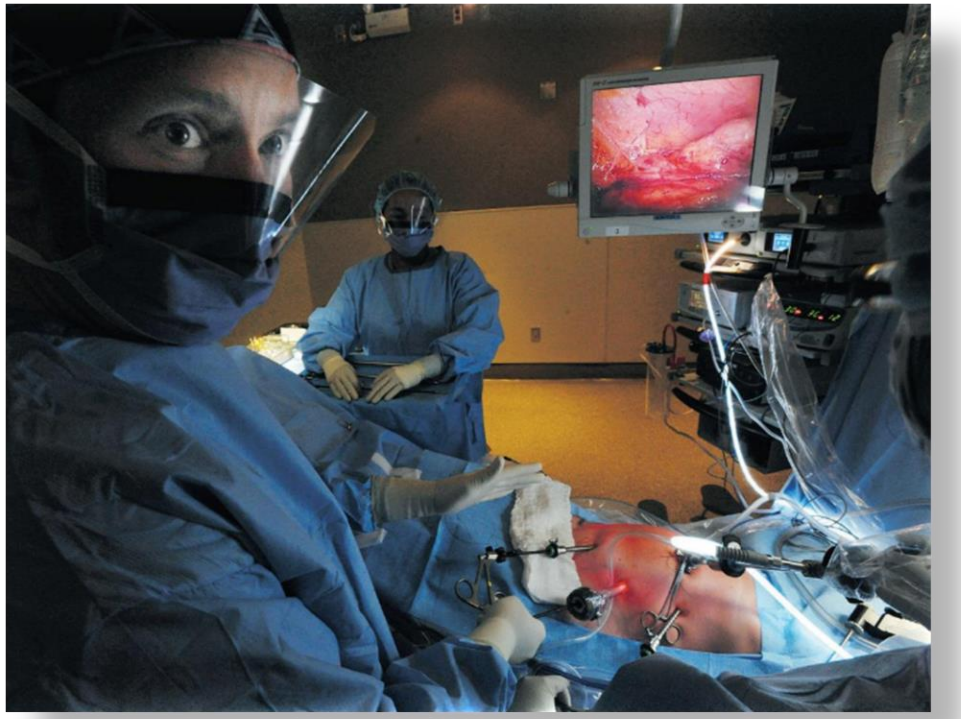
Hagen Kennecke, Providence Cancer Institute, Portland, OR

Study Champions

- Stacy Cohen MD, Medical Oncology, Fred Hutchinson Cancer Center
- Noam Vanderwalde MD, Radiation Oncology, West Cancer Center
- Chris Cann MD, Medical Oncology, Fox Chase Cancer Center
- Steve Nurkin MD, Colorectal Surgery, Roswell Park

Summary

- Early rectal cancer treatment in 2024 is complex
- Options for T1-3_{ab}N0 cancer include:
  - MIS TME
  - Neoadj CRT + TES
  - Neoadj chemo + TES
  - Watch and Wait?
- Optimal treatment includes multidisciplinary conference
- Intensive surveillance critical in organ preservation strategies



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