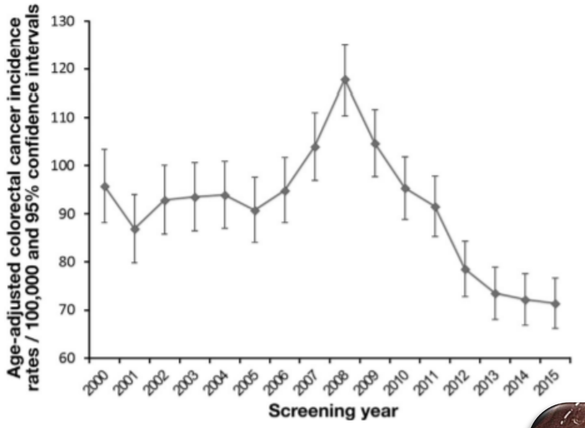
WEO

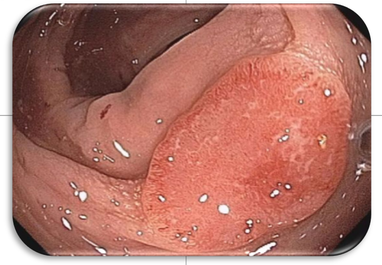
The voice of world endoscopy

Surveillance after endoscopic excision of pT1 malignant polyp. Is that different?

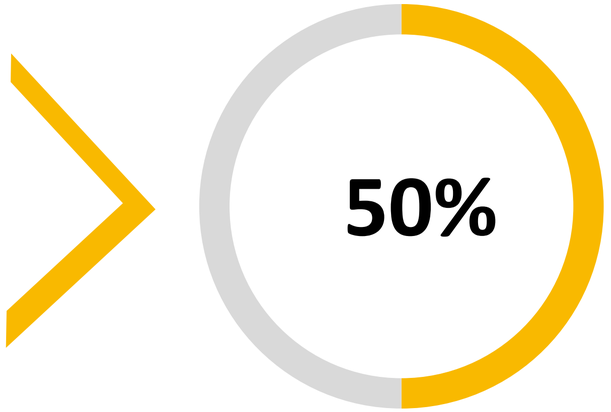
R. Jover/M.Pellisé

Early colorectal cancer





90% can have a complete endoscopic treatment

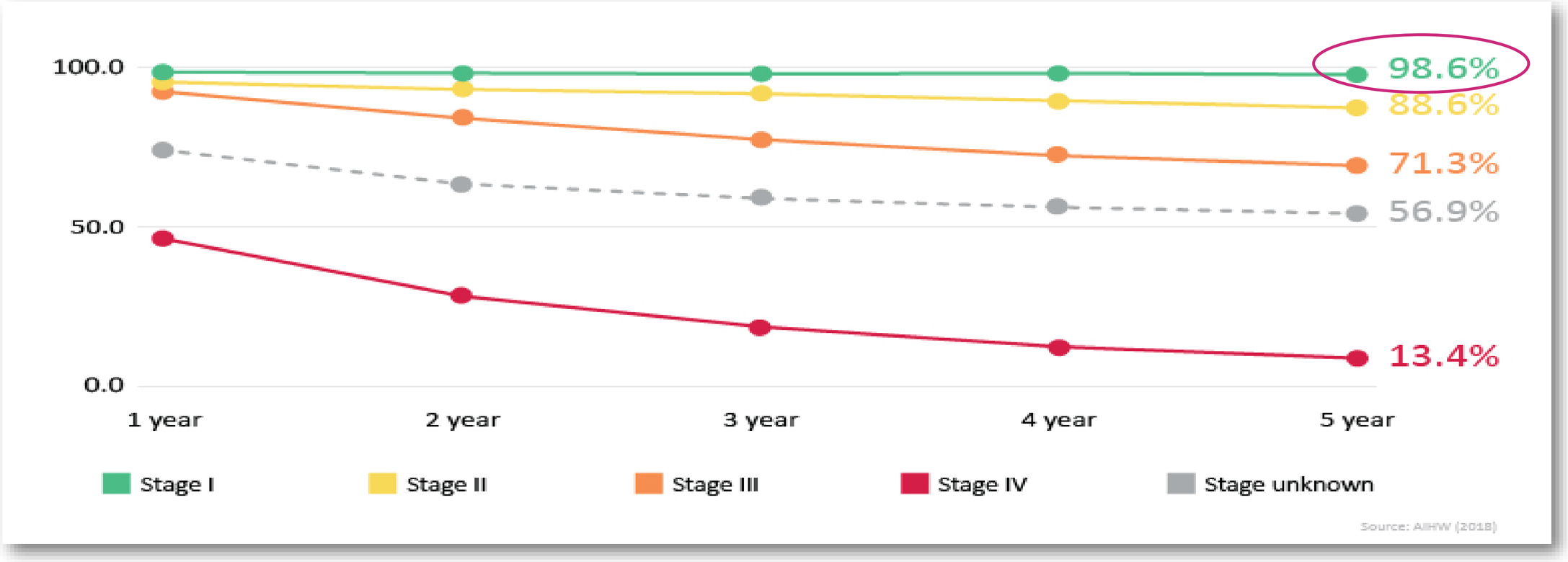


SURGICAL TREATMENT

Theodore R. Levin et al Gastroenterology 2018
Toes Zoutendijk et al. Gut 2017

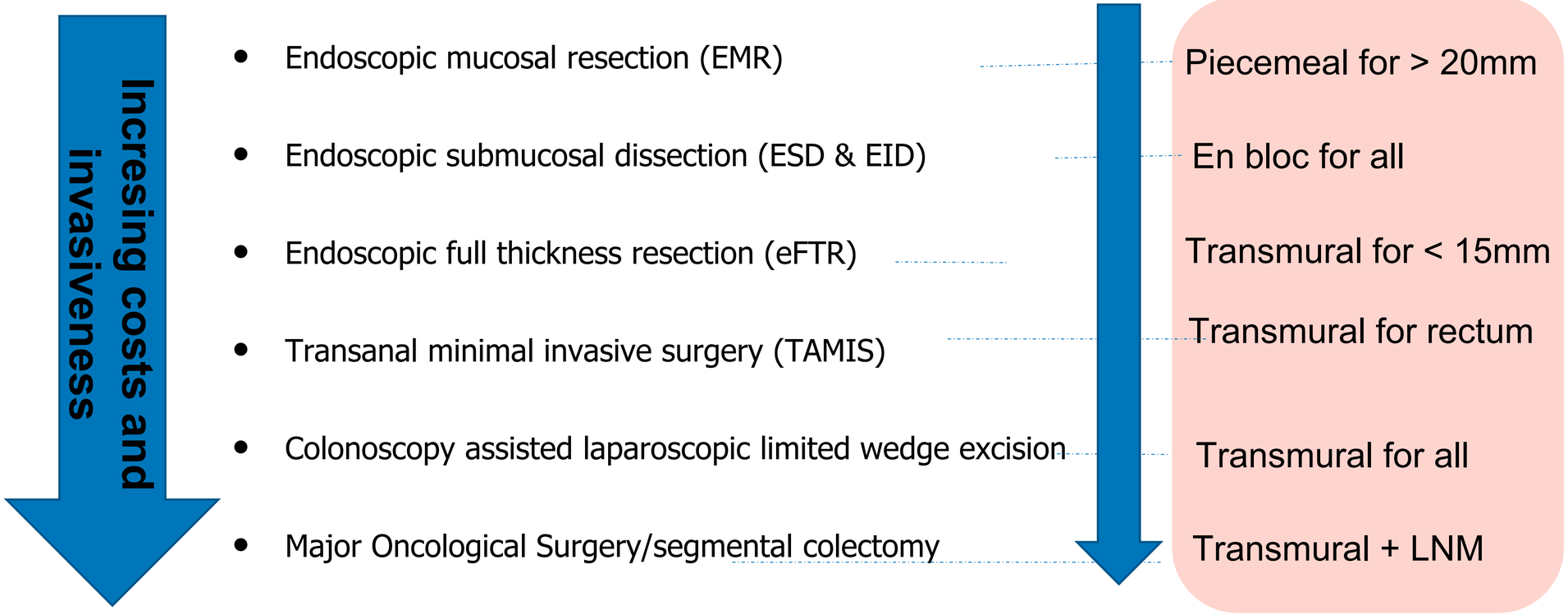
1. Is that different?

