



The Farr Institute  
of Health Informatics  
Research

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21<sup>st</sup> November 2017



# The right outcome measures in organ preservation

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*Manchester BRC*





# CORMAC

CORE OUTCOME RESEARCH MEASURES IN ANAL CANCER



2015-2018  
Rebecca Fish

- First stages: The ‘what’
- Second stages: The ‘how’





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CORE OUTCOME RESEARCH MEASURES IN ANAL CANCER



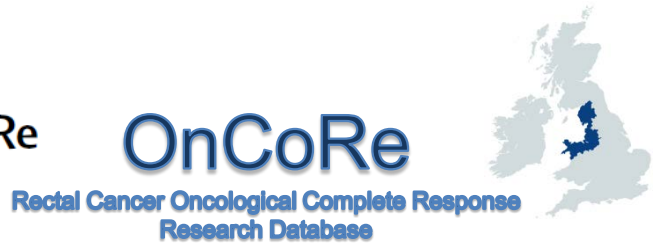
Outcome domains	Absolute numbers	
	Studies	Standardised outcome terms
Survival	78	11
Disease activity	81	7
Life impact	5	6
Delivery of care	11	2*
<b>Toxicity</b>		
Gastrointestinal	72	22
Dermatological	57	6
Haematological	48	6
Musculoskeletal	14	3
Urinary	33	6
Sexual and reproductive	11	6
Constitutional symptoms	12	6
Other toxicities*	35	8
<b>Total</b>	<b>86</b>	<b>83</b>

\*Compliance & patient preference for treatment modality

# Focus on some core outcomes

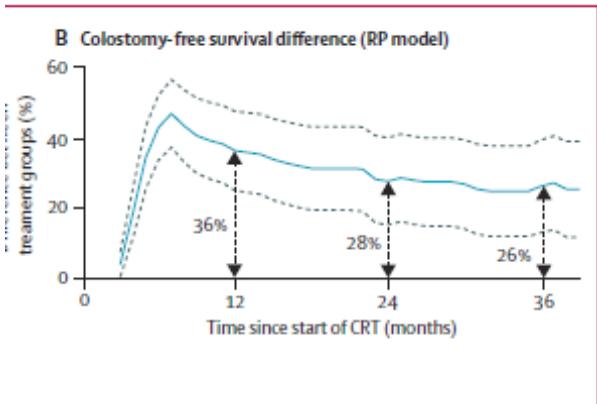
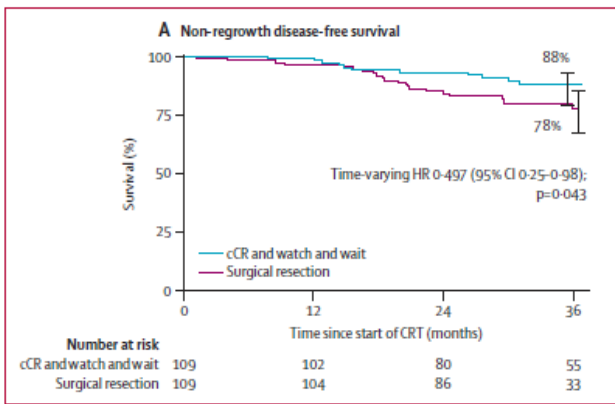
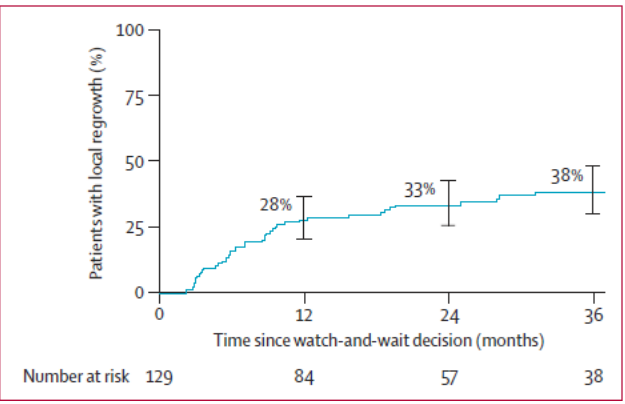
- W&W – subject-specific outcomes
  - local regrowth (actuarial) rate
  - non-regrowth DFS
  - colostomy-free survival
  - distant metastasis rate
- New perspective – composite endpoint

