BMJ Open

Prospective multicentre observational cohort to assess quality of life, functional outcomes and cost-effectiveness following minimally invasive surgical techniques for rectal cancer in 'dedicated centres' in the Netherlands (VANTAGE trial): a protocol

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To cite: Geitenbeek R, Burghgraef T, Hompes R, *et al*. Prospective multicentre observational cohort to assess quality of life, functional outcomes and cost-effectiveness following minimally invasive surgical techniques for rectal cancer in 'dedicated centres' in the Netherlands (VANTAGE trial): a protocol. *BMJ Open* 2022;**12**:e057640. doi:10.1136/bmjopen-2021-057640

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2021-057640).

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Received 22 September 2021
Accepted 01 February 2022

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ABSTRACT

Introduction Total mesorectal excision is the standard of care for rectal cancer, which can be performed using open, laparoscopic, robot-assisted and transanal technique. Large prospective (randomised controlled) trials comparing these techniques are lacking, do not take into account the learning curve and have short-term or long-term oncological results as their primary endpoint, without addressing quality of life, functional outcomes and cost-effectiveness. Comparative data with regard to these outcomes are necessary to identify the optimal minimally invasive technique and provide guidelines for clinical application.

Methods and analysis This trial will be a prospective observational multicentre cohort trial, aiming to compare laparoscopic, robot-assisted and transanal total mesorectal excision in adult patients with rectal cancer performed by experienced surgeons in dedicated centres. Data collection will be performed in collaboration with the prospective Dutch ColoRectal Audit and the Prospective Dutch ColoRectal Cancer Cohort. Quality of life at 1 year postoperatively will be the primary outcome. Functional outcomes, cost-effectiveness, short-term outcomes and long-term oncological outcomes will be the secondary outcomes. In total, 1200 patients will be enrolled over a period of 2 years in 26 dedicated centres in the Netherlands. The study is registered at https://www.trialregister.nl/9734 (NL9734).

Ethics and dissemination Data will be collected through collaborating parties, who already obtained approval by their medical ethical committee. Participants will be included in the trial after having signed informed consent. Results of this study will be disseminated to participating centres, patient organisations, (inter)national society meetings and peer-reviewed journals.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The first large prospective study with quality of life as primary outcome, providing head-to-head comparison of all three minimally invasive techniques, while also assessing functional outcomes and cost-effectiveness.
⇒ Nationwide data will be collected on all minimally invasive techniques, using existing logistic networks of the prospective Dutch ColoRectal Audit and the Prospective Dutch ColoRectal Cancer Cohort.
⇒ Collecting real-life data of standard of practice will provide a high level of evidence and external validity.
⇒ Recommendations for optimal sustainable use of minimally invasive techniques will improve treatment and quality of life for patients with rectal cancer.

INTRODUCTION AND RATIONALE

Surgical resection according to the total mesorectal excision (TME) principle, often preceded by (chemo)radiotherapy, is the primary treatment for rectal carcinoma.[1] TME can be performed by open surgery or minimally invasive techniques such as laparoscopic TME (L-TME), robot-assisted TME (R-TME) and transanal TME (TaTME).[2] As of yet, no clear differences regarding intraoperative, postoperative or oncological outcomes have been described between the three techniques.[3–8]

As treatment of rectal cancer primarily focuses on oncological outcomes, most studies' primary endpoints are short-term postoperative or

long-term oncological results. Less attention has been paid to the effects of treatment on quality of life, the economic analysis or functional outcomes such as sexual outcome, urological and faecal continence and low anterior resection syndrome (LARS). However, quality of life and functional outcomes following minimally invasive TME are of significant importance, as rectal cancer treatment is associated with considerable risk on postoperative morbidity impacting quality of life.[9] In addition, as survival rates are increasing, the effects of preoperative neoadjuvant therapy, postoperative complications and the construction of a (temporary) stoma on quality of life and functional outcomes are becoming more pronounced.[10–14] Furthermore, R-TME and TaTME are suggested to result in more primary anastomosis for low rectal cancers.[15 16] However, the effect on quality of life and functional results remains unknown. This is of special importance as LARS symptoms are highly associated with a low anastomosis.[17–19] Finally, as no clear difference regarding intraoperative, postoperative and long-term oncological outcomes have been described, this urges the need for an analysis of quality of life, functional outcomes and costs.

Current literature comparing the three techniques with regard to quality of life, functional outcomes and cost-effectiveness is limited in number and level of evidence. Available series are small and often retrospective, and therefore, without proper baseline assessment.[20–22] Studies do not account for the effects of the learning curve, while the learning curve is known to confound the assessment of minimally invasive TME outcomes.[23] Lastly, most cost-effectiveness studies are early experience reports, while operating times, which accounts for a substantial part of the costs, tend to decrease with ongoing experience.[24]

In summary, current insight into the quality of life, functional outcomes and economic analysis of the different procedures is limited, due to limited number of studies with low levels of evidence. Therefore, a large prospective trial is needed in order assess these outcomes. This prospective observational multicentre cohort study aims to compare quality of life, functional outcomes and costs of L-TME, R-TME and TaTME performed by surgeons in dedicated centres with profound experience with one of the tree minimally invasive techniques.