Disease free Survival in relation with staging



2. Is that different?

So many different options for resection

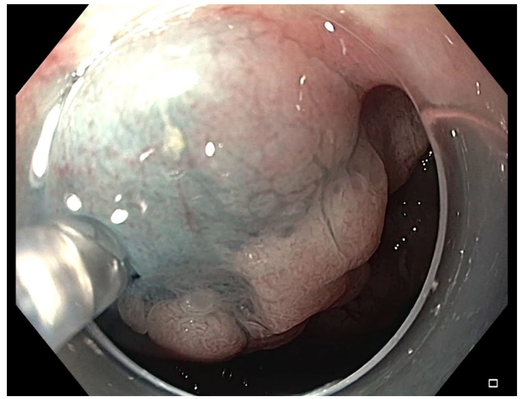


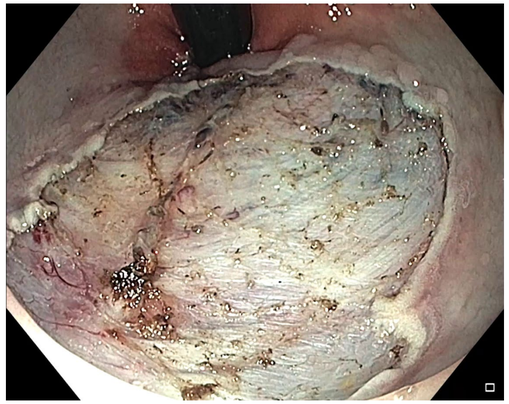
Local treatment CURATIVE if:

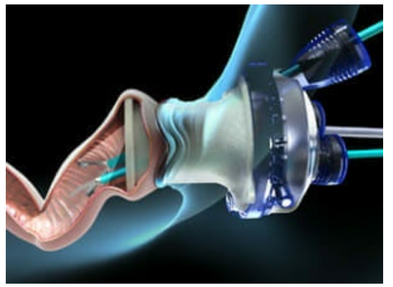
1. **Radicality → *en bloc* R0 resection**

2. **Absence of high risk features:**

- ✓ Poor tumor-differentiation
- ✓ Lymphovascular invasion
- ✓ Intense tumor budding (grade 2-3)
- ✓ *Deep submucosal invasion*







Risk factors of LNM according to international guidelines

	Linfovascular Invasion	Degree of differentiation	Submucosal invasion	Resection Margin	Tumoral Budding
JSCCR 2019	**Yes**	**Poorly differentiated, signet-ring or mucinous adenocarcinoma**	**>1000 µm (T1b)**	**Yes: Positive vertical margin****	**Budding grade 2/3**
NCCN 2021	**Yes**	**Poorly differentiated**	**Not described**	**Yes: Positive Type unspecified*****	**Suggested**
ESMO 2020	**Yes**	**Poorly differentiated**	**Haggit 4 (pedunculated) No clear recommendation in sessile and flat lesions**	**No risk***	**Budding grade 2/3**
ESGE-ESDO 2019	**Yes**	**Poorly differentiated**	**≥ 1000 µm Haggit 4 in pedunculated SM2-3 non pedunculated**	**Yes Positive margin (<1mm) or cannot be assesed**	**Intense tumor budding (unspecified grade)**
ASGE 2020	**Yes**	**Poorly differentiated**	**>1000 µm in non pedunculated No risk in pedunculated**	**Yes: - Positive margin in non pedunculated - <1mm in pedunculated**	**Yes: - Unspecified grade - Only in non pedunculated**

**Positive resection margin (<1mm) is considerer only a risk for local recurrence in ESMO guideline. It is recommended management by excision repetition or local surveillance*

*** Positive vertical margin is defined as carcinoma exposed at the submucosal margin of the resected specimen by JSCCR guideline*

****NCCN guidelines provides multiple definitions for a positive margin of resection, without leaning to a specific definition*

Recurrence and cancer-specific mortality after endoscopic resection meta-analysis

Endoscopically resected without complementary surgery and with ≥12 months of follow-up

Low risk:

7 studies, 650 patients

Recurrence: 1.2% (0.6-2.5%)

Cancer-specific mortality: 0.6% (0.2-1.7%)

High risk:

5 studies, 571 patients

Recurrence: 9.5% (6.7-13.3%)

Cancer-specific mortality: 3.8% (2.4-5.4%)

Antonelli G et al. GIE 2019

Low risk:

36 studies, 1499 patients

Recurrence: 0.7% (0.4-1.2%)

Cancer-specific mortality: 0.1% (0.0-0.7%)

Recurrence: 10 patients; 6 intraluminal/4 distant (2 misclassified as low risk)

High risk:

28 studies, 1023 patients

Recurrence: 7.0% (4.9%-9.9%)

Cancer-specific mortality: 4.5% (3.2-6.3%)

Dang H. Et al CGH 2022

Risk factors for any recurrence

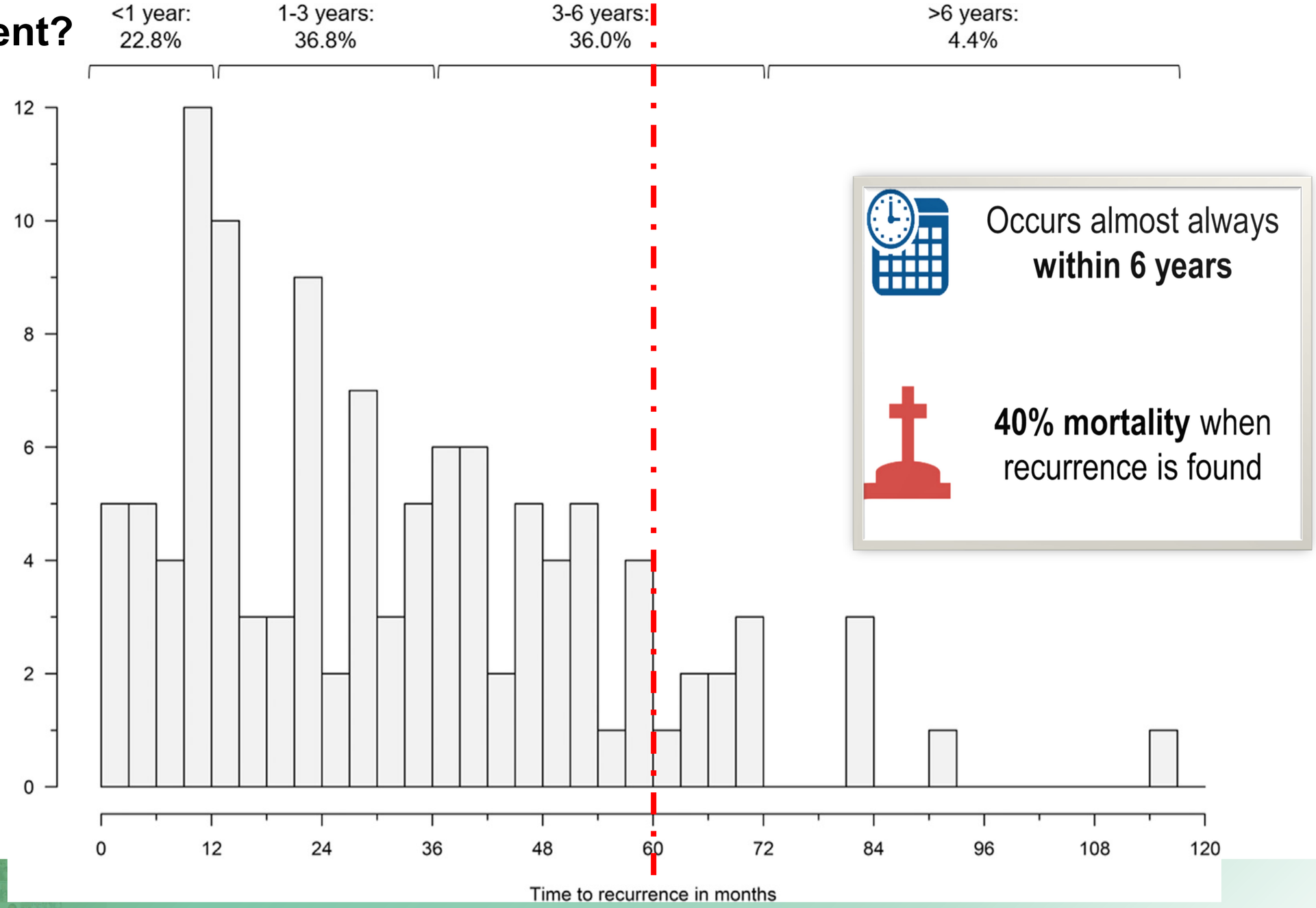
✓ Female
✓ Rectal location
✓ Non-pedunculated
✓ Piecemeal EMR

