## Cure vs. toxicity: Quantifying preferences for non-surgical management of rectal cancer using a discrete choice experiment

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Purpose There is clinical interest in non-surgical management of rectal cancer using higher radiation doses than standard, which entails a trade-off between increased chance of cure and increased risk of toxicity. This study is the first to quantify patient preferences for non-surgical management of rectal cancer, including the cure/toxicity trade-off.

Methods A discrete choice experiment (DCE) was developed with qualitative input and included the attributes: treatment length (4/5/6 weeks); chance of being cancer free two years post-treatment (50/55/60%); side effect risk during treatment (25/30/35%); side effect risk two years post-treatment (5/10/20%) and support available (usual GP/dedicated nurse). The DCE had a Bayesian D-efficient design with four blocks of 10 questions each and was administered to UK rectal cancer patients prior to starting non-surgical treatment. An interim analysis used a latent class model with two preference classes.

**Results** There were 38 participants, 47.4% of whom were female. Their average age was 66.6 years (range 41-82 years). The first preference class had a 74.3% class membership probability. There were no significant preferences for treatment length or support, but the model

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Commented [AA1]: As we've discussed, you can emphasise the lack of data / novelty of this study (from a clinical perspective). You could e.g. add something like "however, no prior studies have quantified this trade-off ", or just stage that "this study is the first to quantify patient preferences (etc)"

Commented [AA2]: For the clinical interpretation, it may be important to state that these were patients who were treated with the intent of non-surgical management. But that may be an irrelevant nuance for you intended audience 😳

Commented [AG3]: This isn't clear what this refers to and you mention in the results about the two preferences but it's not defined.

Commented [AA4R3]: I think this is relatively standard terminology and methodology for the decision making field, so I wouldn't worry too much about explaining it

Commented IEH51: Given this is an interim analysis is the two preference classes pre-defined i.e. Cannot increase next time. Or are you allowing flexibility here if there are multiple latent classes in the future with larger samples.

IF so perhaps two preference classes is a result.

Commented [AG6]: As this is an interim analysis I would state this and say here how many patients you plan to recruit.

Commented [AA7R6]: I agree, would probably be good to state that this represent an interim / preliminary analysis

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coefficients for being cancer free and side effects were statistically significant at the 5%-level. Long-term side effects were more important than short-term. For every 1 percentage point (pp) increase in their chance of being cancer free after two years, participants were willing to accept an extra 5.2 pp risk of short-term side effects, but only a 1.6pp higher risk of long-term side effects. In the second preference class (25, 7% class-membership probability), decisions were dominated by the availability of support, with a preference for a dedicated nurse over participants' usual GP the only significant coefficient.

**Conclusions** Most participants were prepared to accept extra toxicity risks in exchange for a better chance of cure, showing the acceptability of non-surgical management approaches with higher radiation doses. However, participants were more concerned about long-term than short-term side effects. Informing patient decision-making at the time of choosing treatment thus requires follow-up data on long-term toxicity and patient-reported outcomes. For a minority of patients, the care-toxicity trade-off was relatively unimportant, but they had a strong preference for dedicated support. This is the first study of its kind in rectal cancer, and the results will aid clinical practice to better align with patient preferences.

Keywords: Rectal cancer; patient preference; discrete choice experiment; latent class; radiotherapy; non-surgical management

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## Commented [EH8]: Statistically significant?

**Commented [ds9]:** May just be me, but I prefer to see % rather then pp

Commented [AA10R9]: I think there is a risk of misunderstanding when using %, so I'd support keeping percentage points

Commented [EW11R9]: Technically % would be incorrect.

Commented [AG12]: So interesting! :) DSM - agree!

Commented [AA13R12]: Yep!

**Commented [EH14]:** Can see you want to shorten but if space perhaps for clarity may need re-iterate the comparison, i.e. for the same 1pp increase

**Commented [EH15]:** Given fairly small sample size, perhaps worth mentioning number of patients here is it 8,9?

A little confused by this percent, 8/37 = 21.6% 9/37 = 24.3%

With such small number in group, I imagine that's why coefficients were significant

Commented [EW16R15]: It's really probability of being in the class rather than the size of the group – have changed the wording to be more accurate.

**Commented [AA17]:** Again, you could consider emphasising the uniqueness of your study / your data here – if you have the space