Objectives

The primary objective of this study is to compare quality of life at 1 year postoperatively between L-TME, R-TME and TaTME.

Secondary objectives are to compare functional outcomes, cost-effectiveness, short-term outcomes and long-term oncological outcomes of L-TME, R-TME and TaTME.

METHODS AND ANALYSIS

Study setting and design

The VANTAGE trial (prospective multicentre observational cohort to assess quality of life, functional outcomes and cost-effectiveness following minimally inVAsive surgical techNiques for recTAl cancer in 'dedicated centres' by experienced surGEons in the Netherlands) is a prospective observational multicentre study within the routine clinical care setting of patients undergoing minimally invasive TME (figure 1). There are several reasons for not performing a randomised controlled trial (RCT): First, surgeons may not be proficient in all techniques. Requiring surgeons to perform techniques in which they may not be proficient, as an effect of randomisation, may be considered unethical. Second, as surgeons may not be proficient in all three techniques, the experience with the technique might be of a bigger influence than the technique itself.[25] Third, as referral for TME surgery is very limited in the Netherlands, and most centres use one standard procedure, we assume tumour and patient characteristics to be equal between centres and groups. Fourth, RCTs might generate low external validity and reduced generalisability due to their strict inclusion criteria. Contrastingly, this prospective study will generate 'real-life' data reflecting clinical practice.

The trial will be performed in 26 large Dutch teaching centres, both academic and non-academic, with profound experience in one of the three minimally invasive techniques. To be eligible for participation, dedicated centres should have at least 75 TME procedures performed by the dedicated technique. Surgeons performing the procedure should have completed the learning curve, having performed at least 50 procedures of the dedicated technique. According to the standard procedure of the dedicated centre, L-TME will be performed in laparoscopic dedicated centres, R-TME in robot-assisted dedicated centres and TaTME in transanal dedicated centres. Patients that underwent another procedure than the standard technique of the dedicated centre (eg, L-TME in a centre dedicated to R-TME) will be included in an observational study group. These patients will be referred to as the 'non-dedicated' group.

In total, 1200 patients who are planned to undergo L-TME, R-TME or TaTME in dedicated centres will be recruited over a 2-year period. Recruitment is planned to start July 2021. Data collection will be performed by collaborating with existing parties: the prospective Dutch ColoRectal Audit (DCRA) and the Prospective Dutch ColoRectal Cancer Cohort (PLCRC). Local hospitals will provide their local dataset of the DCRA for preoperative baseline characteristics (of patients both before and after receiving neoadjuvant therapy) and short-term outcomes. PLCRC will collect questionnaires regarding quality of life, functional outcomes, cost-effectiveness outcomes and long-term oncological outcomes.

Patient recruitment and consent

All patients planned to undergo L-TME, R-TME or TaTME in participating dedicated centres will be assessed for inclusion in the VANTAGE trial. For study participation, a subject must meet the following criteria:

- Adult patient aged ≥18 years.
- Registered in the DCRA database.