✓ not-Ro; Bd2-3; LVI; Grade3; Deep invasion

	Pooled estimates of any CRC recurrence, % (95% CI; number of studies included in subgroup analyses) Lower risk ——————————————————> Higher risk	
Patient characteristics		
Gender	Males: 1.6 (0.4–6.3; 6 studies)	Females: 4.4 (2.5–7.6; 5 studies)
Tumor characteristics		
Location	Colon: 0.8 (0.2–2.8; 11 studies)	Rectum: 5.7 (2.0–15.2; 11 studies)
Morphology	Ip: 1.0 (0.1–7.2; 9 studies)	Non-Ip: 6.1 (3.5–10.5; 13 studies)
Endoscopic resection		
En bloc vs piecemeal	En bloc: 1.0 (0.4–2.1; 11 studies)	Piecemeal: 4.8 (2.3–9.7; 5 studies)
Endoscopic resection technique used	ESD: 1.8 (0.7–4.1; 12 studies)	EMR: 4.5 (1.6–11.6; 8 studies)
	Snaring: 2.7 (1.9–3.9; 21 studies) eFTR: 2.7 (0.7–10.0; 2 studies)	
Histology		
Overall risk status (not stratified on number of JSCCR criteria used)	Low-risk T1 CRC: 0.7 (0.4–1.2; 36 studies)	High-risk T1 CRC: 7.0 (4.9–9.9; 28 studies)
Margin status	R0: 1.2 (0.4–3.5; 26 studies)	Not-R0: 11.2 (4.9–23.4; 10 studies)
Tumor budding grade	Bd1: 2.6 (1.1–6.0; 7 studies)	≥Bd2: 7.3 (2.8–17.8; 3 studies)
Lymphovascular invasion	Absent: 1.4 (0.7–3.0; 25 studies)	Present: 4.2 (0.6–24.6; 8 studies)
Differentiation grade	Grade 1-2: 2.3 (1.4–3.7; 28 studies)	Grade 3: 19.8 (7.9–41.3; 4 studies)
Invasion depth	Superficial: 1.2 (0.5–3.1; 20 studies)	Deep: 8.5 (5.7–12.5; 11 studies)

Dang H. Et al CGH 2022

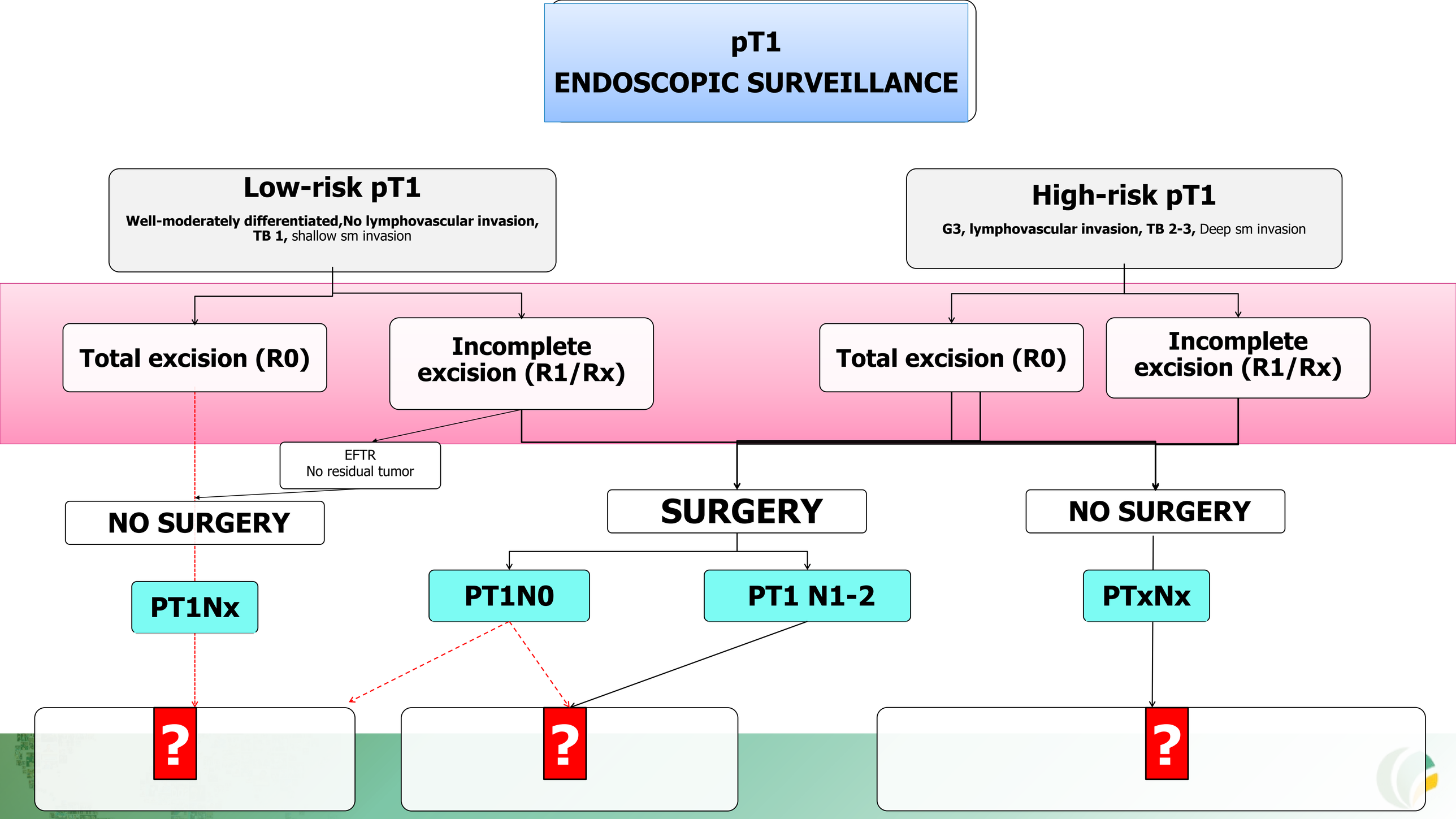
3. Is that different?



