

Shabnam Thapa<sup>1,2</sup>, Katherine Payne<sup>1</sup>, Praveen Thokala<sup>3</sup>, Lee Malcomson<sup>2</sup>, Andrew G Renehan<sup>2</sup>

<sup>1</sup> Manchester Centre for Health Economics, University of Manchester, Manchester, United Kingdom

<sup>2</sup> Manchester Cancer Research Centre, Division of Cancer Sciences, University of Manchester, Manchester, United Kingdom

<sup>3</sup> School of Health and Related Research, University of Sheffield, Sheffield, United Kingdom

## Introduction

In patients with rectal cancer who achieve clinical complete response after neoadjuvant chemoradiotherapy, watch-and-wait (W&W) is a novel management strategy with potential to avoid major surgery but this is not yet routine practice. Observational studies have shown that watch-and-wait strategy is safe and have similar oncological outcomes compared with surgery in these group of patients (1).

Evidence of cost-effectiveness of watch-and-wait strategy will better inform policy decision making on whether to endorse and implement this strategy of organ preservation. Hence, we undertook a systematic review of economic evaluation in this question.

## Aim



To produce a critical summary of the available economic evidence for the use of a watch-and-wait strategy in people with clinical complete response following neoadjuvant chemoradiotherapy for rectal cancer.

## Methods

We searched MEDLINE and Embase, English language only, until March 2022 to identify published studies undertaking full economic evaluation (cost-effectiveness analysis, cost-utility analysis, cost-benefit analysis). Studies were selected according to the inclusion and exclusion criteria set according to the PICO framework ( see Figure 1).

Figure 1. Inclusion and Exclusion criteria for the selection of studies

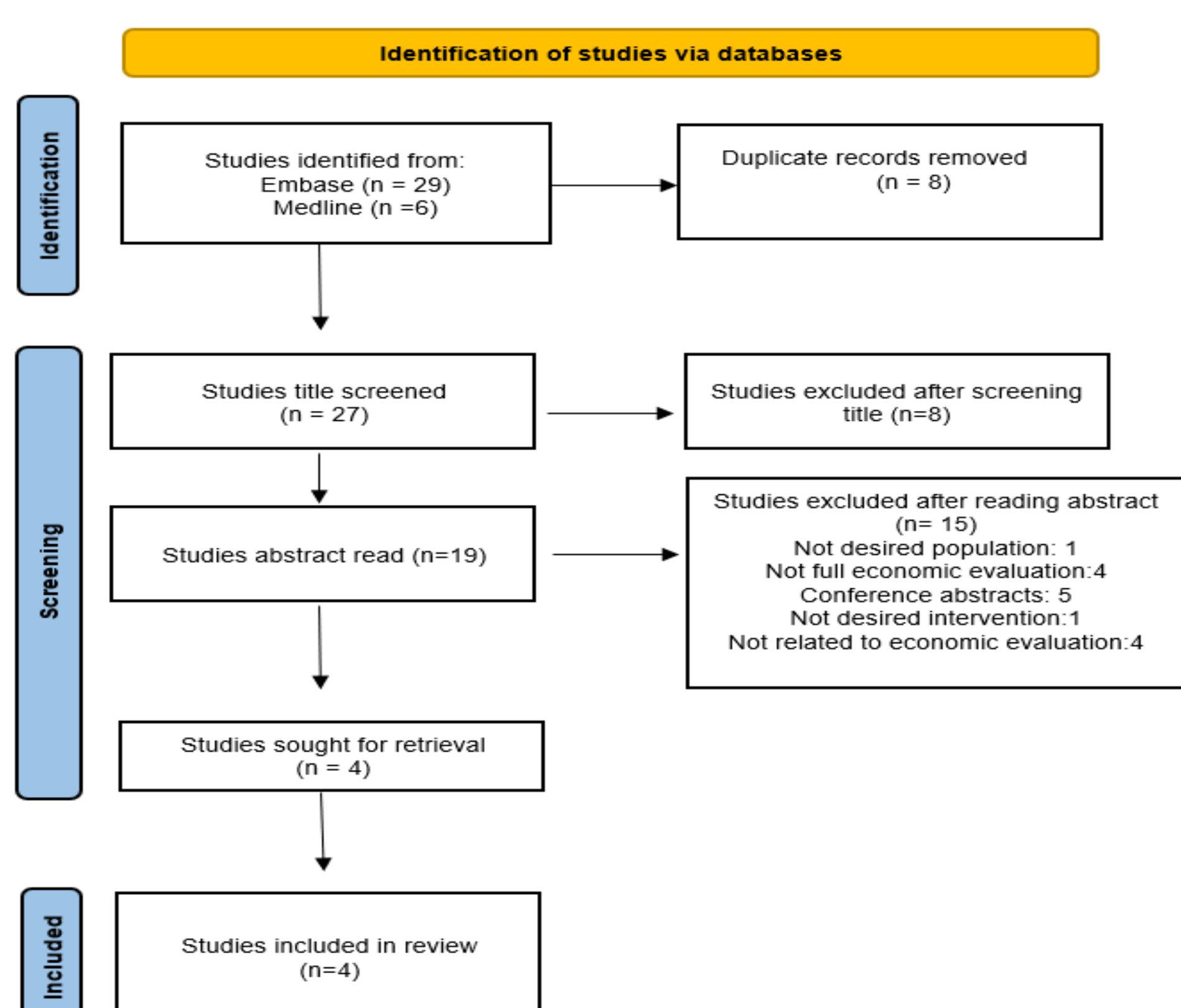
Characteristics	Inclusion criteria	Exclusion criteria
Population	Adults (18 years and above) with locally advanced rectal cancer who have achieved clinical complete response following neoadjuvant chemoradiotherapy	Adults with locally advanced rectal cancer who have not achieved clinical complete response or who are near clinical complete response following neoadjuvant chemoradiotherapy
Intervention	Only studies following Watch-and-wait strategy i.e. active surveillance	Studies not undertaking watch-and-wait strategy
Comparator	Resection surgery	Other procedures such as endoscopic micro-dissection surgery
Study design	Full economic evaluation either model-based decision analytic study or prospective study	Studies not undertaking full economic evaluation
Language	English language	Languages other than English
Publication	Only published studies in journals will be included	Abstracts, dissertation and unpublished studies