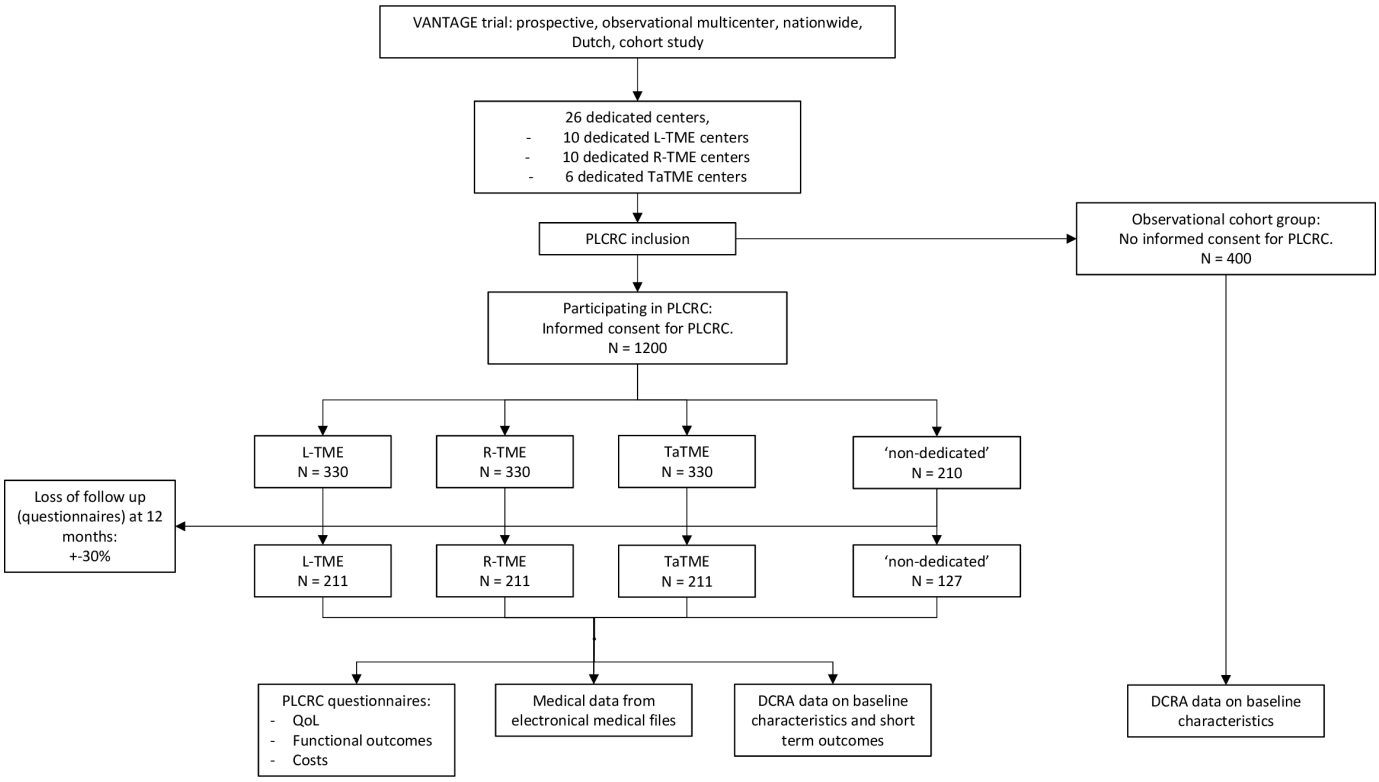

Figure 1 Flow chart of patients participating in the Vantage trial including patients in the observational cohort group. TME performed using a 'non-dedicated' technique for a specific centre. DCRA, Dutch ColoRectal Audit; L-TME, laparoscopic TME; PLCRC, Prospective Dutch ColoRectal Cancer Cohort; QoL, quality of life; R-TME, robot-assisted TME; TaTME, transanal TME; TME, total mesorectal excision.

- Diagnosed with rectal cancer defined as the lower border of the tumour under the sigmoidal take off.[26]
- Undergoing elective and curative minimally invasive TME in a dedicated centre.

There are no predefined exclusion criteria. Local research nurses or surgical residents in participating hospitals will coordinate identification of patients eligible to participate in the PLCRC, a prospective cohort study. The PLCRC is currently including patients in all participating hospitals. Patients eligible for inclusion will be informed by the local surgical resident or research nurse, under supervision of a consulting surgeon, in the outpatient clinic prior to elective hospitalisation for surgical rectal resection. Patients willing to participate will be asked to sign the informed consent form (ICF). If patients sign the ICF, and are included in PLCRC, they are automatically included in the VANTAGE trial. Additionally, patients who are not willing to participate will be registered, to allow for assessment of the representativeness of the included patients.

Outcomes

The primary endpoint will be health-related quality of life based on the Physical Functioning score of the European Organization for Research and Treatment for Cancer (EORTC) Quality of Life Questionnaire-Core questionnaires (QLQ-C30)[27 28] at 1 year following L-TME, R-TME or TaTME.

The following secondary endpoints will be assessed:

- Quality of life outcomes: emotional, social and symptom status.
- Functional outcomes: sexual, urogenital and defecation status.
- Economic analysis: total costs, cost–utility and cost-effectiveness.
- Short-term outcomes: perioperative, postoperative and histopathological outcomes.
- Long-term oncological outcomes: overall survival, disease-free survival, local recurrence and systematic recurrence.
- Long-term stoma outcomes: stoma-related complications, permanent stoma rate, readmission, reintervention.

Data collection

Data will be collected prospectively in collaboration with the DCRA and PLCRC (figure 2).