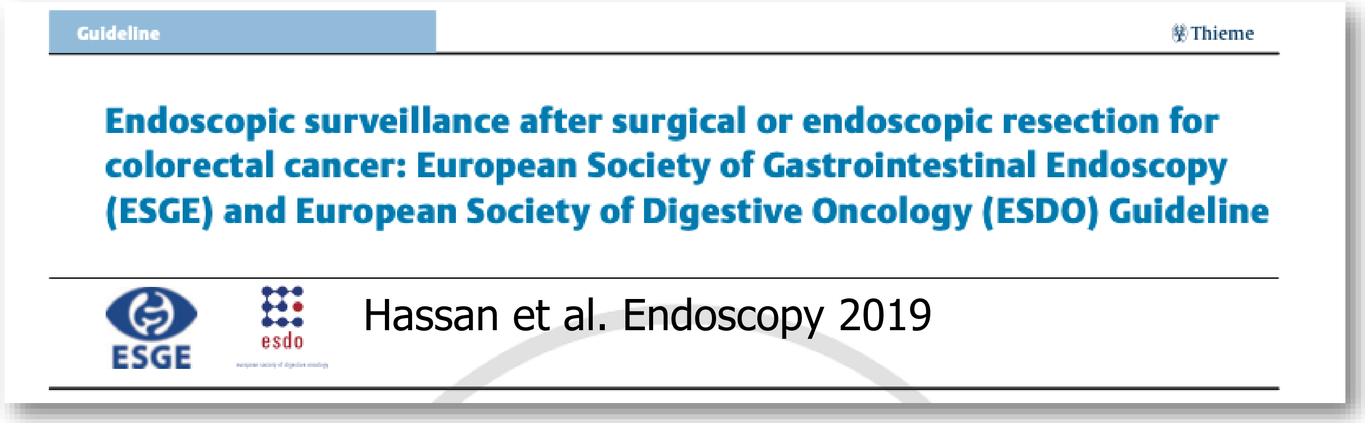
Dang H. Et al CGH 2022

Surveillance of pT1 polyps

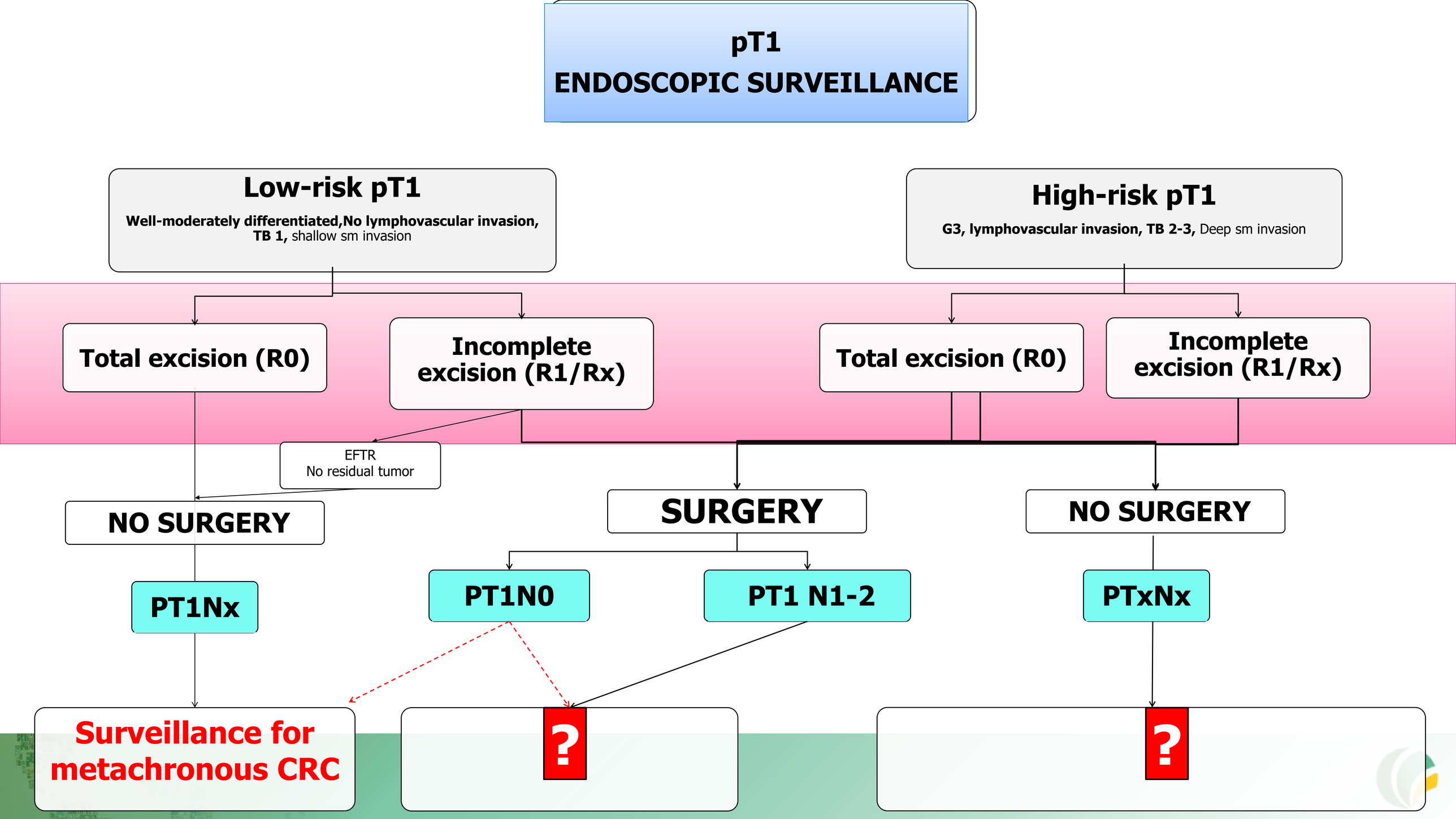
- **No RCT published** (ongoing: LOCAL trial in Netherlands; EPOS IV)
- **No study specifically directed to address surveillance**
- **Indirect data that addresses prognosis of pT1**
  - ✓ **Heterogeneity and deficiencies in reporting histology**
  - ✓ **Heterogeneity and deficiencies in reporting endoscopic data**
  - ✓ **Surgical series**
- **Different definitions for Risk**
- **Only specific subgroup analysis**
- **Different outcomes measures**
  - ✓ **None uses luminal recurrence as an specific end-point**


pT1
ENDOSCOPIC SURVEILLANCE
Low-risk pT1
Well-moderately differentiated,No lymphovascular invasion, TB 1, shallow sm invasion
High-risk pT1
G3, lymphovascular invasion, TB 2-3, Deep sm invasion
Total excision (R0)
Incomplete excision (R1/Rx)
Total excision (R0)
Incomplete excision (R1/Rx)
EFTR
No residual tumor
NO SURGERY
SURGERY
NO SURGERY
PT1Nx
PT1N0
PT1 N1-2
PTxNx
?
?
?

Surveillance T1Nx/0 Low-Risk



In patients with a low-risk pT1 CRC treated by endoscopy with an R0 resection, we suggest the same surveillance schedule as for any CRC. (Weak recommendation, Low quality of evidence)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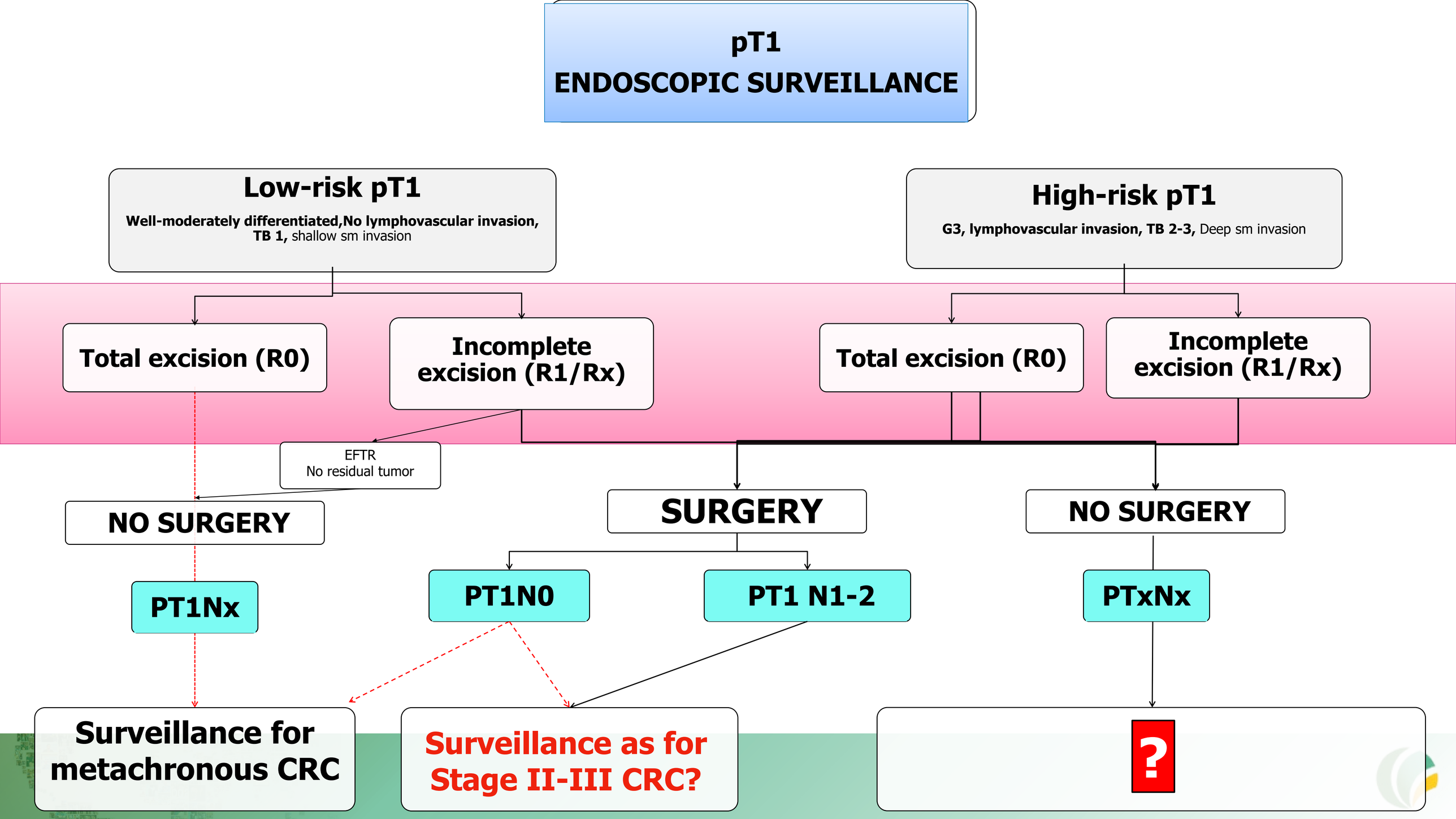
NO SURGERY
SURGERY
NO SURGERY
PT1Nx
PT1N0
PT1 N1-2
PTxNx
Surveillance for metachronous CRC
?
?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EFTR
No residual tumor
NO SURGERY
SURGERY
NO SURGERY
PT1Nx
PT1N0
PT1 N1-2
PTxNx
Surveillance for metachronous CRC
Surveillance as for Stage II-III CRC?
?

