

How to approach the elderly patient with muscle-invasive bladder cancer?

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**11th Belgian Multidisciplinary
Meeting on Urological Cancers**

Conflicts of interest

- Research funding from CRUK, PCUK, MRC, NIHR, PCUK, Elekta AB
- Honoraria from Bayer PLC, Janssen, AZ, ASTRO, ASCO, Roche, Merck
- Editor in Chief, BMJ Oncology



Underutilisation of radical therapy

- US and UK data
- Use of aggressive therapy decreased with age and poor social economic status

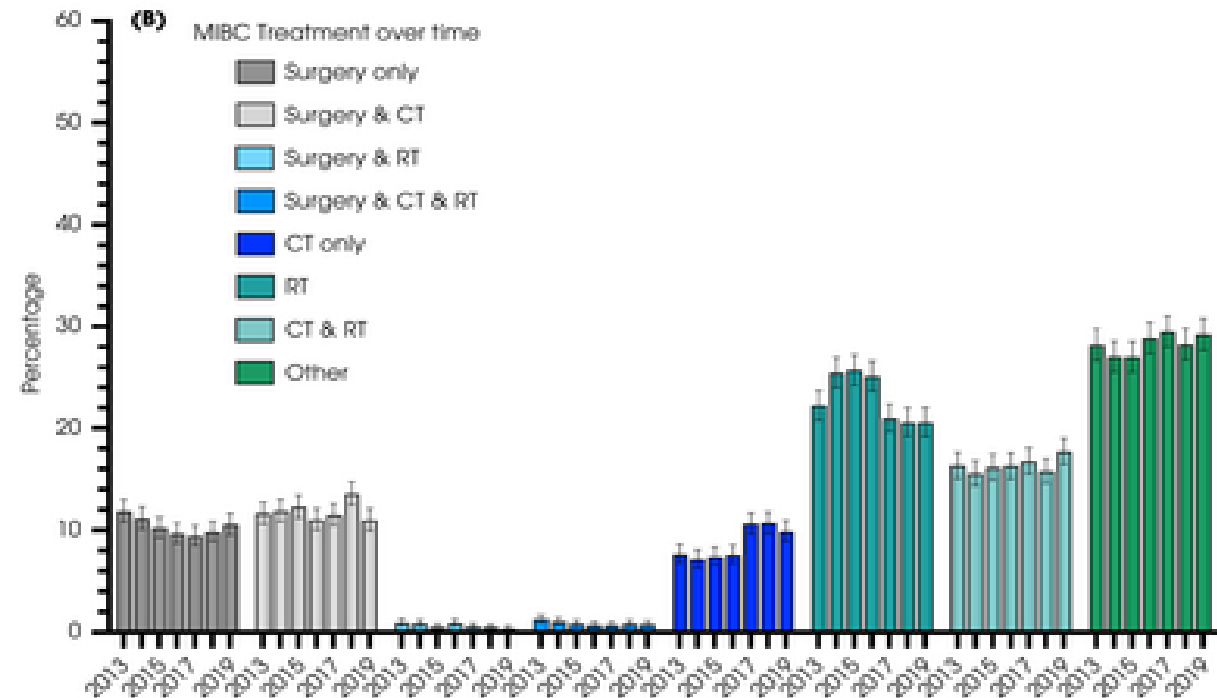
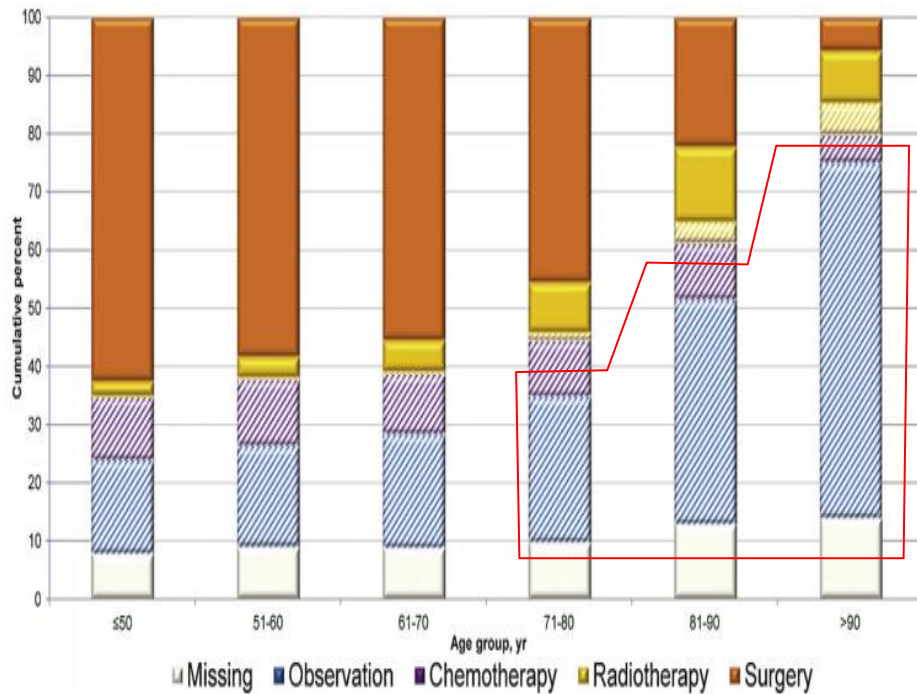


Fig 1 - Distribution of primary therapies received by patients with muscle-invasive bladder cancer by age group. Aggressive therapies are shown in solid colors, nonaggressive therapies are shown in striped colors.