# Watch-and-wait approach versus surgical resection after chemoradiotherapy for patients with rectal cancer (the OnCoRe project): a propensity-score matched cohort analysis



Andrew G Renehan, Lee Malcomson, Richard Emsley, Simon Gollins, Andrew Maw, Arthur Sun Myint, Paul S Rooney, Shabbir Susnerwala, Anthony Blower, Mark P Saunders, Malcolm S Wilson, Nigel Scott, Sarah T O'Dwyer

- In 129 patients from multiple centres (4 regions, UK), third local re-growths
- W&W is oncologically safe
- Approximately a 1/4 patient destined for avoid permanent colostomy



# Local failure definition: local regrowth

- Local re-growth
  - Intra-luminal (majority)
  - Mesorectal (uncommon)
- Drop use of 'local recurrence'

OnCoRe (44/ 129)	
Intra-luminal	42
Mesorectal	2

Consensus Statement

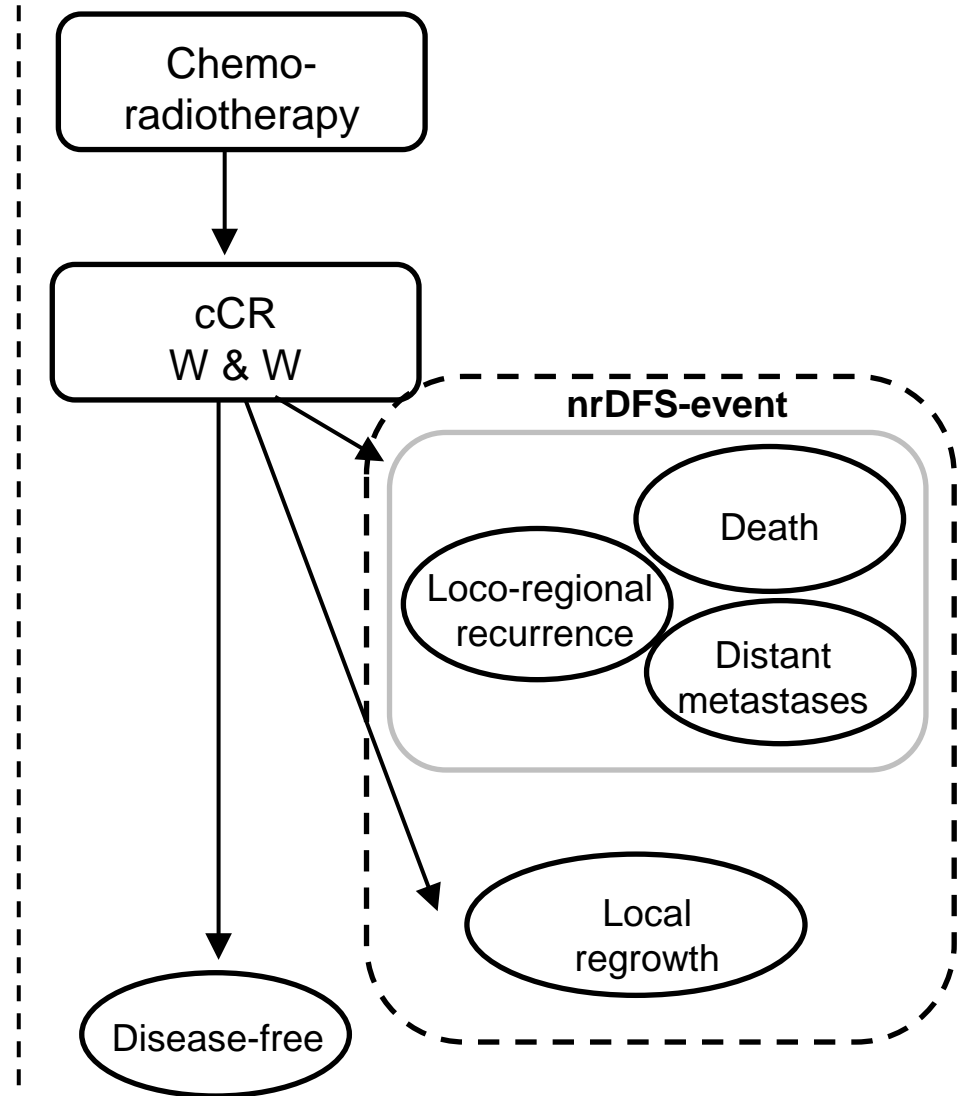
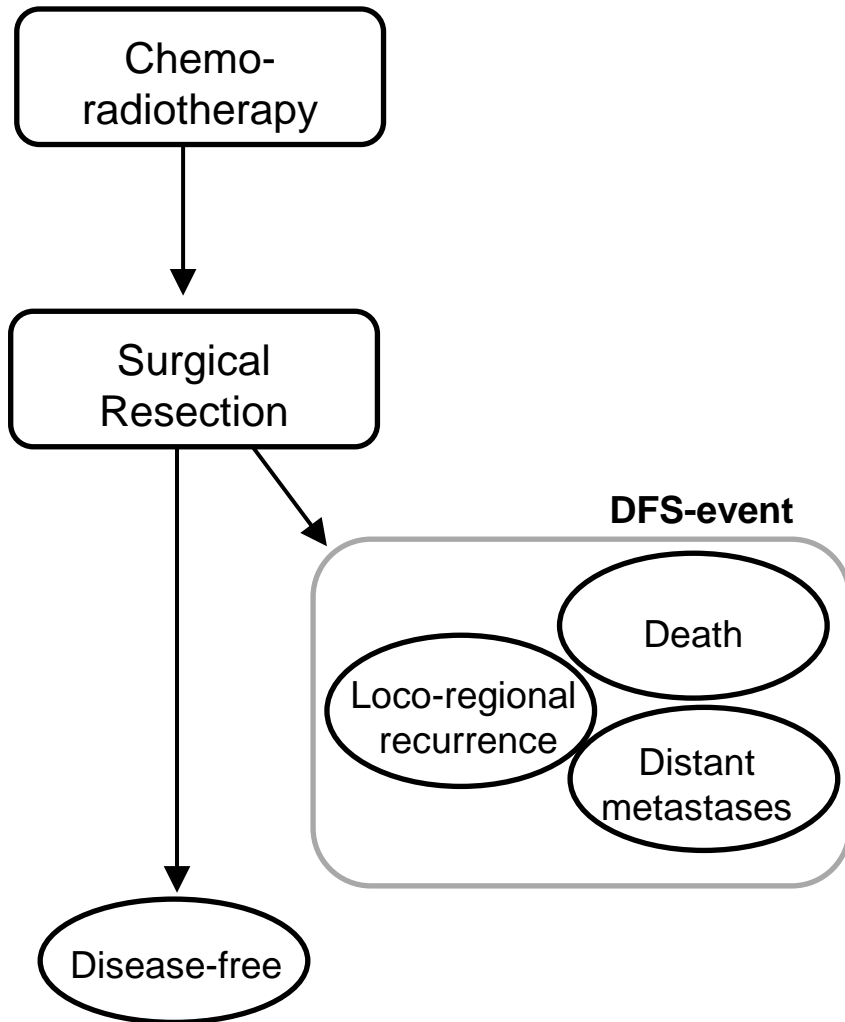
doi:10.1111/codi.12627