Identified studies from electronic search were screened in multiple stages; screening of title, abstract and full text. Data from included studies were extracted using bespoke data extraction form. The Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) was used to critically appraise the quality of reporting for the identified economic evaluation (2).

## Results

A total of 34 studies were identified from Embase (n= 29) and Medline (n=6). After multiple stage screening, a total of four studies were included in the review (see figure 2 for the screening process).

Figure 2: PRISMA flowchart for selection of studies in systematic review



## Results

All four selected studies have been conducted in last five years; two were from the USA, one from Spain and one from the UK. They all were decision-analytic model based studies with 75% of studies having lifetime horizon. All studies were conducted from payers' perspective.

Figure 3: Result of economic evaluation from included studies

Study	Intervention	Comparator	Model type	Results
Rodriguez-Pascual J et al, 2022, Spain	Watch-and-wait strategy	Standard resection (SR) and Robotic Rectal Resection (RRR)	State transition Markov model with six health states Time Horizon: Lifetime Discount rate: 3% Perspective: Payer	WW dominant over SR (-£75,486.75, +2.04 QALYs) and RRR (-£75,486.75, +0.41 QALYs)
Cui CL et al, 2021, USA	Watch-and-wait strategy	Low anterior resection (LAR) and Abdominoperineal resection (APR)	State Transition Markov Model Time Horizon: 5-year Discount rate: 3% Perspective: Payer	WW dominant over vs LAR (-\$23,984, + 0.17 QALYs) vs APR (-\$16,760.63, + 0.23 QALYs)
Miller J A et al, 2020, USA	Watch-and-wait strategy	Low anterior resection (LAR) and Abdominoperineal resection (APR)	State transition Markov model with seven health states. Time Horizon: Lifetime Discount rate: 3% Perspective: Payer	WW dominant over LAR (\$-28,500, + 0.527 QALYs) vs APR (-\$32,100, + 0.601 QALYs)
Christopher Rao et al, 2017, UK	Watch-and-wait strategy	Radical surgery (RS)	Decision tree linked with state Transition Markov model with five health states. Time Horizon: Lifetime Discount rate: 3.5% Perspective: Payer (NHS)	WW dominant over RS in age 60 cohort (-£8094.54, + 0.63 QALYs); and age 80 cohort (-£6274.24), + 0.56 QALYs)

Footnote: 1) Surgical Oncology. 2022 May 1;41:101710. 2) Annals of surgical oncology. 2022 Mar;29(3):1894-907. 3) J Natl Cancer Inst. 2020 Aug 1;112(8):792-801. doi: 10.1093/jnci/djaa003. PMID: 31930400. 4) Diseases of the Colon & Rectum. 2017 Jan 1;60(1):30-42.

All four studies reported watch-and-wait strategy to be dominant over surgery i.e. less costly and yield more benefits. Results of sensitivity analysis also suggest watch-and-wait strategy is cost-effective over surgery. However, results were sensitive to rates of local regrowth and distant metastases in watch-and-wait group.

## Conclusion

Compared with standard surgical resection, watch-and-wait strategy appears to be cost-effective but there was considerable uncertainty, especially in relation to patients' wider well-being. Large scale economic evaluation studies along with inclusion of wider perspectives (quality of life, patient reported outcomes) is required to assess value of this novel strategy.

## References

1. Renehan AG, Malcomson L, Emsley R, Gollins S, Maw A, Myint AS, Rooney PS, Susnerwala S, Blower A, Saunders MP, Wilson MS. The Lancet Oncology. 2016 Feb 1;17(2):174-83.
2. Husereau D, Drummond M, Augustovski F, De Bekker-Grob E, Briggs AH, Carswell C, et al. BMJ. 2022 Jan 11 [cited 2022 Feb 8];376.