Surveillance after resection of local CRC Stage II and III

80% of relapses
occur during the first 3 years and an additional 15% between the 3rd and 5th year

metachronous primary cancer with an incidence of 0.7-1.7% within the first 2 years

ESMO 2020

		3	6	9	12	15	18	21	24	27	30	33	36	42	48	54	60
	CEA	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Colonoscopy				x								x				
High risk	Abdominal/chest CT scan		(x)		x		(x)		x		(x)		x				

ASCO/NCCN/ASCRS/UK

Table 3 Published Colorectal Cancer Surveillance Guidelines

	History and Physical	CT (Chest/Abdomen/Pelvis)	CEA	Colonoscopy
ASCO (stage II/III)	Every 3–6 mos × 3 yrs; every 6 mos at years 4 and 5	Annually × 3 yrs if high risk	Every 3 mos for at least 3 yrs	At 3 yrs and then every 5 yrs thereafter
NCCN (stage I–III)	Every 3–6 mos × 2 yrs; every 6 mos in years 3–5	Annually for up to 5 yrs, especially if high risk	Every 3–6 mos × 2 yrs; every 6 mos in yrs 3–5	At years 1 and 4, then every 5 yrs
ASCRS (stage I–III)	At least every 4 mos for 2 yrs	None	At least every 4 mos for 2 yrs	Every 3 yrs
UK (stage I–III)	None	CT of abdomen and pelvis only, once within 2 yrs	None	Every 5 yrs

ASCO = American Society of Clinical Oncology; ASCRS = American Society of Colon and Rectal Cancer Surgeons; CEA = carcinoembryonic antigen; NCCN = National Comprehensive Cancer Network; UK = United Kingdom 2010 guidelines.

Clinic Hospital

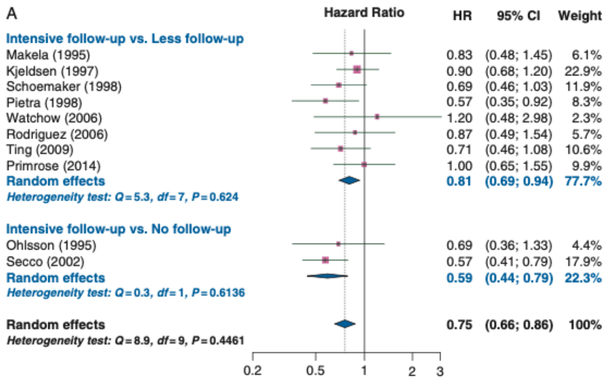
	3 m	6 m	9 m	12m	15m	18m	21m	24m	30m	36m	42m	48m	54m	60m
Physical exam & symptoms	X	X	x	x	x	x	x	x	x	x	x	x	x	x
CEA	X	X	x	x	x	x	x	x	x	x	x	x	x	x
CT chest & abd				x						x				x
Colonoscopy				x								x		

Intensive follow-up strategies improve outcomes in nonmetastatic colorectal cancer patients after curative surgery: a systematic review and meta-analysis

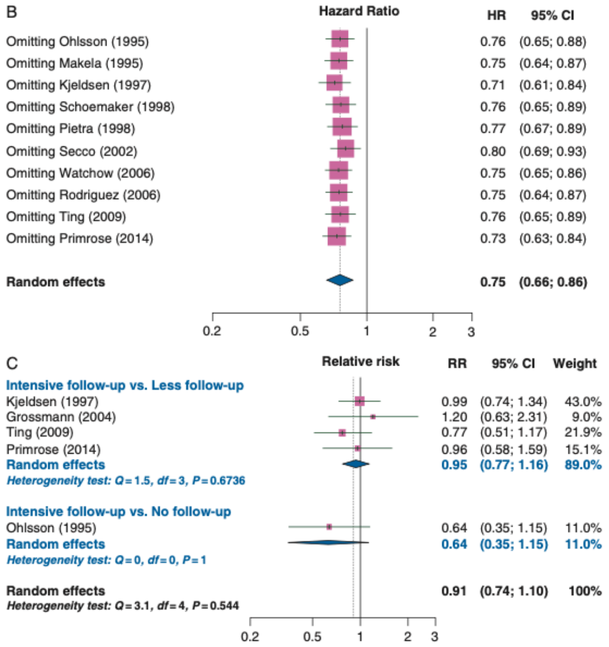
S. Pita-Fernández[1,2*], M. Alhayek-Aí[1], C. González-Martín[2], B. López-Calviño[1,2], T. Seoane-Pillado[1,2] & S. Pértega-Díaz[1,2]

Annals of oncology 2015

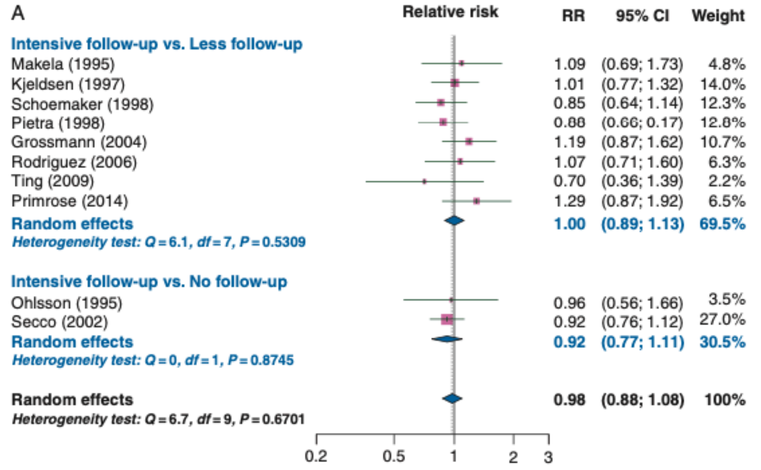
Overall survival rate after curative resection of colorectal cancer



