Valorization
Colorectal cancer is the second most frequent type of cancer in male and third most common malignancy in women. Rectal cancer mainly affects middle-aged and elderly individuals, with more than 75% of patients being diagnosed at age 60 years or older. Nevertheless, also younger patients, under 40 years of age, are increasingly affected. The rectum is localized in the pelvis and is surrounded by uro- and genital organs. To date, the only curative treatment for rectal cancer is surgery, although improvements are made with less invasive approaches (e.g. wait and see). In early stage rectal cancer (cT1-T2), less invasive treatment is possible with local tumor resection (e.g. transanal endoscopic microsurgery (TEM)). In case of more advanced disease (cT2+/N+), neo-adjuvant radiotherapy and total mesorectal excision (TME) surgery is needed in order to achieve curation. In case of locally advanced disease (LARC), the tumour involves surrounding structures and intensified treatment regimens are needed to downsize the tumor. If after neo-adjuvant treatment, the tumor still invades the surrounding structures, extended resections are needed with an en-bloc removal of the affected organs. This often results in a colo- and/or urostomy. In addition, with removal of genital organs, these resections affect urologic and sexual function. But also in non-advanced disease stage (T2+), urologic and sexual dysfunction is seen after surgery. For both the clinician and the patient, knowledge on the influence of treatment strategies on patients’ health related quality of life (HRQL) is extremely important. Nowadays, patient-reported outcome and quality of life are increasingly important. However, the last decades research on primary or recurrent rectal cancer focused primarily on improving oncological outcome. In addition, HRQL was not actively discussed during the past international expert consensus meetings. The current approach to rectal cancer requires knowledge of the influence of the treatment, on the patients’ HRQL. Patients need to be well informed about the choices that can be made regarding their treatment and they should participate actively in the decision making process. In this thesis, the effect of tumour stage and subsequent treatment, extent of surgery and influence of a permanent stoma on HRQL was investigated. In general, we can conclude that despite the intensive treatment regimens and major surgery these patients have to endure, their HRQL after treatment can be considered good. In addition, a permanent stoma does not influence HRQL in a negative way. In patients with a low rectal tumor, who will suffer more from the complications or functional problems of a low anastomosis, a permanent stoma needs to be discussed prior to surgery. Especially in frail or elderly patients, a permanent stoma is feasible while maintaining a good HRQL.

The negative impact of curative treatment on sexual function, as found in this thesis, calls for further attention and awareness to alleviate this problem in sexually active patients. For optimal consultation, sexual dysfunction due to surgery should be actively discussed during a patients visit.

With the use of data from the Netherlands Cancer Registry, age related differences in treatment and outcome were investigated in this thesis. Young patients are less
commonly seen during daily practice and less research on tumor characteristics and outcome of treatment in this particular patient group is available. We observed that young patients present with more advanced stage of disease and have more unfavourable tumor characteristics compared to middle aged-aged patients. Despite these unfavourable characteristics, survival rates are equal and young age is even a prognosticator for better survival. Young patients received adjuvant chemotherapy more often compared to middle-aged patients. This was associated with improved survival in young patients with pN1 or stage III disease. Nevertheless, the additional survival benefit of adjuvant chemotherapy has to be interpreted with caution, and further research will be needed to assess the effect of adjuvant chemotherapy in young rectal cancer patients. Elderly patients are at risk of not being treated according to the national guidelines. They are a difficult heterogeneous group of patients with often multiple comorbidities and often poor clinical condition. Due to their age and physical condition, they are more often treated with a non-curative intent. Furthermore, they are also underrepresented in clinical studies and current guidelines do not focus on elderly patients. Therefore, evidence on how to treat the elderly patient with rectal cancer is scarce.

Little is known about how elderly patients with LARC or LRRC endure intensive treatment regimens including, neo-adjuvant therapy followed by major rectal surgery and multi-visceral resections. In our study, including only LARC or LRRC patients, morbidity was high regardless of age in LARC patients. In LRRC, differences in morbidity were observed but were not statistically different. One-month mortality was equal for both treatment groups and regardless of age. However, after one year, an almost threefold increase in mortality was observed in elderly LARC patients compared to younger LARC patients. A similar increase in mortality was seen in LRRC patients, but this was not age related. This study highlights that elderly patients can be treated according to the guidelines with neo-adjuvant treatment and major surgery, but improvements are needed in patient selection or (pre/re)habilitation programs in order to lower the one-year post-operative mortality. Particularly in advanced cases there is enough time for optimizing the patient prior to surgery in the interval between neo-adjuvant treatment and definitive surgery. Future studies focusing on the role of a pre-habilitation program during the waiting period on post-operative outcome in elderly with LARC and LRRC cases are warranted.

This thesis has addressed several issues in HRQL and morbidity of treatment between various age groups. We were not able to detect major differences in quality of life with general HRQL questionnaires. Future research should focus more on the differences between pre- and post-treatment HRQL and the influence of sexual support on general HRQL. Furthermore adequate selection of elderly patients with awareness of the
morbidity of this locally progressive disease in relation to the impact of surgery on morbidity and mortality could improve outcome and quality of life.

Finally, the modern approach to rectal cancer should be a more individualised approach. Driven by international guidelines, the physicians do not only need to inform their patients on the different treatment possibilities, oncological outcome and morbidity, but also on the influence of treatment on HRQL. This thesis provides insight in age related differences in rectal cancer treatment and HRQL after treatment. It provides an insight in a more individualised treatment approach for daily practice. We should not only focus on optimal oncological outcome but also on functional results and subsequent quality of life of our patients after treatment. Ultimately, the optimal strategy in rectal cancer treatment should be shared decision making.