Report from a consensus meeting: response to chemoradiotherapy in rectal cancer – predictor of cure and a crucial new choice for the patient

On behalf of the Champalimaud 2014 Faculty for 'Rectal cancer: when NOT to operate'

*Heald, Beets, Carvalho Colorectal Disease 2014*

# Non-regrowth disease-free survival (nrDFS)



# DFS – colorectal cancer

**Table 2.** Consensus agreement of the contribution of nine different events to the definition of six endpoints in adjuvant studies with cancer patients

Event	Endpoint*					
	DFS	RFS	TTR	TTF	CSS	OS
Locoregional recurrence	E	E	E	E	I	I
Distant metastases	E	E	E	E	I	I
Second primary, same cancer	E	I	I	E	I	I
Second primary, other cancer	E	I	I	E	I	I
Death from same cancer	E	E	E	E	E	E
Death from other cancer	E	E	C	E	C	E
Non-cancer-related death	E	E	C	C	C	E
Treatment-related death	E	E	C	E	C	E
Loss to follow-up	C	C	C	C	C	C

\* DFS = disease-free survival; RFS = relapse-free survival; TTR = time to recurrence; TTF = time to treatment failure; CSS = cancer specific survival; OS = overall survival; E = event; C = censor; I = ignore.

For W&W after cCR	
	nrDFS
Locoregional recurrence	E
Distant metastases	E
Second primary, same	E
Second primary, other	E
Death same cancer	E
Death other cancer	E
Non-cancer death	E
Treatment-related death	E
Lost to follow-up	C
Local regrowth	I

## Endpoints in Adjuvant Treatment Trials: A Systematic Review of the Literature in Colon Cancer and Proposed Definitions for Future Trials

*JNCI 2007*

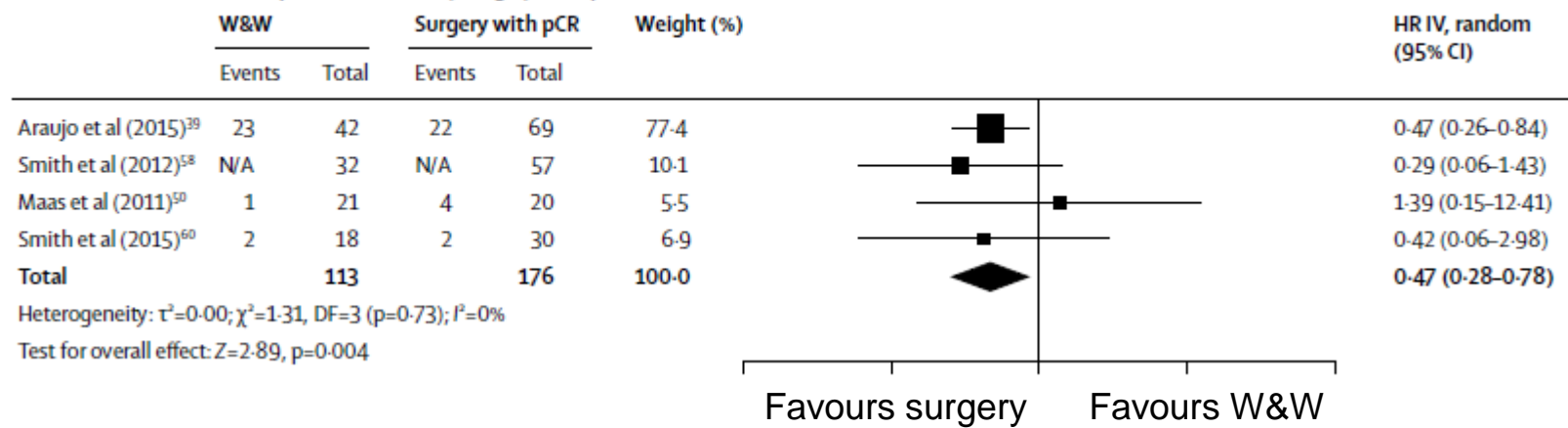


# A watch-and-wait approach for locally advanced rectal cancer after a clinical complete response following neoadjuvant chemoradiation: a systematic review and meta-analysis