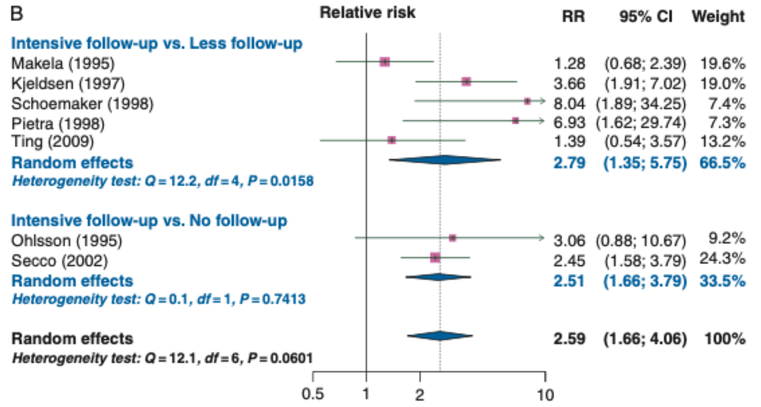
Cancer-specific survival



Detection of total recurrences after curative resection of colorectal cancer



Detection of asymptomatic recurrences after curative resection of colorectal cancer



More intensive follow-up =

+ overall survival rate
+ probability of detecting asymptomatic recurrences
+ curative surgery attempted at recurrences
- shorter recurrence detection time

Not associated with a greater detection of total recurrences, or **a decrease in mortality related to disease**, even though there is a trend toward a protective effect

Effect of More vs Less Frequent Follow-up Testing on Overall and Colorectal Cancer–Specific Mortality in Patients With Stage II or III Colorectal Cancer: The COLOFOL Randomized Clinical Trial

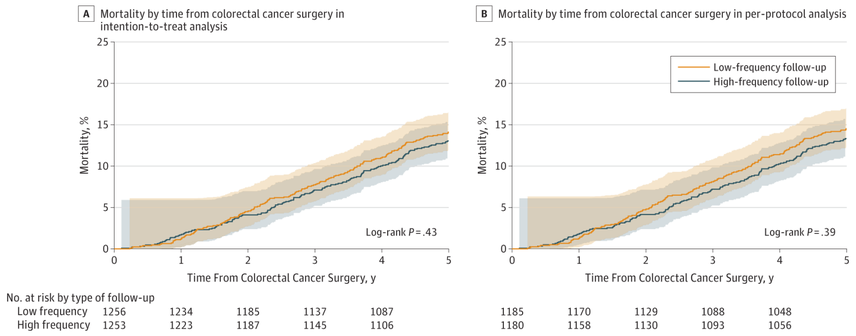
JAMA. 2018;319(20):2095-2103. doi:10.1001/jama.2018.5623

2006 -2010
2555 CRC Stage II and III

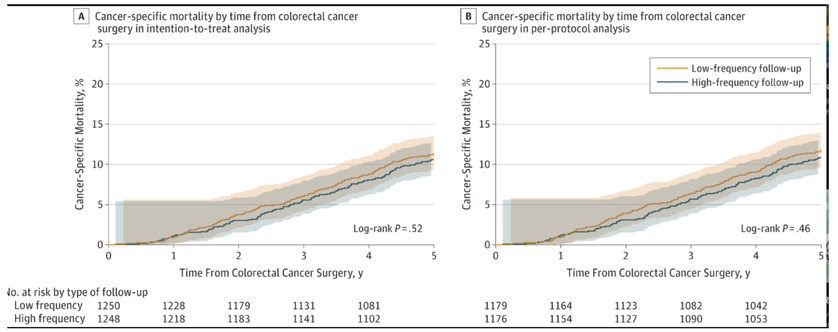
Randomised 1:1

High-frequency group: multislice contrast-enhanced CT of the thorax and abdomen and CEA at: 6, 12, 18, 24, and 36 months after surgery.

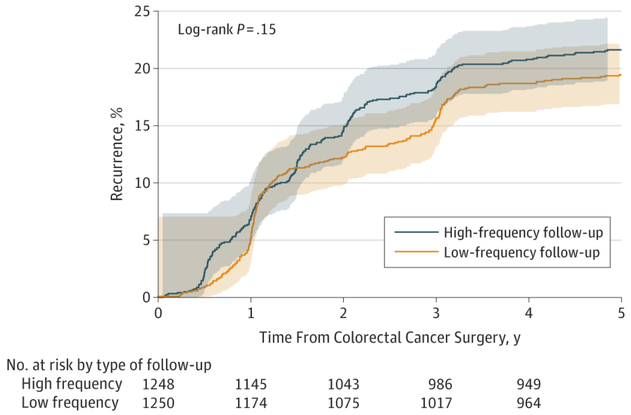
Low-frequency group: multislice contrast-enhanced CT of the thorax and abdomen and CEA at: 12 and 36 months after surgery.



Overall Mortality by Time From Colorectal Cancer Surgery



Cancer specific Mortality by Time From Colorectal Cancer Surgery



Secondary Outcome of Colorectal Cancer–Specific Recurrence

No significant rate reduction in 5-year overall mortality or colorectal cancer–specific mortality

Colorectal cancer–specific recurrence was detected earlier, but this did not translate into a reduced mortality rate.