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- US and UK data
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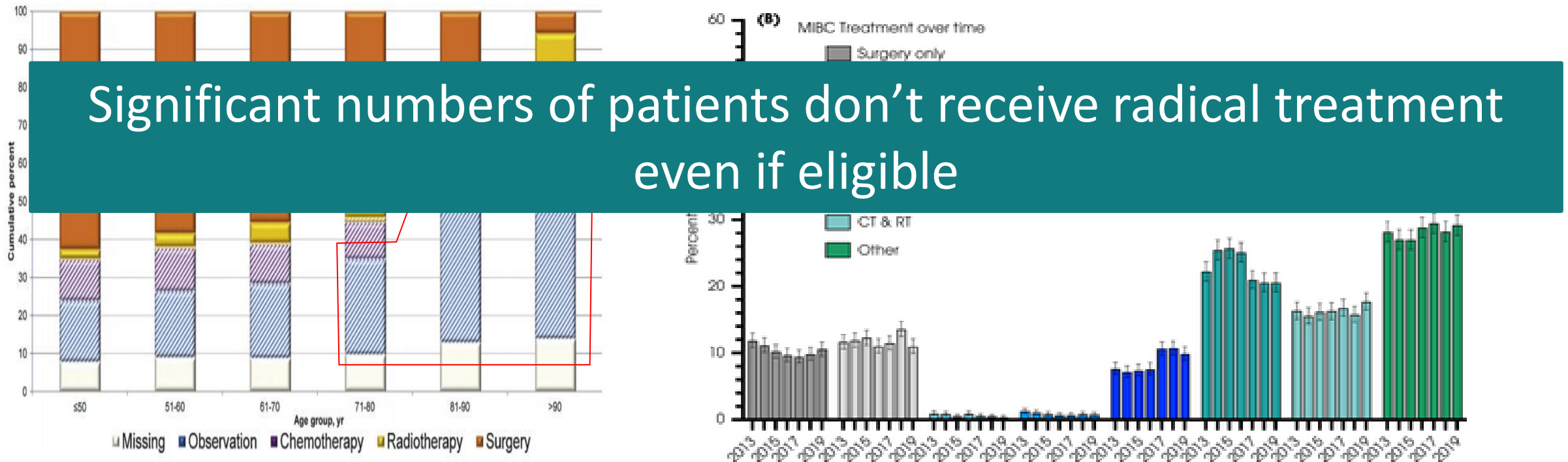
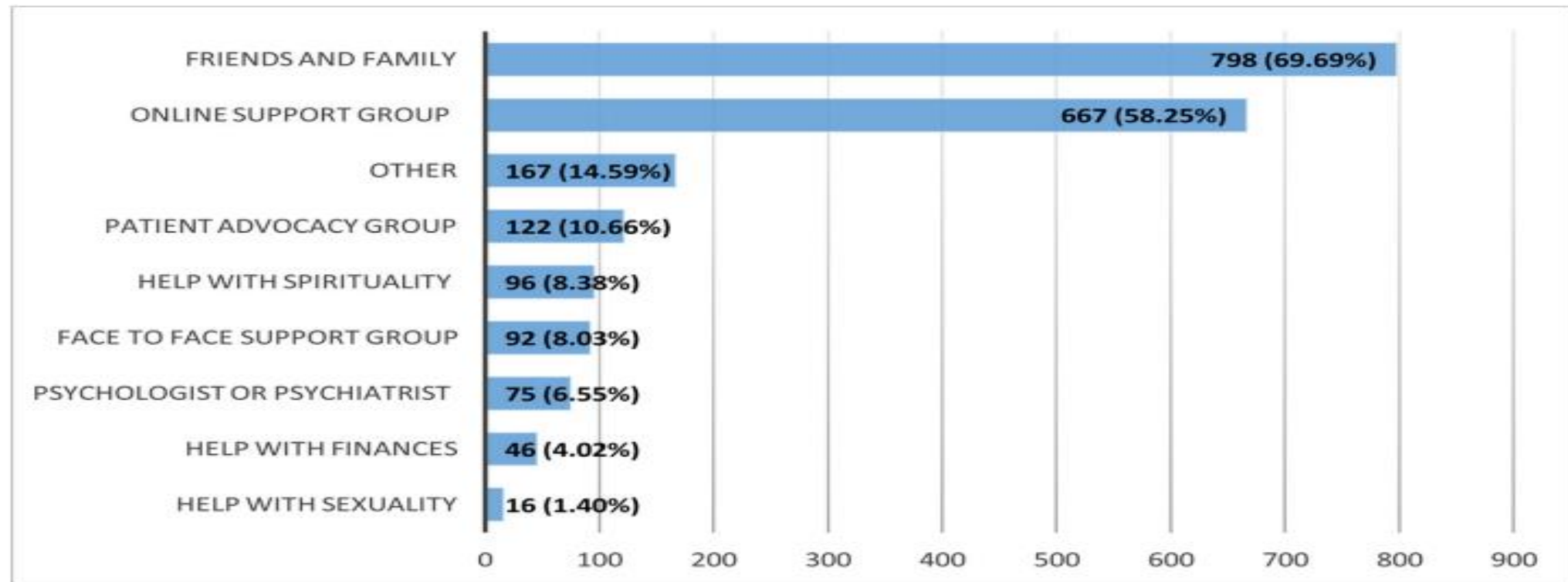


Fig 1 - Distribution of primary therapies received by patients with muscle-invasive bladder cancer by age group. Aggressive therapies are shown in solid colors, nonaggressive therapies are shown in striped colors.

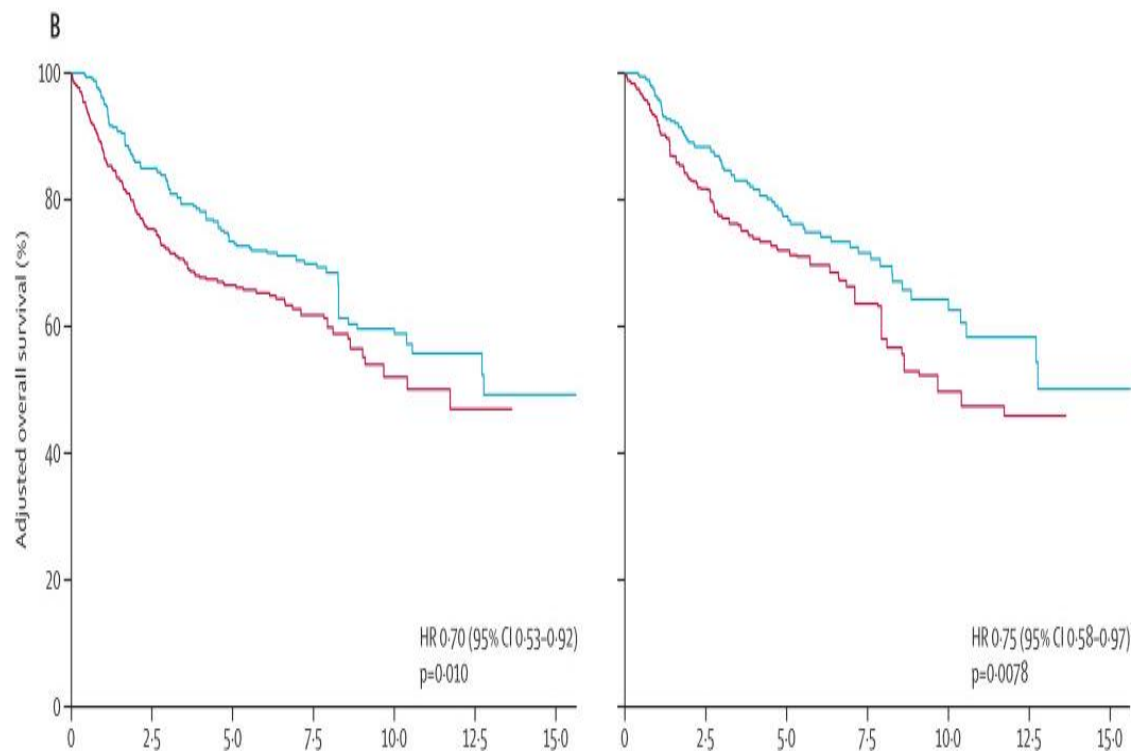
Bladder cancer patients are poorly served when it comes to patient experience

- Data from multiple countries show that bladder patients are poorly served compared to other cancer patients.