Fahima Dossa, Tyler R Chesney, Sergio A Acuna, Nancy N Baxter

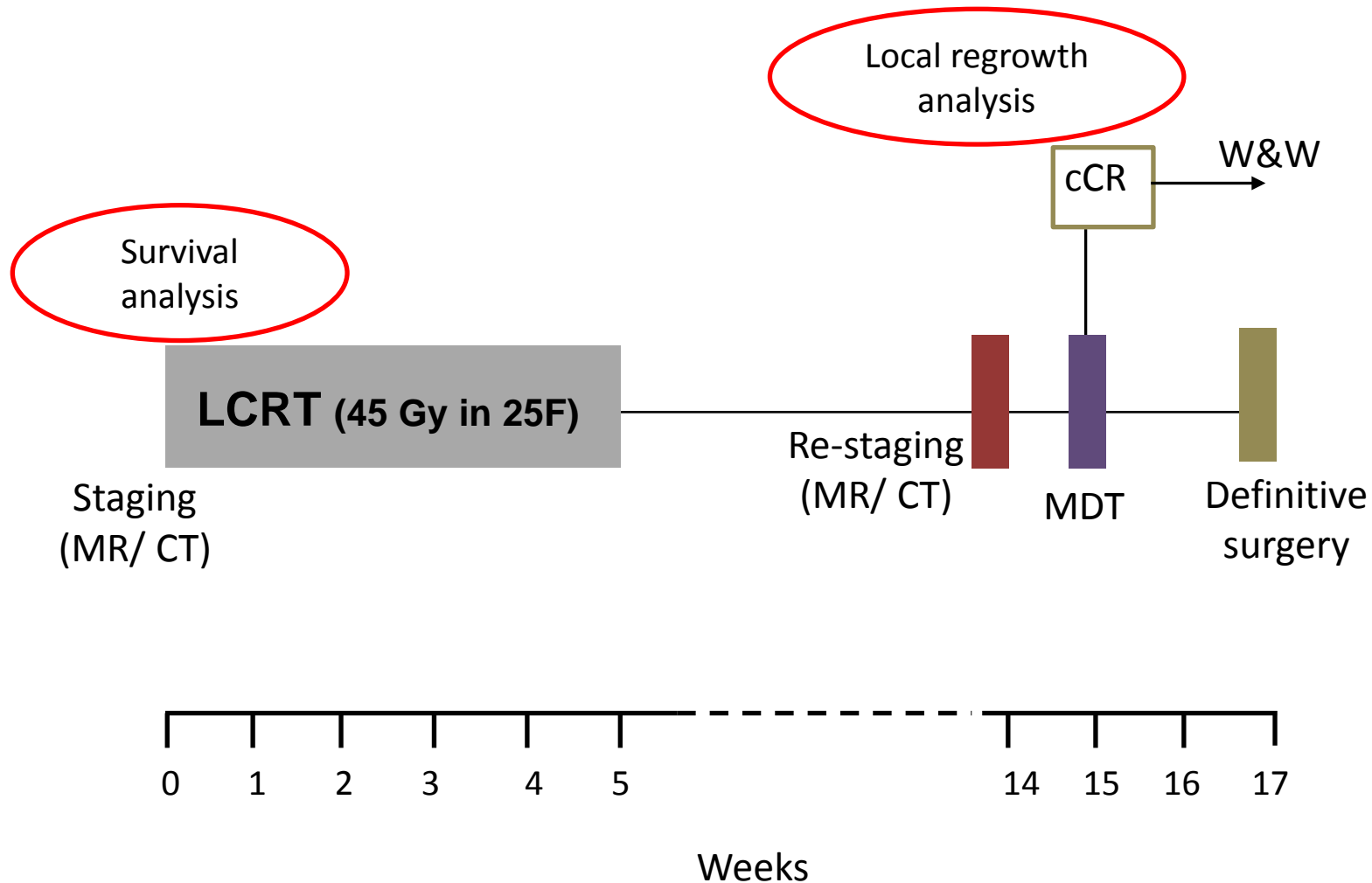
## A Disease-free survival for patients treated by surgery with pCR vs W&W



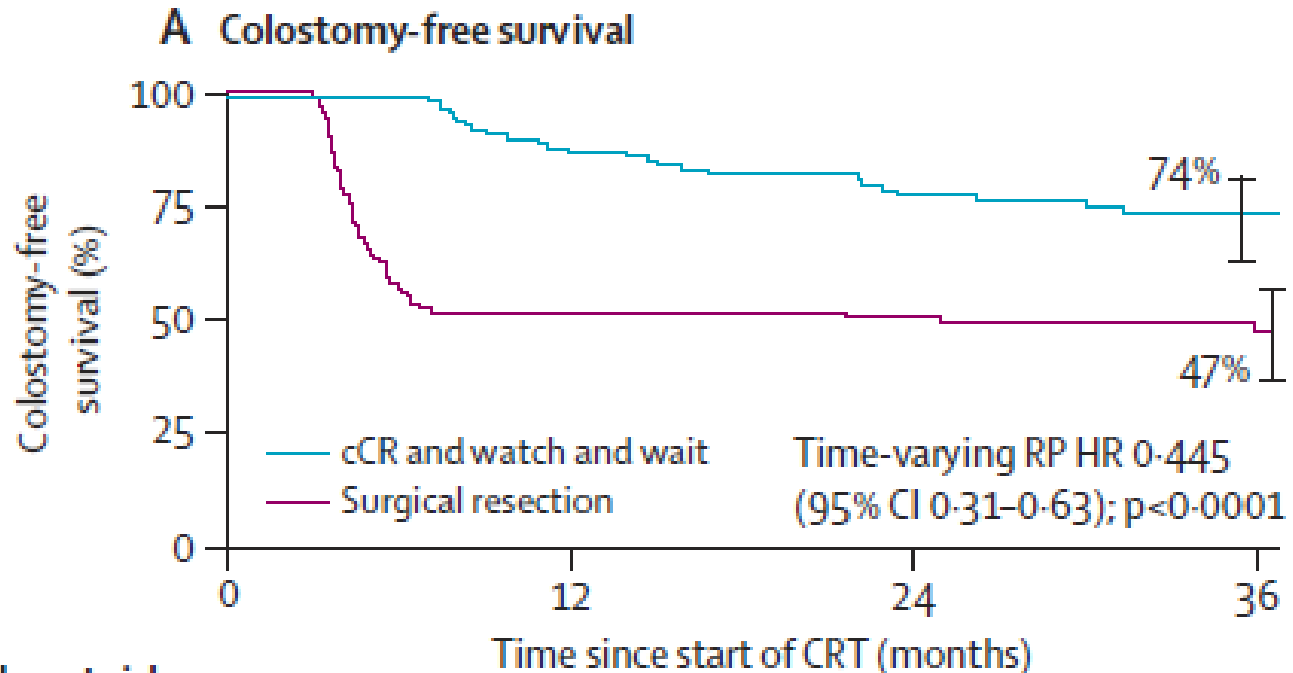
Watch-and-wait approach for rectal cancer: concepts of a subject-specific method