Date of download: 10/2/2022
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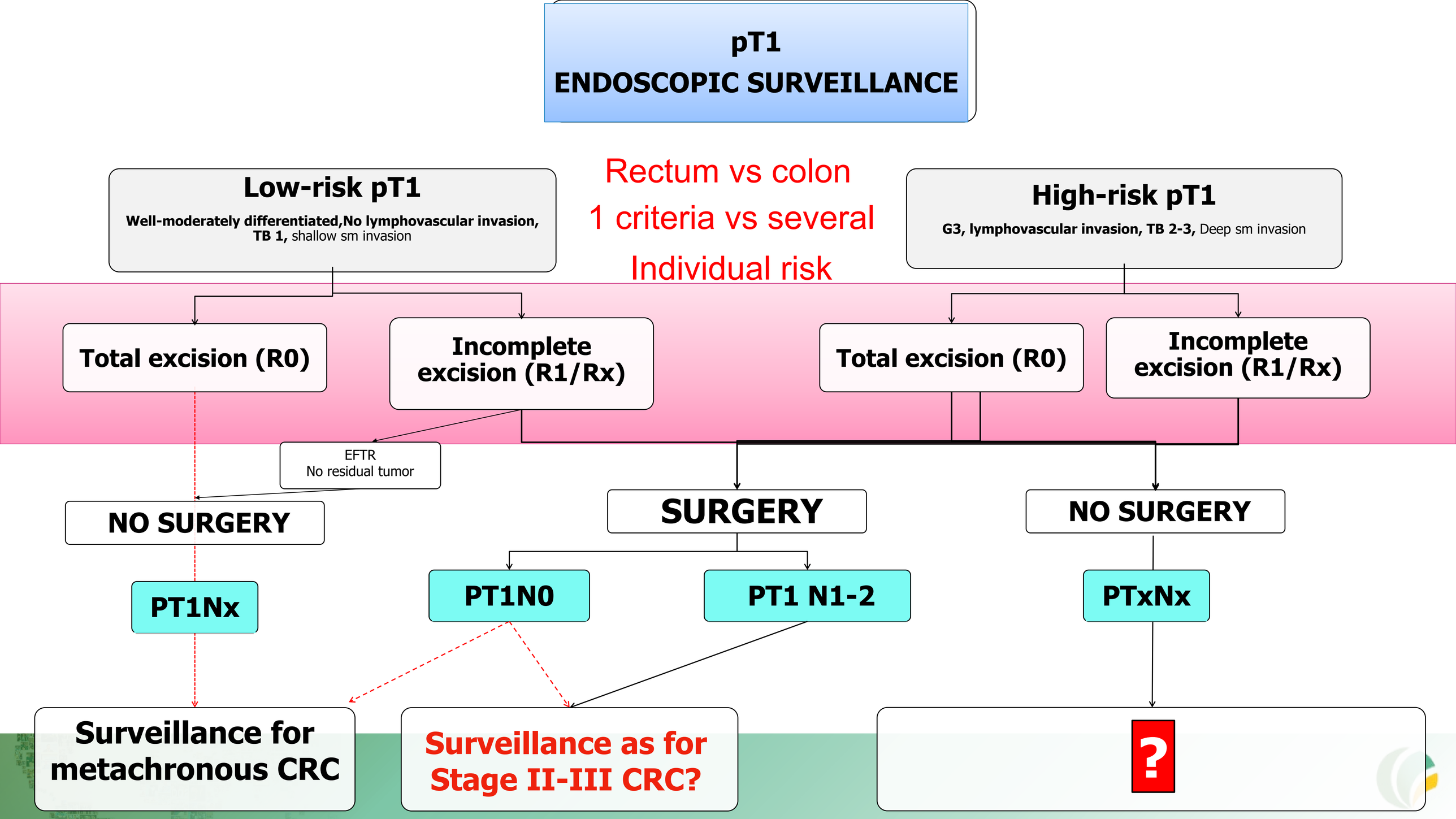
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Rectum vs colon
1 criteria vs several
Individual risk
High-risk pT1
G3, lymphovascular invasion, TB 2-3, Deep sm invasion
Total excision (R0)
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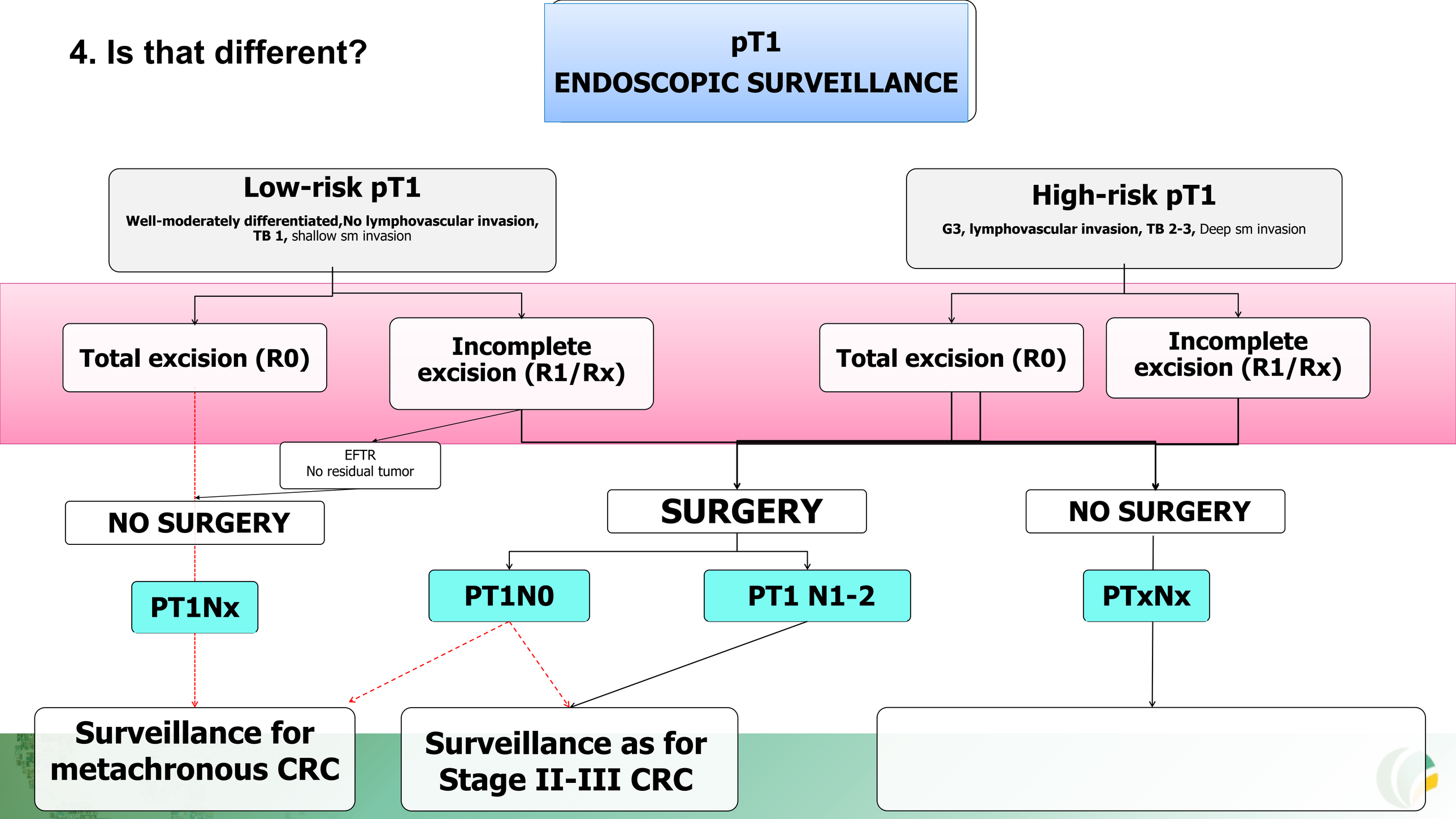

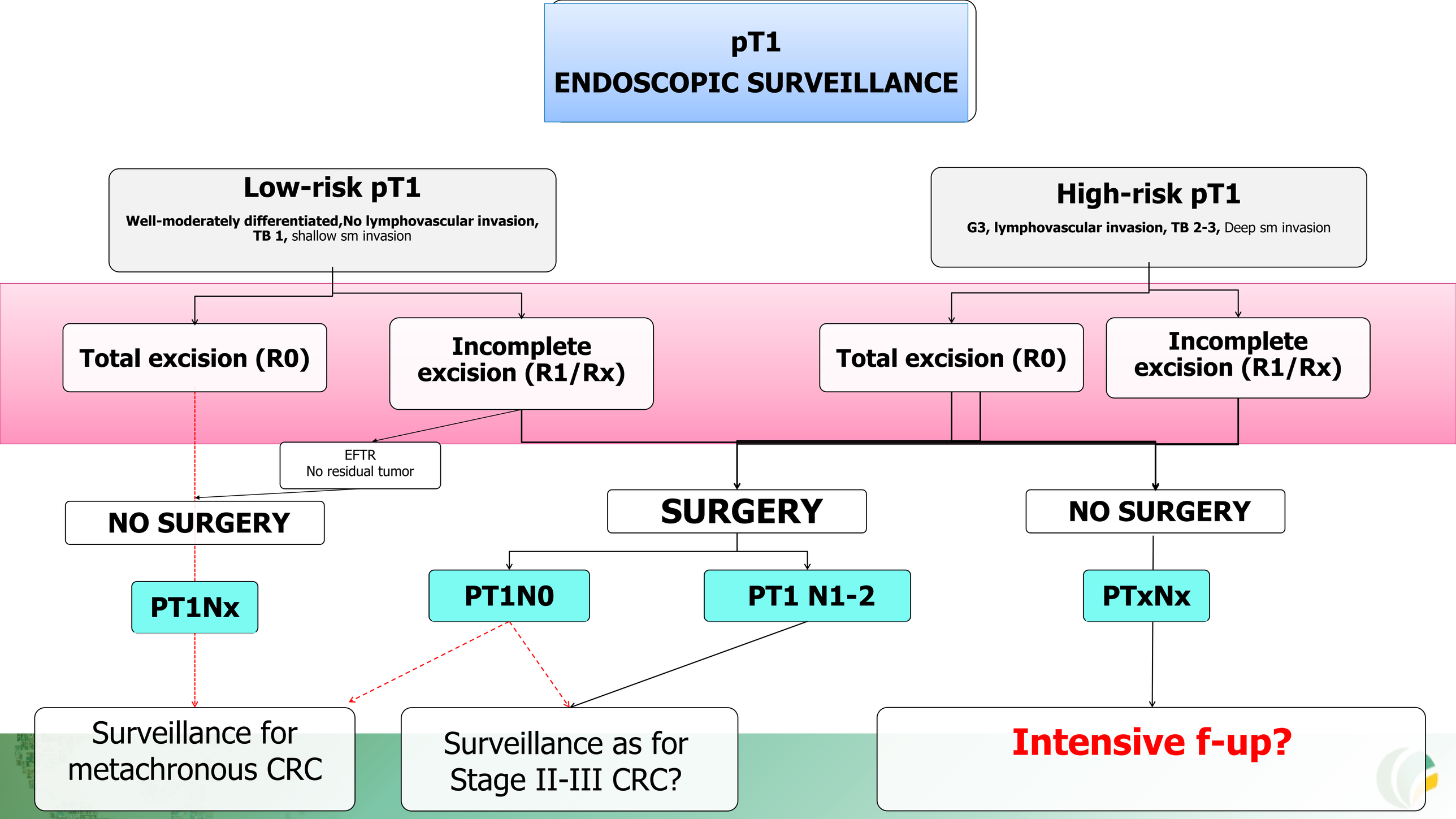
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PT1 N1-2
PTxNx
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Surveillance as for Stage II-III CRC?
Intensive f-up?