Makaroff et al. Eur.Urol. 2023
Elliott et al. J. Cancer Policy. 2019

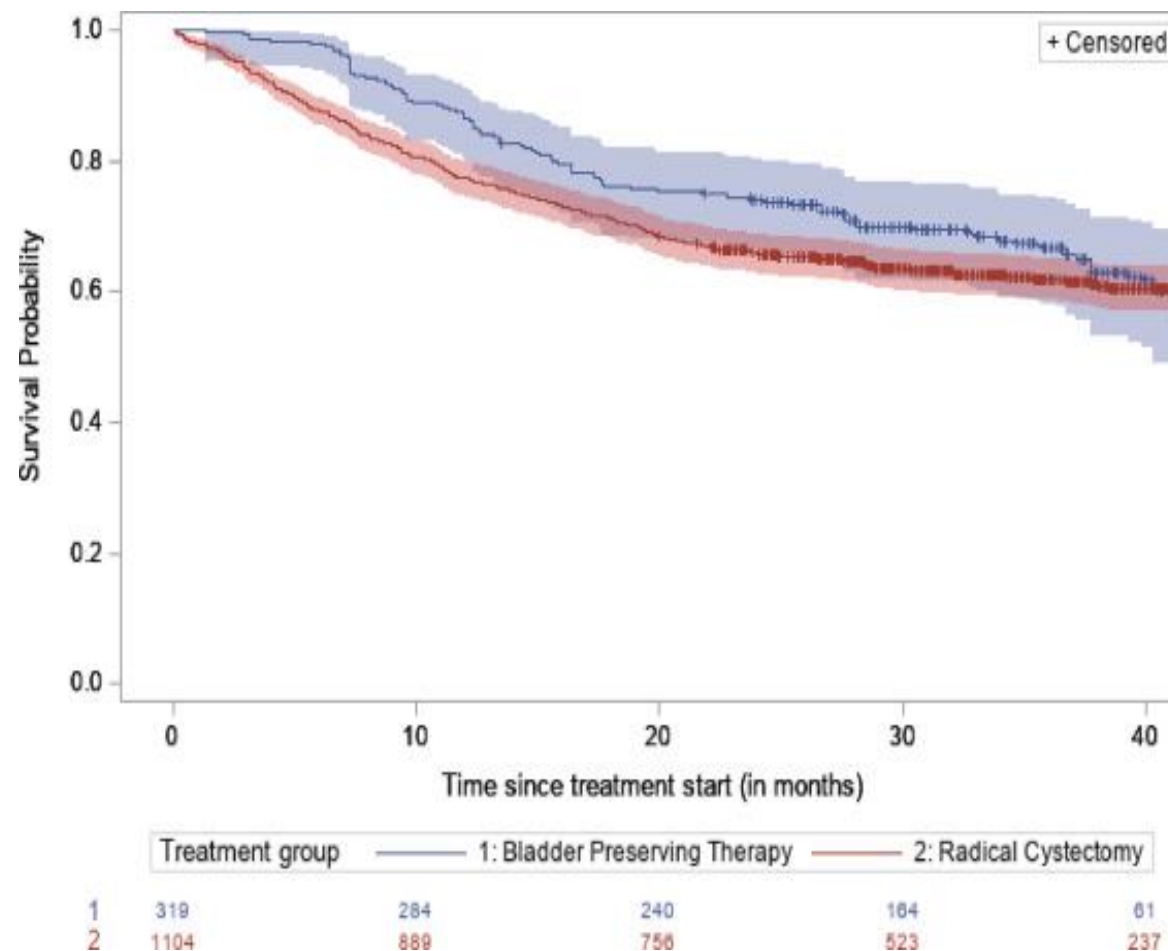
Overall survival: Contemporary data



Number at risk

(number censored)

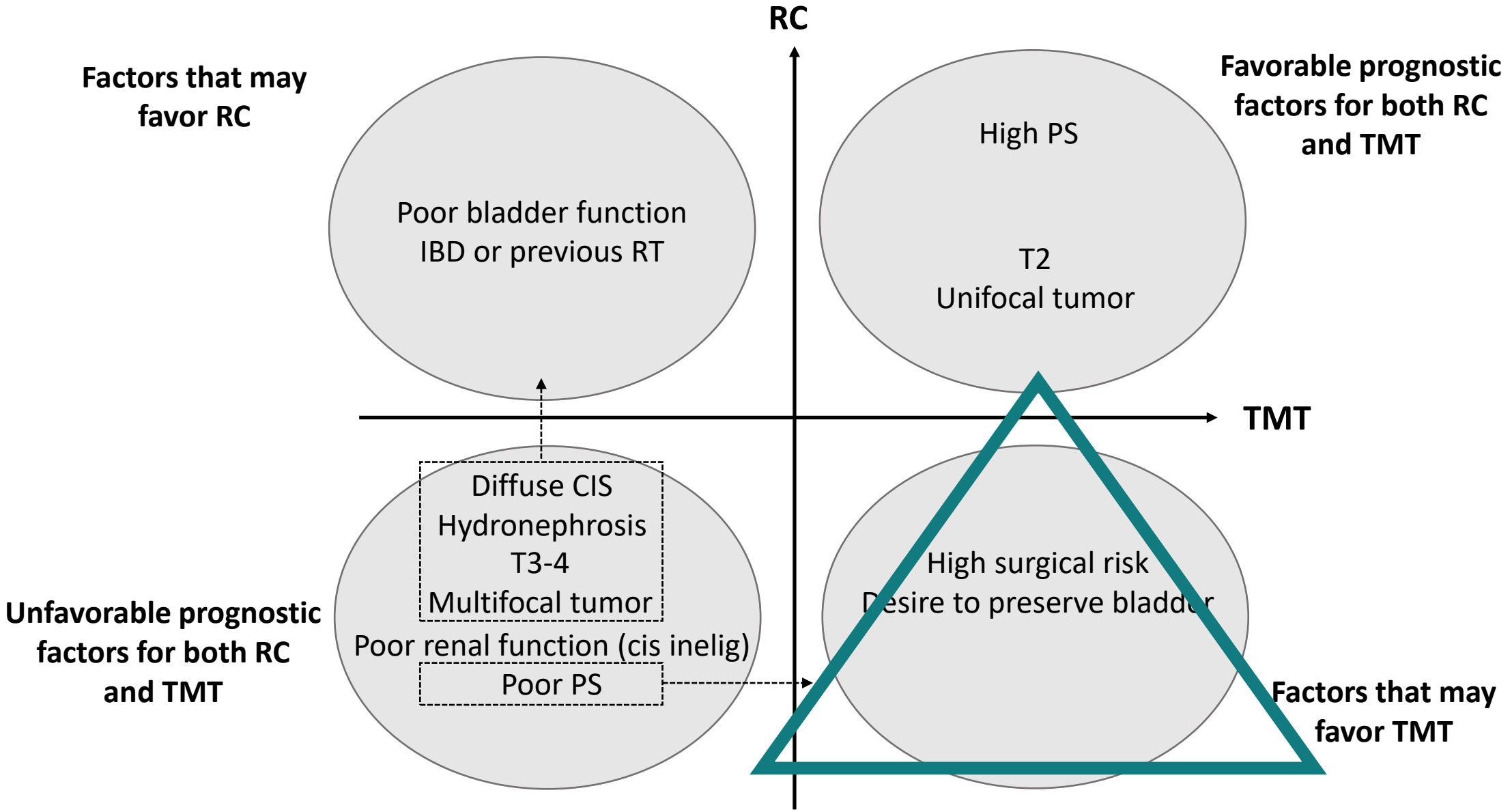
Radical cystectomy	440 (0)	289 (45)	179 (123)	82 (211)	28 (257)	6 (277)	0 (283)	837 (0)	595 (124)	403 (325)	172 (408)	62 (451)	16 (467)	0 (467)
Trimodality therapy	282 (0)	222 (23)	138 (82)	76 (136)	43 (163)	19 (184)	2 (199)	282 (0)	222 (59)	138 (113)	76 (140)	43 (161)	19 (176)	2 (177)