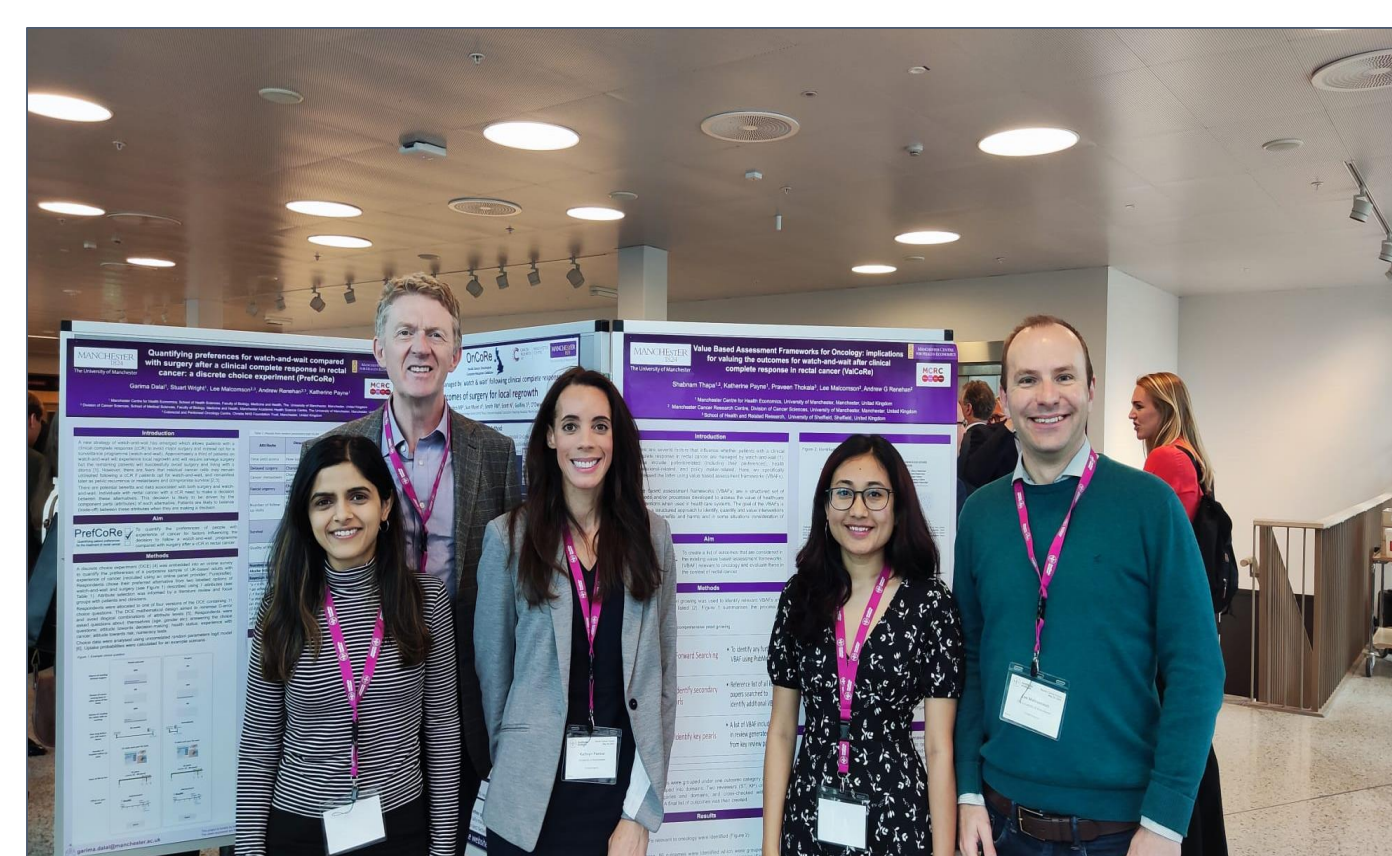
## Research in Context

This work is from PhD project that is a part of and funded by European Union's Horizon 2020 Research and Innovation Programme; CAST. CAST, an 11 centre EU consortium is working towards implementing novel approaches in deciding when or whether surgery is needed in patients with rectal cancer.

CAST has a network of Early Stage Researchers (ESRs) who are enrolled in PhD programs in different universities across Europe. It is mandatory to have non-home country students in these PhD programs. This network of students collaborate in multiple projects and work towards the goal of CAST.



ESRs in annual CAST meeting held at Karolinska University, Stockholm, 2022



Team Renehan (from Manchester Cancer Research) at Rectal Cancer Forum, Stockholm, 2022.

I am a health economist embedded within a clinical research in Manchester and also a part of wider European clinical research team. Through my PhD project, I am bringing health economics perspective in the programme and working towards valuing consequences related to watch-and-wait strategy and surgery in patients with rectal cancer to better inform policy decision making.