PLCRC will provide the current study with:

- Quality of life outcomes, collected through EORTC-QLQ-C30 questionnaire and EORTC-QLQ-ColoRectal Cancer module-29[28] sent at baseline, 3, 6, 12, 18 and 24 months postoperative. This data will include: all quality of life endpoints.
- Functional outcomes, collected through LARS Questionnaire,[29] Macoy Female Sexuality Questionnaire,[30] International Index of Erectile Function,[31] Urogenital

	Collected at time									
	Screening	Baseline	Surgery	3m	6m	12m	18m	24m	36m	60m
Informed consent	X									
Demographics	X									
Surgeon's experience	X									
Center's experience	X									
(Pre-)operative assessment										
Preoperative assessment (MRI)		X								
Preoperative treatment (neoadjuvant)		X								
Intra-operative characteristics			X							
Post-operative characteristics				X						
Pathological characteristics				X						
Quality of life questionnaires										
QLQ-C30		X		X	X	X	X	X		
QLQ-CR29		X		X	X	X	X	X		
EQ-5D		X		X	X	X	X	X		
Functional questionnaires										
LARS		X		X	X	X	X	X		
MSFQ		X		X	X	X	X	X		
IIEF		X		X	X	X	X	X		
UDI-6		X		X	X	X	X	X		
IIQ-7		X		X	X	X	X	X		
Costs										
Total costs			X	X	X	X		X	X	X
WAI		X		X	X	X	X	X		
iMCQ				X	X	X	X	X		
Long term outcomes										
Overall survival									X	X
Disease free survival									X	X
Local recurrence									X	X
Systemic recurrence									X	X
Long term stoma complications & reinterventions/readmissions									X	X

Figure 2 Study schedule of questionnaires and data collected. DCRA, Dutch ColoRectal Audit; EQ-5D, EuroQol Five Dimensions Health Questionnaire; IIEF, International Index of Erectile Function; IIQ-7, Incontinence Impact Questionnaire; iMCQ, iMTA Medical Consumption Questionnaire; LARS, Low Anterior Resection Syndrome Questionnaire; MFSQ, Macoy Female Sexuality Questionnaire; PLCRC, Prospective Dutch ColoRectal Cancer Cohort; QLQ-C30, Quality of Life Questionnaire-Core questionnaire; QLQ-CR29, Quality of Life Questionnaire-ColoRectal Cancer module; UDI-6, Urogenital Distress Inventory; WAI, Work Ability Index.

Distress Inventory-6 and Incontinence Impact Questionnaire-7[32] sent at baseline, 3, 6, 12, 18 and 24 months postoperative. This data will include: all functional endpoints.

- Cost-effectiveness and cost–utility outcomes, collected through the EuroQol Five Dimensions Health Questionnaire (EQ-5D)[33] and the Work Ability Index (WAI)[34] at baseline, 3, 6, 12, 18 and 24 months postoperative. And through the iMTA medical consumption questionnaire (iMCQ) at 3, 6, 12, 18 and 24 months postoperative.
- Long-term oncological and stoma outcomes,collected at three and 5 years postoperative. These data will include: stoma characteristics, recurrence and survival.

The DCRA will provide the current study with:

1. Short-term outcomes and baseline characteristics, collected at 90 days postoperative. These data will include: patient characteristics (demographics, comorbidity, history and complications), imaging characteristics (tumour location and cTNM staging), perioperative characteristics (strategy, (neo)adjuvant therapy, length of stay and mortality) and histopathological characteristics (tumour type, (yp)stage, lymph node involvement, radical resection and quality of TME).

Also, this study will collect additional data of patients included in the VANTAGE trial that is not provided through PLCRC or DCRA:

- Patient characteristics: previous (transanal) resections and stoma type prior to surgery.
- Preoperative characteristics: tumour distance on colonoscopy, clinical staging subclassification and location of metastasis.
- Imaging characteristics including preoperative and postneoadjuvant CT/MRI imaging: sigmoidal take-off,[26] low rectal tumours defined according to the English Low Rectal Cancer Development Programme (LOREC) definition[35] and ycTNM staging.
- Treatment characteristics: intent of therapy, wait and see approach and reasons for not using the dedicated technique.

- Perioperative characteristics: number of teams operating (TaTME), dedicated operating theatre assistants and type of Da Vinci used (R-TME), reason for conversion, surgical timestamps, anastomosis type and configuration.
- Long-term oncological and stoma outcomes: anastomotic leakage (type and grade), readmissions, reinterventions and cause of death.

Definitions and grades

Preoperative morbidity was graded according to the American Society of Anesthesiologists' (ASA) classification of Physical Health.[36] Serious preoperative morbidity was defined as having ASA-score of ≥3. Postoperative complications were graded according to the Clavien-Dindo classification.[37] Major complications were defined as complications with Clavien-Dindo grade III–V. Low rectal cancer was defined according to the LOREC definition as an adenocarcinoma with its lower edge at, or below, the origin of the levators on the pelvic sidewall.[35] The sigmoidal take-off is an anatomic, image-based definition of the junction of the mesorectum and mesocolon and can be identified as the mesocolon elongates as the ventral and horizontal course of the sigmoid on axial and sagittal views respectively on cross-sectional imaging.[26] Quality of TME will be assessed using a three-tiered classification consisting of complete, nearly complete and incomplete TME.[38] Overall survival will be defined as being alive follow-up. Disease-free survival will be defined as being alive without recurrent disease at follow-up. Local recurrence will be defined as tumour deposit located in the pelvic cavity, with pathological proven adenocarcinoma, or growth on consecutive imaging if histopathological confirmation was absent. Systematic recurrence will be defined as any distant metastasis, either pathologically proven or as a lesion suspect for metastasis on imaging that showed growth on consecutive imaging. Location of local recurrence will be classified according to the classification by Georgiou *et al*.[39] Anastomotic leakage will be registered until 1-year postoperative, defined and graded according by the International Study Group of Rectal Cancer.[40]