Zlotta et al: Lancet Oncology 2023

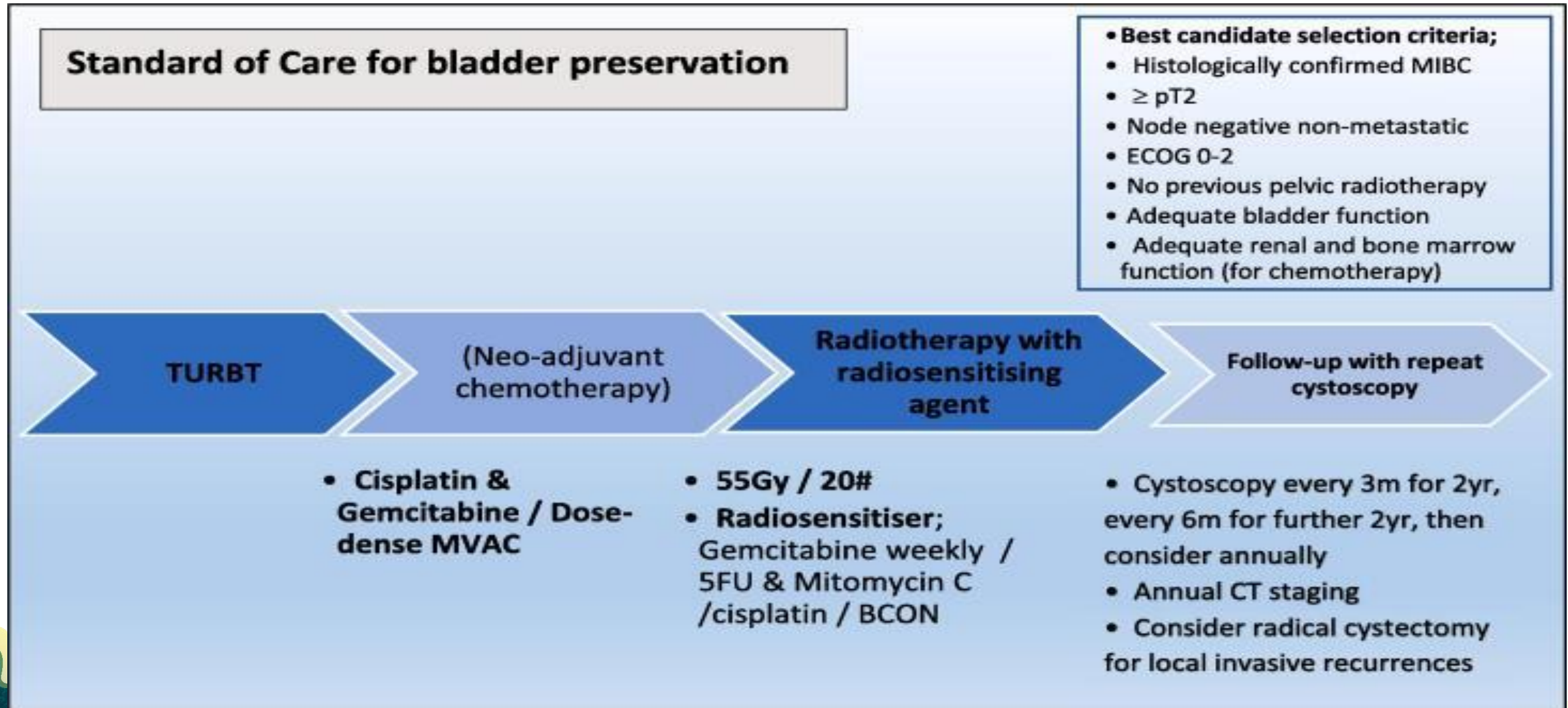
Bruch et al. IJROBP 2023

Factors that may impact treatment choice

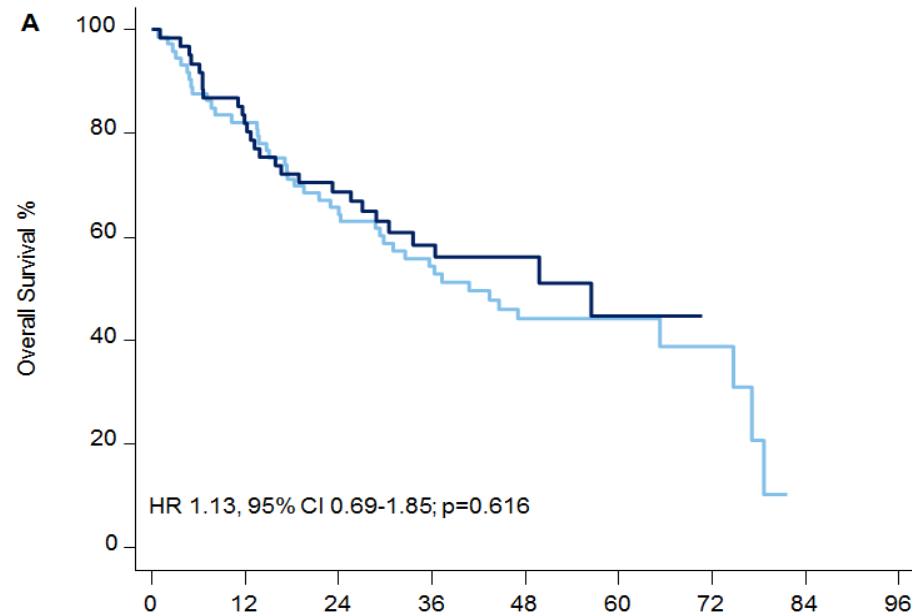


(caveats: comparative data limited/absent; each case is unique!)

Management of localised muscle-invasive bladder cancer

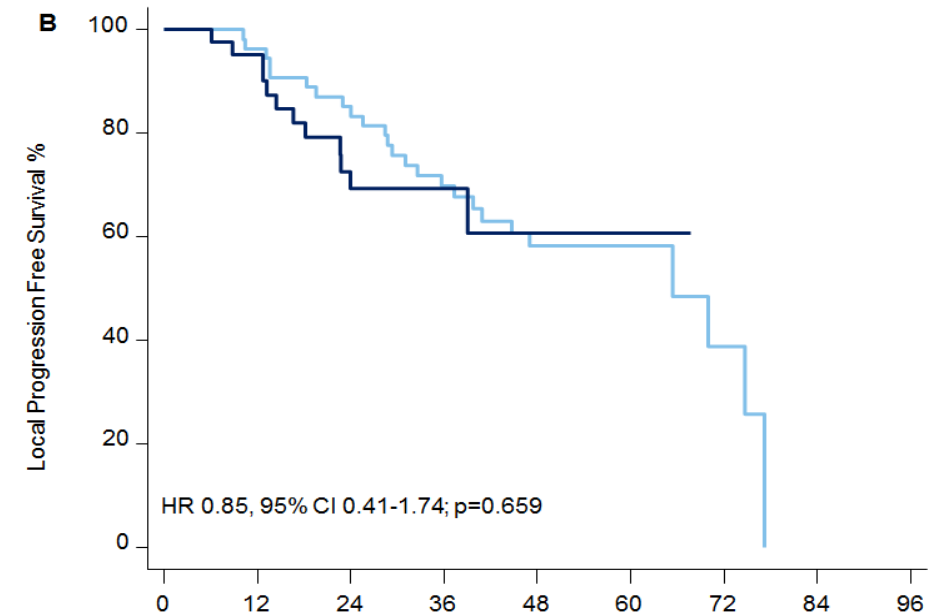


Use a radiosensitiser, any radiosensitiser



Numbers at risk

		0	12	24	36	48	60	72	84	96
—	CON	73	60	48	36	24	14	6	0	0
—	GemX	61	50	38	25	12	6	0	0	0



Numbers at risk

		0	12	24	36	48	60	72	84	96
—	CON	54	52	46	34	23	9	4	0	0
—	GemX	45	37	21	12	3	1	0	0	0