# Time zero (for W&W setting)



# Colostomy-free survival



Number at risk		Time since start of CRT (months)			
		0	12	24	36
cCR and watch and wait	109	90	68	46	
Surgical resection	109	56	53	20	

Figure 4: Colostomy-free survival for the 218 patients in the matched analysis cohort

# Colostomy-free survival

(lessons from anal cancer)



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MANCHESTER  
The University of Manchester

COMET  
INITIATIVE

NHS  
National Institute for  
Health Research

The Christie  
NHS Foundation Trust

Author	Definition
James et al. (8)	All pre-treatment colostomies not reversed within 8 months after starting treatment or any colostomies after treatment
Peiffert et al. (9)	Colostomy for progression, relapse or complication; reversed colostomies excluded
Yeung et al. (33)	Colostomy including diverting colostomy and colostomy from salvage APR
Meulendijks et al. (24)	Colostomy, excluding colostomies reversed during follow-up
Franco et al. (26)	Submission to definitive colostomy excluding preventative colostomies
El-Hadaad et al. (21)	First colostomy
Kichenadasse et al. (46)	Sphincter not intact at last follow-up

# 3-year distant metastasis rates

## Matched analysis

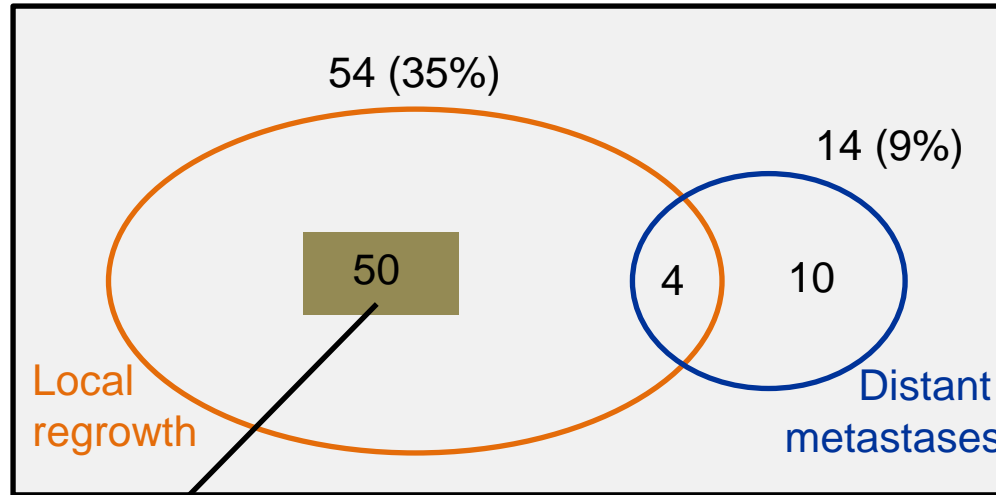
OnCoRe (2015)	n	3-year distant mets	P
Standard resection pathway	109	14%	0.08*
cCR	109	8%	