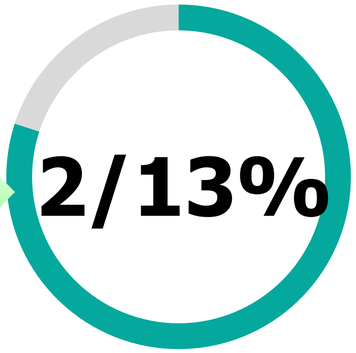
Intensive surveillance after High Risk pT1 that do not undergo surgery

Rectum	6	12	18	24	30	36	42	48	54	60
Scar surveillance	X	X	X	X		X		X		X
MRI rectum	X	X	X	X		X		X		X
CEA	X	X	X	X	X	X	X	X	X	X
Full colonoscopy		X						X		

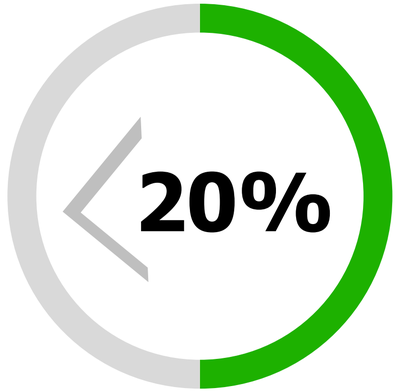
Colon	6	12	18	24	30	36	42	48	54	60
Scar surveillance	X	X		X		X		X		X
CT thorax-abdomen		X		X		X		X		X
CEA	X	X	X	X	X	X	X	X	X	X
Full colonoscopy		X						X		

Dutch pT1CRC Working group

With current clinicopathological criteria: 38-77% of T1 CRC patients are classified as high-risk:



have LNM



have residual tumor

80%

Overtreatment

Over surveillance

Intermediate Risk group

Overwater A. Gut 2018; Ozawa T. Gastroenterology 2018; Richards CH. Gut 2018; Backes Y. Gastroenterology 2017

Jen-Hao Yeh et al. Clin Gastroenterol Hepatol

EpiT1 Consortium

Pais Vasco
Basurto
Cruces
Urduliz
HU Donostia
HU Araba
Goierri-Alto Urola

Madrid
H. Puerta de Hierro
H. Mostoles
H. 12 de Octubre
H. Ramon y Cajal

Galicia
H. Ourense

Cantabria
H. Marques de Valdecillas

Castilla y Leon
H. S R Aranda Duero
H. Rio Hortega

Aragon
H. Zaragoza

Canarias
H. Tenerife

33 Healthcare Centers

Catalunya
Hospital Clinic
H. Bellvitge
H. Gral de Catalunya
H. Sagrat Cor
Parc Tauli
H. Terrassa
H. Moises Broggi
H. Vall d`Hebron
H. Althaia
H. Granollers
H. Palamos

C. Valenciana
H. Clinico Valencia
IVO
H.Alicante

Murcia
HCU Arrixaca

Andalucia -Sevilla
H. Virgen del Rocio

I. Baleares- Mallorca
H. Inca

Financed by:

Project 201932

Project PI 19/01050

3161 pT1 CRC

RECURRENCE

3.54%

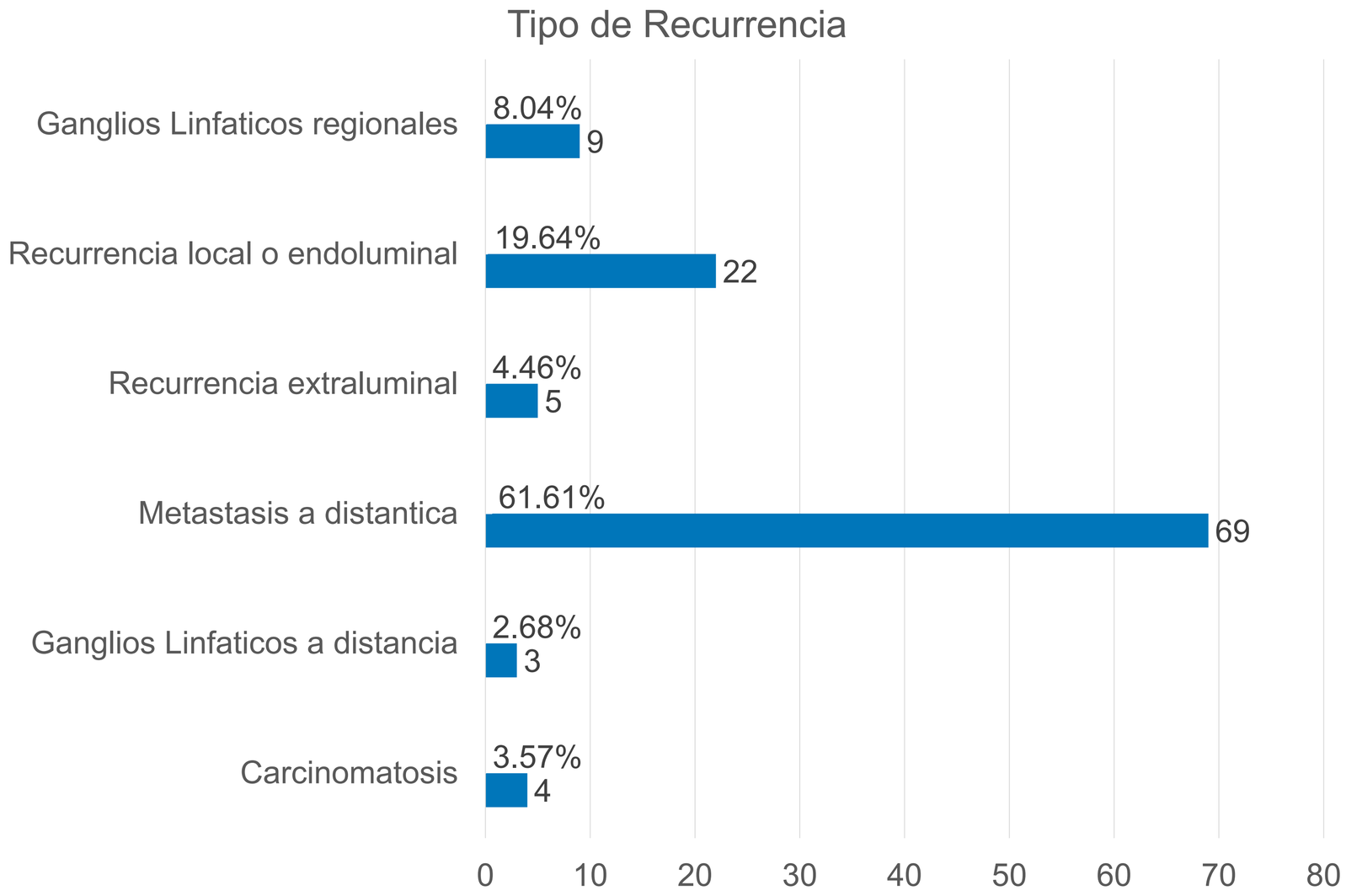
(112/3161)

1.01%

Metachony (32/3161)

0.7%

Endoluminal recurrence
22/ 3161



Summary

Why different?

- ✓Survival 95% irrespective of treatment modality
- ✓Two very different situations: low vs. high risk
- ✓Distant recurrences in 5% of cases, only if high-risk features and with bad prognosis
- ✓Local treatment in 50% of cases at least: wide variability in type of treatment
- ✓High risk criteria can be refined. **OVERTREATMENT**

R0 & good prognosis don‘t need oncological follow-up

Many open questions for the rest

WEO

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