Comparison of radiosensitisers

	Advantages	Disadvantages
MMC+5FU	Level I evidence Well tolerated No increased long term toxicity	Requires central access Capecitabine unproven Avoid in cardiac morbidity
GemX	Phase II and IPD evidence Well tolerated No increased long term toxicity	Requires less infrastructure Can cause more GI toxicity
Cisplatin	Used widely throughout the World (not in UK) No increased long term toxicity	Small RCT, underpowered Avoid in renal comorbidity Requires less infrastructure
BCON	Level I evidence Well tolerated No increased long term toxicity Cost-effective	Many are unfamiliar Can cause nausea and diarrhoea



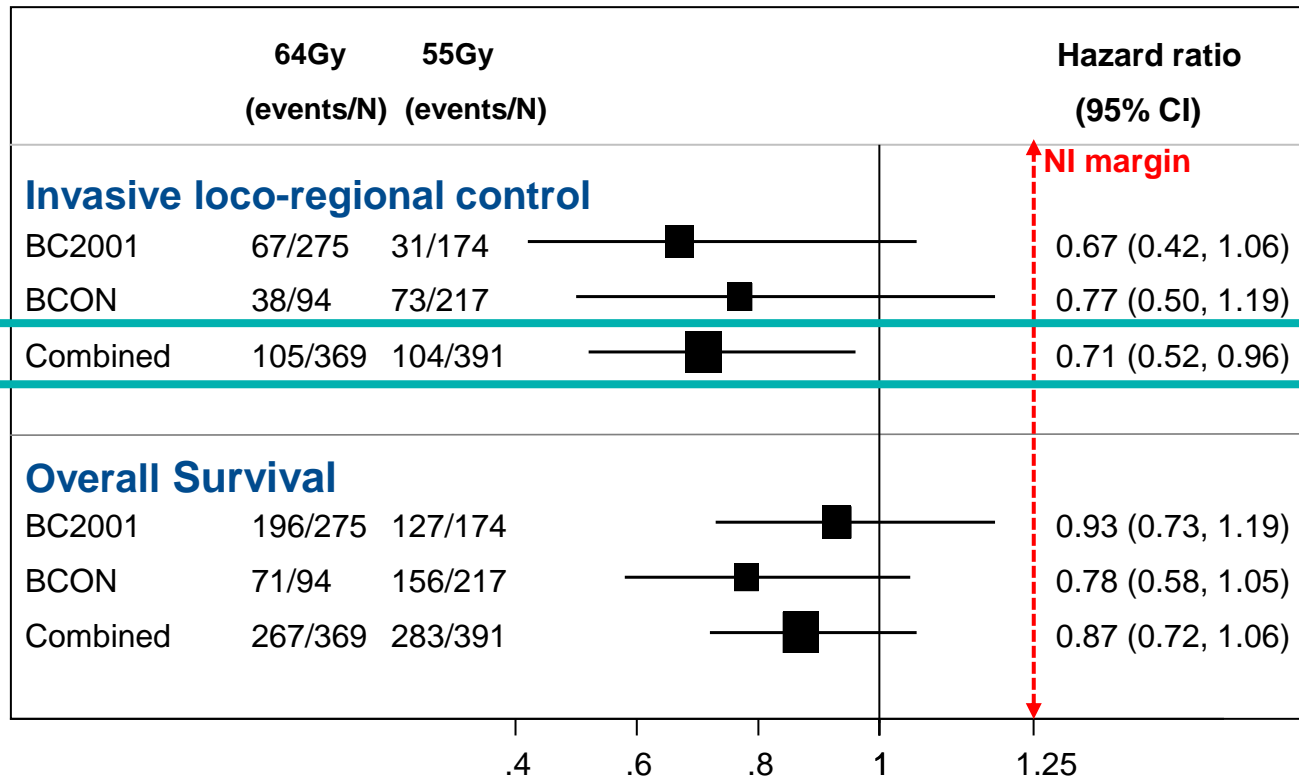
Current radiosensitisation: UK practice

Median age: 73 years

	20 fractions	32 fractions
N	150	131
Receiving NAC	77 (51%)	56 (43%)
Gemcitabine/cisplatin	65 (84%)	49 (88%)
Accelerated MVAC	4 (5%)	0
Carboplatin/gemcitabine	1 (1%)	7 (12%)
Other	7 (9%)	0
N	137	112
Receiving CRS	92 (67%)	78 (70%)
5FU/Mitomycin	36 (39%)	63 (81%)
Gemcitabine	36 (39%)	6 (8%)
Cisplatin	3 (3%)	1 (1%)
Carbogen/nicotinamide	17 (18%)	7 (9%)
Both NAC and CRS	58 (39%)	51 (39%)
No NAC/CRS	36 (24%)	32 (24%)

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64Gy vs 55Gy comparison – ILRC & OS



← 55Gy better 64Gy better →

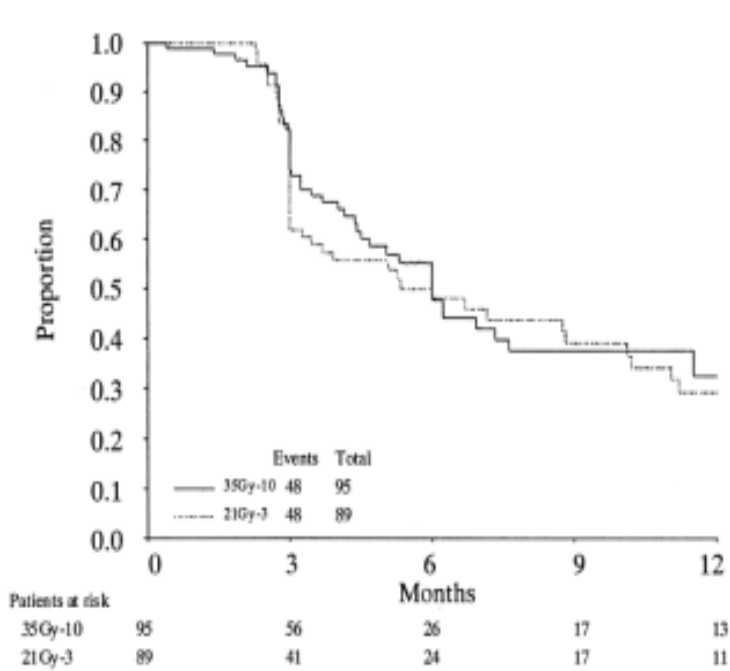
95% CI excludes non-inferiority margin (p-value < 0.001) AND excludes null difference (superiority p-value 0.026)

55Gy ILRC benefit also seen in patients receiving RT alone: HR 0.72 [CI 0.49-1.05]