Statistical analysis

Sample size calculation

The sample size of the prospective cohort regarding the three minimally invasive techniques was determined based on a clinically meaningful difference of 5 points on the Physical Functioning score of the EORTC QLQ-C30 questionnaire.[41 42] The power calculation was performed taking into account difference in independent means, an SD of 15, a power of 0.90 and a two-sided interval.[43 44] This resulted in a total of 211 patients required within each group. Based on results of our soon published retrospective cohort study, we estimate 15%, 15% and 30% of the patients in, respectively, the L-TME, R-TME and TaTME centres will not undergo the standard technique of the dedicated centre ('non-dedicated' group). Therefore, we will include 127 patients in the 'non-dedicated' group. Taking into account a 30% lost to follow-up of questionnaires at 12 months, we will enrol 1200 patients in this study. Accounting for a 75% inclusion rate (as is for PLCRC at the time of writing), 1500 patients need to be screened. Since we expect that each centre would perform around 40 procedures per year, we expect that in the Dutch centres 400 L-TME, 400 R-TME and 240 TaTME patients will be screened within 1 year. Therefore, in order to enrol all necessary patients we expect to include patients for 2 years.

Comparative analysis

Analysis will be performed with support of an experienced statistician. Categorical or dichotomous outcomes will be presented as absolute numbers and percentages. Descriptive outcomes will be reported as median with IQR or mean with SD. A three-arm analysis will be performed for the different primary and secondary outcomes. Additionally, pairwise comparisons of the 'non-dedicated' group with L-TME, R-TME and TaTME will be performed.

Quality of life and functional outcomes analysis

To compare between group differences of quality of life questionnaires and functional results questionnaires at different time points, linear mixed-effects models will be used to take into account the intrasubject correlation between the repeated measurements. Two years was chosen, since factors known to influence quality of life and functional outcomes following TME only rarely occur after this period.

Short-term and long-term outcomes analysis

Depending on the distribution univariate analyses will be done using independent sample t-test and Mann-Whitney U test for independent data. The dependent sample t-test and the signed rank test will be used for non-normally distributed paired data. The χ^2 test or Fisher's exact test will be used for unpaired binary and categorical data.

Economic analyses

For the economic analyses of the three techniques, cost–utility and cost-effectiveness will be assessed using a lifelong time horizon, with modelling of results after 2 years. Modelling after 2 years was chosen, since factors known to influence utility or costs following TME only rarely occur after this period. Comparison will be done using pairwise comparison between the techniques. The economic analyses will be performed according to the Dutch guideline regarding economic evaluations in healthcare.[45]

Cost–utility analysis

Cost differences per technique will be analysed and compared with gained utility (in QALY). Cost data will be assessed using a bottom up micro costing approach, the electronic patient record, iMCQ, WAI, EQ-5D and the financial information system from participating centres. The cost utility analysis will be performed from a societal perspective and a lifelong time horizon.

Cost-effectiveness analysis

The incremental cost-effectiveness ratio will be calculated to represent cost differences between the three techniques relative to the difference in the proportion of patients with a particular outcome. Outcomes of interest will include, but are not limited to: permanent stoma rate, primary anastomosis, major morbidity (Clavien-Dindo >grade III) and length of stay.

Cost categories used and costs collected per category will include:

- Costs made in healthcare: theatre costs, hospitalisation costs, outpatient costs.
- Costs made by patients and family: transportation costs and healthcare materials payed by patients.
- Costs made by other institutions: productivity losses and rehabilitation costs.

Lost to follow-up or replacement of participants

Subjects can leave the study without consequences and no further follow-up will be performed. Patients who withdraw during the study will not be replaced and are not likely to jeopardise study power as sample size calculation accounted for a loss to follow-up of 30%. Analysis will be done according to the 'intention-to-treat' principle. Lost to follow-up will be assessed for bias, and intention-to-treat analysis will be performed.

Patient and public involvement

This study protocol was written in accordance with the GRIPP2 reporting guidelines.[46] Patients and patient organisations were involved as research partners in all aspects of the development of this study protocol and actively contributed to identifying the lack of understanding, the need for evidence, and the research question. Patients and patient organisations will remain involved throughout all execution phases of the research and provide feedback on the results to ensure findings are presented to directly benefit patients. Results will be disseminated through a collaboration with the patient organisations, ensuring results of this study adjusted for a non-specialist audience reach the intended patient population.