\*In OnCoRe, we set statistical significance at  $< 0.01$

# Distant metastasis



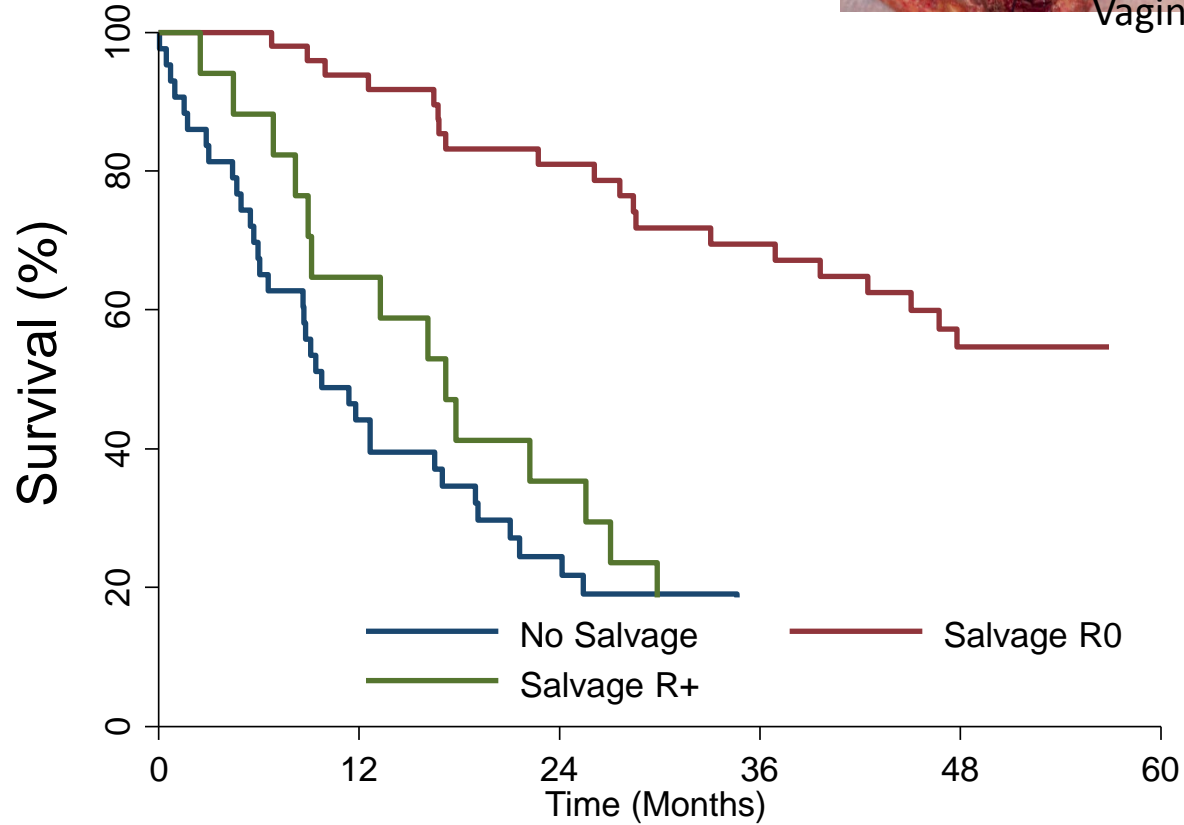
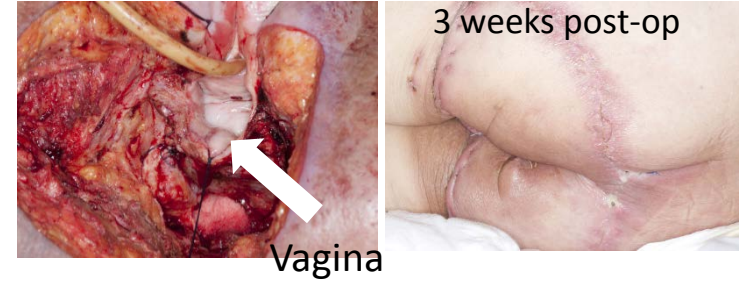
Updated N: 156 (2005-2016)



	n	R0
Local excision	none	
Resection surgery	42 (84%)	41
Papillon local therapy	3	
No treatment/ chemotherapy	5	

# Anal cancer: post-salvage survival

(2004 to 2014, N: 66)



Number at risk

No Salvage	43	19	9	6	4	3
Salvage R0	49	45	36	30	21	19
Salvage R+	17 (26%)	11	6	2	1	1

Thank you