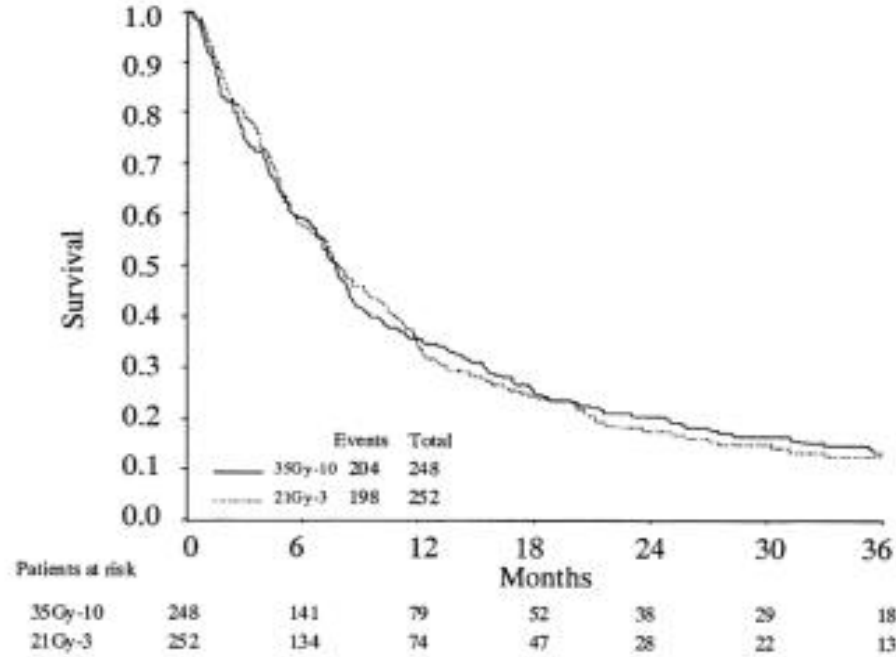
Palliative radiotherapy: the evidence

MRC BAO9 trial: 35 Gy/10# v 21 Gy/3#

Time to deterioration of symptoms

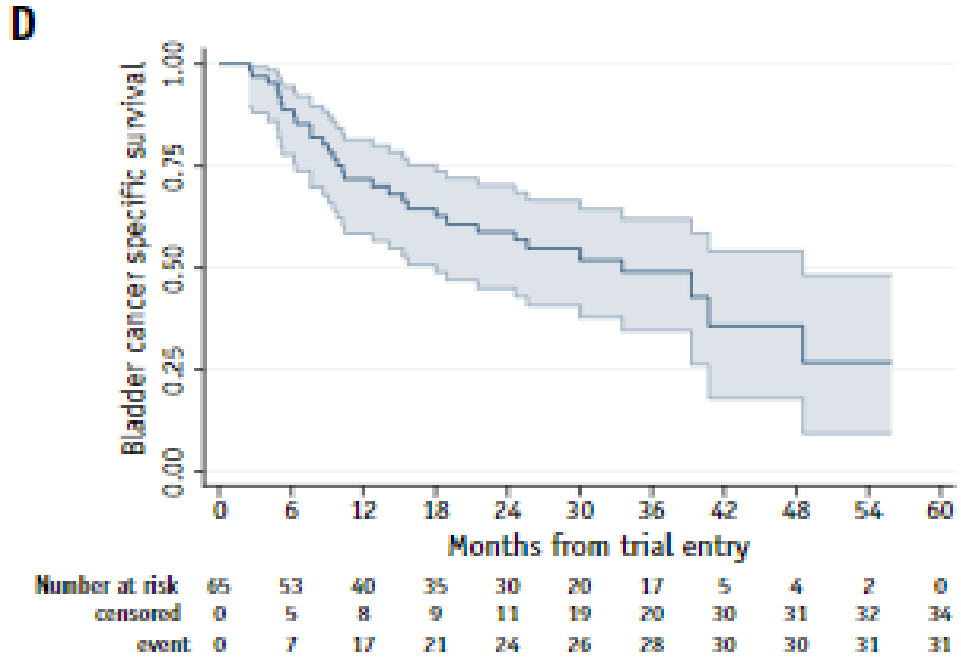
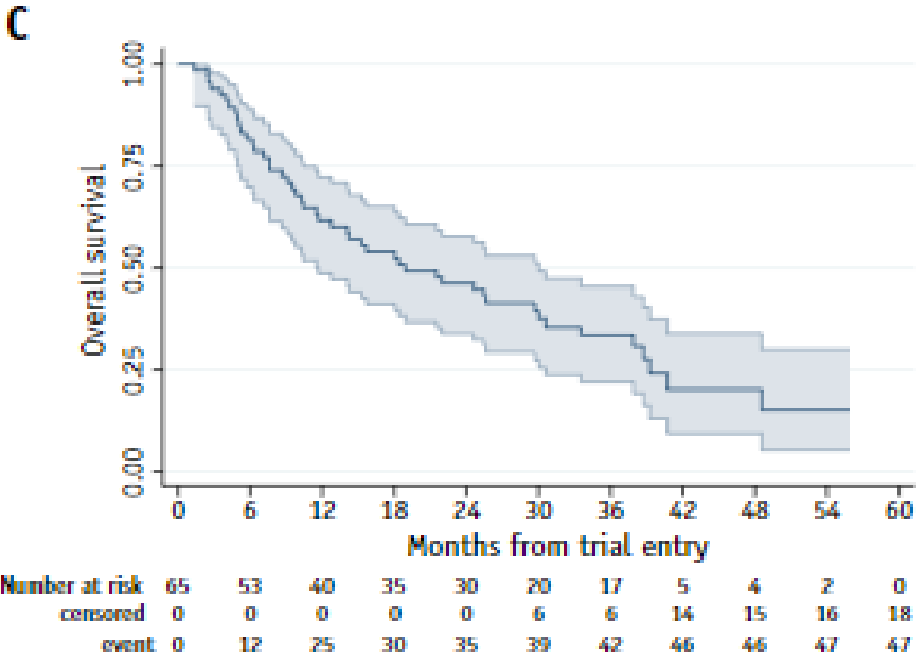


Overall survival

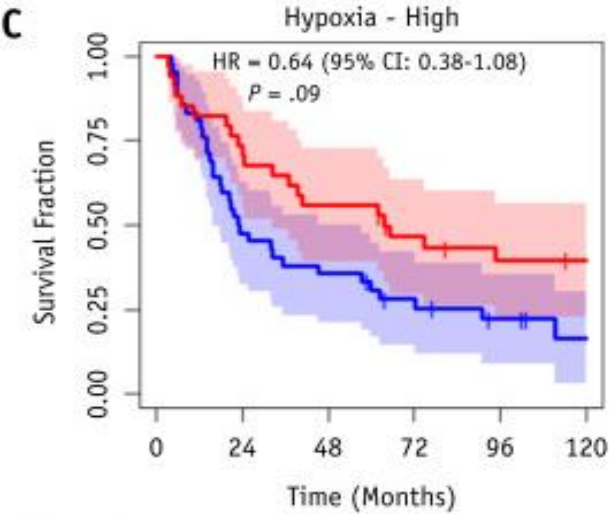


HYBRID trial: 36 Gy in 6# over 6 weeks

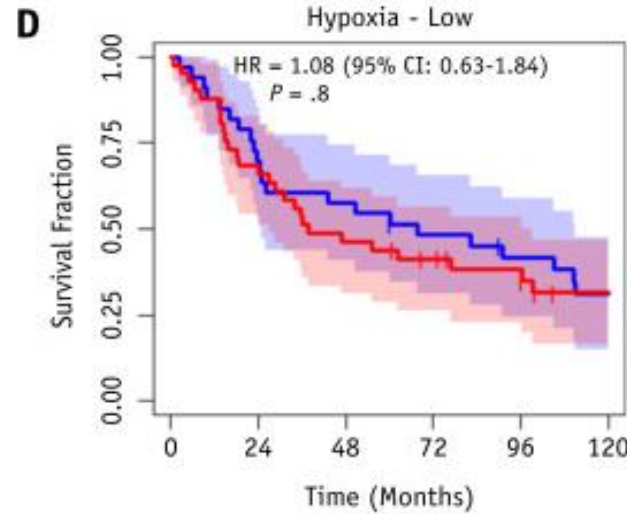
Adaptive plan of the day technique – better prognosis than BA09 trial