Data management and missing data

All data will be collected in the secure online database CASTOR (www.castoredc.com). Data will be handled in compliance with the Dutch Medical Treatment Agreement Act (WGBO) and patients will be pseudonymised. Analysis will be performed to assess quality and completeness of data. Discrepancies and missing data will be reported back to participating centres to be clarified by the local investigator. All data and documents will be stored on a password-protected hospital network drive for a minimum of 15 years.

ETHICS AND DISSEMINATION

The VANTAGE trial will collect data in two groups of pseudonymised patients:

- This study will, from patients included in PLCRC: (1) receive questionnaires sent by PLCRC regarding quality of life, functional outcomes and costs; (2) receive relevant medical data from the patients' electronic medical file (this includes the patients' DCRA data). Patients included in PLCRC provided informed consent for this data to be collected and shared in the context of scientific research. Approval from the regional medical ethical committee of the University Medical Centre Utrecht (METC), and approval from the local medical ethical committees of all participating centres has been obtained (see online supplemental file A).
- This study will, from patients not included in PLCRC, collect DCRA data regarding baseline characteristics. These patients did not provide informed consent. For this part of data collection, informed consent has been waived, and approval by the regional medical ethical committee of the University Medical Centre Groningen (METC) has been obtained. Using this data a comparison can be made regarding the baseline characteristics of the patients included in the PLCRC cohort, and those not included in PLCRC. Therefore, these data are essential to assess the representativeness of the included PLCRC patients in the cohort compared with the total of patients receiving TME in participating dedicated centres.

This trial will be conducted in accordance with the principles of the Declaration of Helsinki and Good Clinical Practice. Patients are not at any increased risk as all three minimally invasive techniques are currently performed as standard of practice and patient burden is deemed low as patients are only required to fill in questionnaires. Findings of the VANTAGE trial will be disseminated to all disciplines involved in care for rectal cancer surgery, through articles in peer-reviewed journals, national and international oncology meetings.

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Acknowledgements We would kindly like to thank participating patient organisations and all collaborators of the MIRECA (Minimally Invasive RECtal CArcinoma surgery) study group for their participation in the development of this study project and protocol.

Collaborators MIRECA study group: G.J.D. van Acker, T.S. Aukema, H.J. Belgers, F.H. Beverdam, J.G. Bloemen, K. Bosscha, S.O. Breukink, P.P.L.O. Coene, R.M.P.H. Crolla, P. van Duijvendijk, E.B. van Duyn, I.F. Faneyte, S.A.F. Fransen, A.A.W. van Geloven, M.F. Gerhards, W.M.U. van Grevenstein, K. Havenga, I.H.J.T. de Hingh, C. Hoff, G. Kats, J.W.A. Leijtens, M.F. Lutke Holzik, J. Melenhorst, M.M. Poelman, A. Pronk, A.H.W. Schiphorst, J.M.J. Schreinemakers, C. Sietses, A.B. Smits, I Somers, E.J. Spillenaar Bilgen, H.B.A.C. Stockmann, A.K. Talsma, P.J. Tanis, J.

Tuynman, E.G.G. Verdaasdonk, F.A.R.M. Warmerdam, H.L. van Westreenen, D.D.E. Zimmerman.

Contributors Substantial contributions to the conception and design of the work: RG, TB, RH, DZ, MD, MP, AR, PV and EC. Drafting the article: RG and TB. Revising the article critically for important intellectual content: RH, DZ, MD, MP, AR, PV and EC. Final approval of the version to be published: RG, TB, RH, DZ, MD, MP, AR, PV and EC. All authors agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The MIRECA Taskforce for Minimally Invasive Rectal Carcinoma surgery consists of all local investigators responsible for patient recruitment in their respective centres. They all provided insight and feedback during the conception and design of the work.

Funding This work was supported by Intuitive Surgical grant number (V20201105).