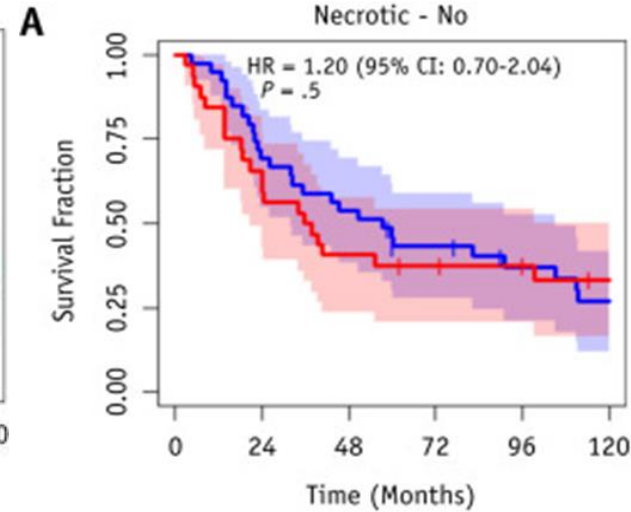
Biomarkers and BCON



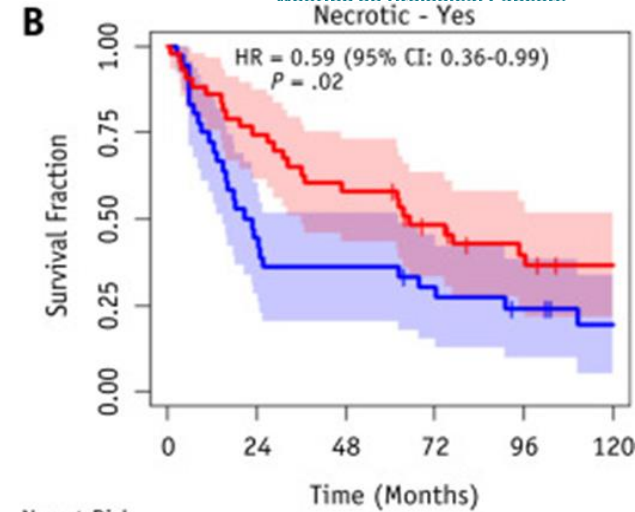
No. at Risk						
RT:	42	20	15	10	6	3
RT + CON:	34	25	19	14	11	10



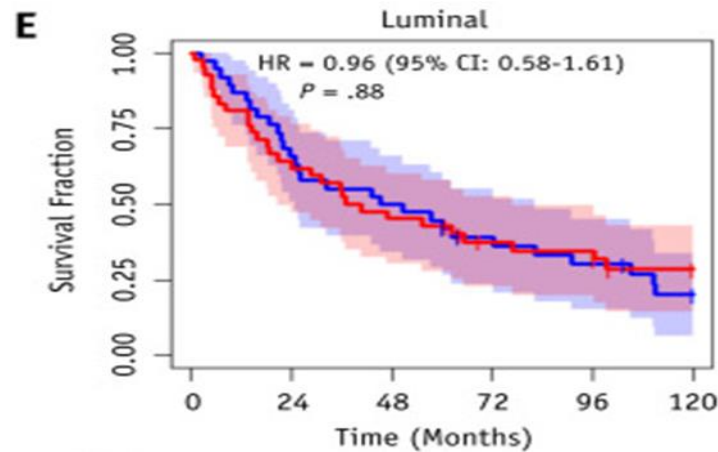
No. at Risk						
RT:	33	23	19	15	12	9
RT + CON:	41	28	19	15	12	7



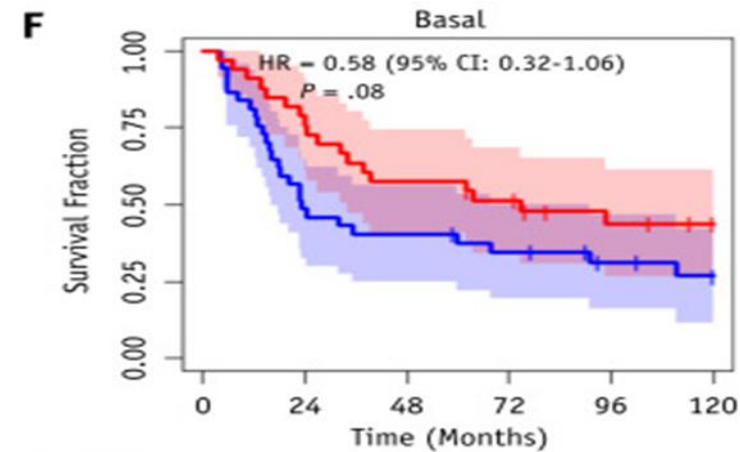
No. at Risk						
RT:	39	27	21	15	11	8
RT + CON:	32	21	13	11	10	7



No. at Risk						
RT:	36	16	13	10	7	4
RT + CON:	43	32	25	18	13	10



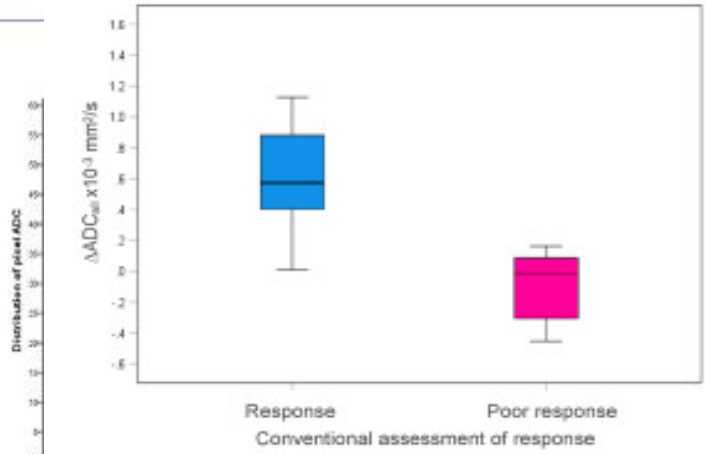
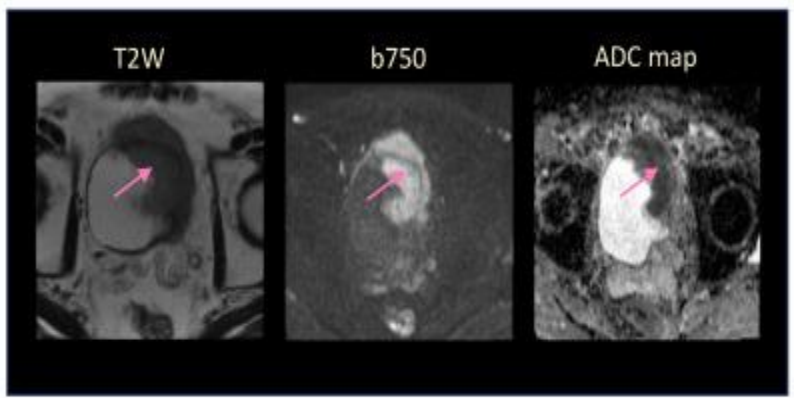
No. at Risk						
RT:	38	25	19	13	10	6
RT + CON:	42	27	19	13	12	8