Competing interests EC is proctor for Intuitive Surgical and (financial) support from this organisation has been received for the submitted manuscript. All other authors declare: no support from any organisation for the submitted work; no financial relationships with organisations that may have an interest in the submitted work in the previous 3 years; and no other relationships or activities that could appear to have influenced the submitted work.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

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REFERENCES

1 Heald RJ, Husband EM, Ryall RD. The mesorectum in rectal cancer surgery--the clue to pelvic recurrence? *Br J Surg* 1982;69:613–6.
2 Massarotti H, Wexner SD. *Laparoscopic exposure of critical anatomy in rectal cancer surgery: techniques and examples*. Japan: Springer, 2018.
3 Rubinkiewicz M, Zarzycki P, Witowski J, *et al*. Functional outcomes after resections for low rectal tumors: comparison of transanal with laparoscopic total mesorectal excision. *BMC Surg* 2019;19:79.
4 van der Pas MH, Haglind E, Cuesta MA, *et al*. Laparoscopic versus open surgery for rectal cancer (color II): short-term outcomes of a randomised, phase 3 trial. *Lancet Oncol* 2013;14:210–8.
5 Kang S-B, Park JW, Jeong S-Y, *et al*. Open versus laparoscopic surgery for mid or low rectal cancer after neoadjuvant chemoradiotherapy (COREAN trial): short-term outcomes of an open-label randomised controlled trial. *Lancet Oncol* 2010;11:637–45.
6 Stevenson ARL, Solomon MJ, Lumley JW, *et al*. Effect of laparoscopic-assisted resection vs open resection on pathological outcomes in rectal cancer: the ALaCaRT randomized clinical trial. *JAMA* 2015;314:1356–63.
7 Fleshman J, Branda M, Sargent DJ, *et al*. Effect of Laparoscopic-Assisted resection vs open resection of stage II or III rectal cancer on pathologic outcomes: the ACOSOG Z6051 randomized clinical trial. *JAMA* 2015;314:1346–55.
8 Jayne DG, Guillou PJ, Thorpe H, *et al*. Randomized trial of laparoscopic-assisted resection of colorectal carcinoma: 3-year results of the UK MRC CLASICC trial group. *J Clin Oncol* 2007;25:3061–8.
9 Borstlap WAA, Westerduin E, Aukema TS, *et al*. Anastomotic leakage and chronic presacral sinus formation after low anterior resection. *Ann Surg* 2017;266:870–7.
10 Siegel R, Desantis C, Jemal A. Colorectal cancer statistics, 2014. *CA Cancer J Clin* 2014;64:104–17.
11 Lange MM, van de Velde CJH. Urinary and sexual dysfunction after rectal cancer treatment. *Nat Rev Urol* 2011;8:51–7.
12 Costa P, Cardoso JM, Louro H, *et al*. Impact on sexual function of surgical treatment in rectal cancer. *Int Braz J Urol* 2018;44:141–9.
13 Couwenberg AM, de Beer FSA, Intven MPW, *et al*. The impact of postoperative complications on health-related quality of life in older patients with rectal cancer; a prospective cohort study. *J Geriatr Oncol* 2018;9:102–9.
14 Downing A, Glaser AW, Finan PJ, *et al*. Functional outcomes and health-related quality of life after curative treatment for rectal cancer: a population-level study in England. *Int J Radiat Oncol Biol Phys* 2019;103:1132–42.
15 Burghgraef TA, RMPH C, Verheijen PM. Robot-assisted total mesorectal excision versus laparoscopic total mesorectal excision: a retrospective propensity score matched cohort analysis in experienced centres, 2020. Available: https://onlinelibrary.wiley.com/doi/full/10.1111/codi.15332
16 Hol JC, Burghgraef TA, Rutgers MLW, *et al*. Comparison of laparoscopic versus robot-assisted versus transanal total mesorectal excision surgery for rectal cancer: a retrospective propensity score-matched cohort study of short-term outcomes. *Br J Surg* 2021;108:1380–7.
17 Grass JK, Perez DR, Izbicki JR, *et al*. Systematic review analysis of robotic and transanal approaches in Tme surgery- a systematic review of the current literature in regard to challenges in rectal cancer surgery. *Eur J Surg Oncol* 2019;45:498–509.
18 Detering R, Roodbeen SX, van Oostendorp SE, *et al*. Three-Year nationwide experience with transanal total mesorectal excision for rectal cancer in the Netherlands: a propensity score-matched comparison with conventional laparoscopic total mesorectal excision. *J Am Coll Surg* 2019;228:235–44.
19 Emmertsen KJ, Laurberg S. Low anterior resection syndrome score: development and validation of a symptom-based scoring system for bowel dysfunction after low anterior resection for rectal cancer. *Ann Surg* 2012;255:922–8.
20 Kamali D, Reddy A, Imam S, *et al*. Short-Term surgical outcomes and patient quality of life between robotic and laparoscopic extralevator abdominoperineal excision for adenocarcinoma of the rectum. *Ann R Coll Surg Engl* 2017;99:607–13.
21 Veltcamp Helbach M, Koedam TWA, Knol JJ, *et al*. Quality of life after rectal cancer surgery: differences between laparoscopic and transanal total mesorectal excision. *Surg Endosc* 2019;33:79–87.
22 Panteleimonitis S, Ahmed J, Harper M, *et al*. Critical analysis of the literature investigating urogenital function preservation following robotic rectal cancer surgery. *World J Gastrointest Surg* 2016;8:744.
23 Corrigan N, Marshall H, Croft J, *et al*. Exploring and adjusting for potential learning effects in ROLARR: a randomised controlled trial comparing robotic-assisted vs. standard laparoscopic surgery for rectal cancer resection. *Trials* 2018;19:339.
24 Morelli L, Di Franco G, Lorenzoni V. Structured cost analysis of robotic TME resection for rectal cancer: a comparison between the da Vinci Si and Xi in a single surgeon's experience. *Surg Endosc Other Interv Tech* 2018;0.
25 Rockall TA. Transanal total mesorectal excision: the race to the bottom. *Br J Surg* 2021;108:3–4.
26 D'Souza N, de Neree Tot Babberich MPM, d'Hoore A, *et al*. Definition of the rectum: an international, Expert-based Delphi consensus. *Ann Surg* 2019;270:955–9.
27 Aaronson NK, Ahmedzai S, Bergman B, *et al*. The European organization for research and treatment of cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst* 1993;85:365–76.
28 Stiggelbout AM, Kunneman M, Baas-Thijssen MCM, *et al*. The EORTC QLQ-CR29 quality of life questionnaire for colorectal cancer: validation of the Dutch version. *Qual Life Res* 2016;25:1853–8.
29 Hupkens BJP, Breukink SO, Olde Reuver Of Briel C, *et al*. Dutch validation of the low anterior resection syndrome score. *Colorectal Dis* 2018;20:881–7.
30 McCoy NL. The McCoy female sexuality questionaire. *Qual Life Res* 2000;9:739–45.
31 Rosen RC, Riley A, Wagner G, *et al*. The International index of erectile function (IIEF): a multidimensional scale for assessment of erectile dysfunction. *Urology* 1997;49:822–30.

32 Utomo E, Korfage IJ, Wildhagen MF, *et al*. Validation of the urogenital distress inventory (UDI-6) and incontinence impact questionnaire (IIQ-7) in a Dutch population. *Neurourol Urodyn* 2015;34:24–31.
33 Devlin NJ, Brooks R. EQ-5D and the EuroQol group: past, present and future. *Appl Health Econ Health Policy* 2017;15:127–37.
34 Ilmarinen J, Tuomi K, Klockars M. Changes in the work ability of active employees over an 11-year period. *Scand J Work Environ Health* 1997;23 Suppl 1:49–57.
35 Moran BJ, Holm T, Brannagan G, *et al*. The English national low rectal cancer development programme: key messages and future perspectives. *Colorectal Dis* 2014;16:173–8.
36 Daabiss M. American Society of Anaesthesiologists physical status classification. *Indian J Anaesth* 2011;55:111–5.
37 Dindo D, Demartines N, Clavien P-A. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004;240:205–13.
38 Nagtegaal ID, van de Velde CJH, van der Worp E, *et al*. Macroscopic evaluation of rectal cancer resection specimen: clinical significance of the pathologist in quality control. *J Clin Oncol* 2002;20:1729–34.
39 Georgiou PA, Tekkis PP, Constantinides VA, *et al*. Diagnostic accuracy and value of magnetic resonance imaging (MRI) in planning exenterative pelvic surgery for advanced colorectal cancer. *Eur J Cancer* 2013;49:72–81.
40 Rahbari NN, Weitz J, Hohenberger W, *et al*. Definition and grading of anastomotic leakage following anterior resection of the rectum: a proposal by the International Study group of rectal cancer. *Surgery* 2010;147:339–51.
41 Fayers PM*et al*. Eortc QLQ-C30 scoring manual the EORTC QLQ-C30 introduction. *EORTC QLQ-C30 Scoring Man* 2001;30:1–67.
42 Cocks K, King MT, Velikova G, *et al*. Evidence-Based guidelines for determination of sample size and interpretation of the European organisation for the research and treatment of cancer quality of life questionnaire core 30. *J Clin Oncol* 2011;29:89–96.
43 Van Engelen E. Uitgebreide toelichting van Het meetinstrument European organization for research and treatment for cancer quality of life questionnaire (EORTC QLQ-C30). *EJCM Swinkels-Meewisse* 2013:1–8.
44 Couwenberg AM, Burbach JPM, Intven MPW, *et al*. Health-Related quality of life in rectal cancer patients undergoing neoadjuvant chemoradiation with delayed surgery versus short-course radiotherapy with immediate surgery: a propensity score-matched cohort study. *Acta Oncol* 2019;58:407–16.
45 Hakkaart L, van der Linden N, Bouwmans C. Richtlijn voor Het uitvoeren van economische evaluaties in de gezondheidszorg. *Zorginstituut Ned* 2016;120.
46 Staniszewska S, Brett J, Simera I. GRIPP2 reporting checklists: tools to improve reporting of patient and public involvement in research. *BMJ* 2017;358:3453.