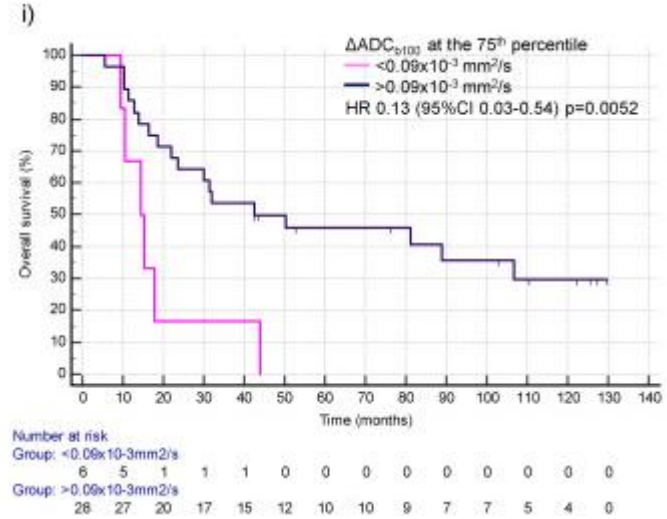
No. at Risk						
RT:	37	18	15	12	8	6
RT + CON:	33	26	19	16	11	9

Functional MRI in radiotherapy

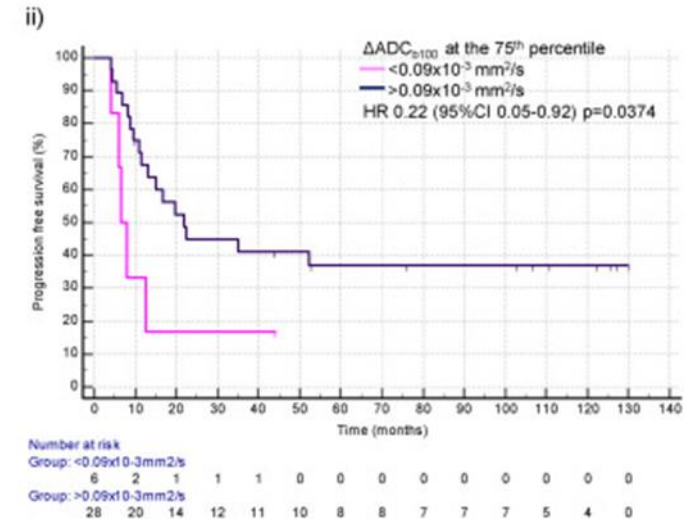
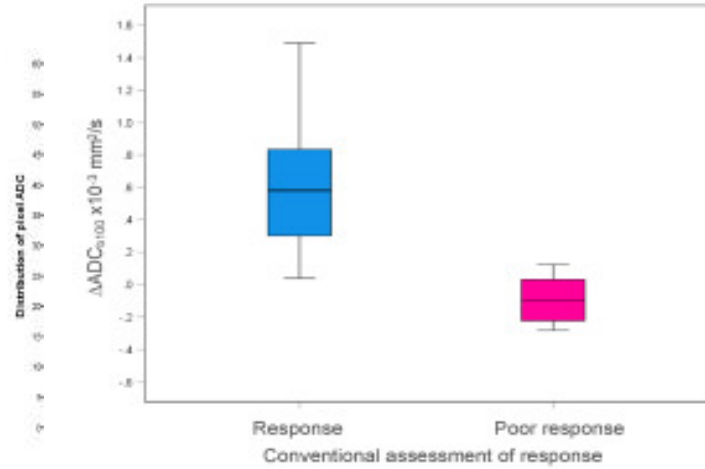
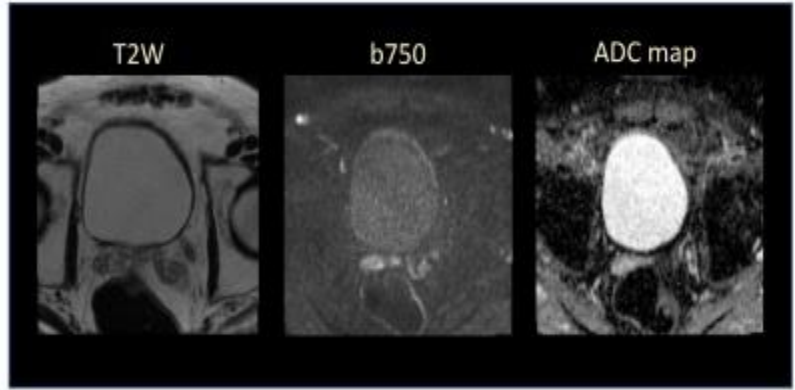
Baseline MRI analysis



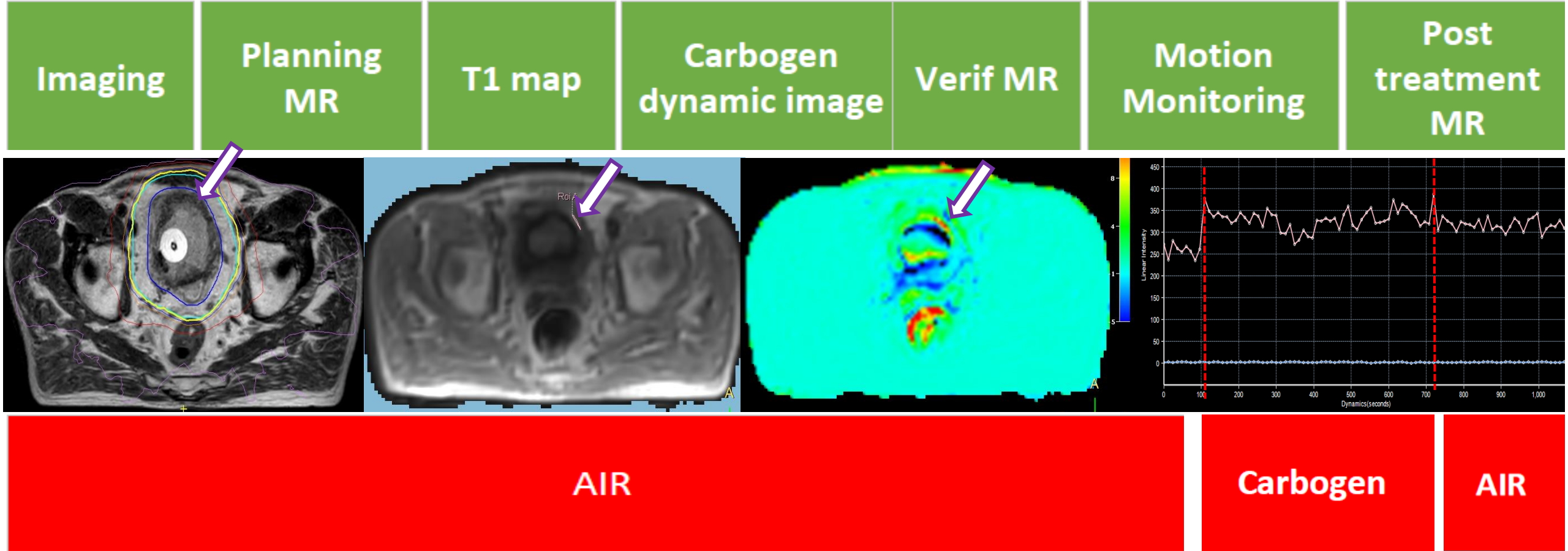
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Post radiotherapy MRI analysis



Bladder hypoxia with carbogen imaging



How should we treat the elderly patient?

- Treat as other patients – co-morbidities affect prognosis more than age
- Treat!
- Consider:
 - Neoadjuvant chemotherapy
 - Hypofractionation
 - Advanced RT techniques: daily adaptive, MR guidance
 - Shorter overall treatment times
 - Predictive biomarkers: tissue and imaging



Questions?



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