Purpose of review
To study the recent literature on health-related quality of life (HRQOL) in patients after radical cystectomy followed by urinary diversion.

Recent findings
General consensus regarding which urinary diversion is superior in terms of HRQOL has not been reached. Although there is an increase in studies favoring the orthotopic neobladder, overall quality of these studies is poor. Other studies suggest that HRQOL outcomes in different types of urinary diversions is similar and that other factors, such as age, comorbidities and sex are more important instead. Patient choice, in consultation with the treating surgeon should be the determinant of which urinary diversion is performed. Furthermore, sexual function can play an important role in HRQOL. However, practice shows that counselling on the option of sexual-preserving techniques is still not implemented in routine clinical practice. Furthermore, studies regarding differences in HRQOL after urinary diversion between male and female individuals are lacking.

Summary
Thorough preoperative counselling on the different types of urinary diversion and options for sexual-preserving techniques decreases decision regret and increases HRQOL in patients after radical cystectomy.

Keywords
health-related quality of life, ileal conduit, orthotopic neobladder, radical cystectomy, urinary diversions

INTRODUCTION
Radical cystectomy followed by urinary diversion is the golden standard for treatment of muscle invasive bladder cancer (MIBC) and in selected patients with high-risk nonmuscle invasive bladder cancer (NMIBC) [1]. In some cases, functional disorders and/or congenital anomalies are also indications for urinary diversion with or without cystectomy. Over the years, a variation of continent and incon tinent urinary diversions have been developed and described. However, nowadays the ileal conduit and orthotopic neobladder (ONB) are the most commonly utilized urinary diversions following cystectomy [2]. General consensus on which urinary diversion gives the best outcomes in terms of health-related quality of life (HRQOL) has not been reached. This is partly as high-level evidence is still lacking [3,4]. Studies on HRQOL after radical cystectomy often have methodological limitations like small sample size and a retrospective and cross-sectional design. However, in recent years, there is an increase in prospective studies regarding patients with MIBC. Also the number of studies using validated questionnaires specifically for HRQOL in MIBC or after radical cystectomy, like the EORTC-QLQ-BLM30 and FACT-VCI is increasing. This has improved the overall quality of the studies [5]. In the current review, we study the recent literature on HRQOL in patients with an ileal conduit or ONB following cystectomy. We will also examine other
There is no general consensus on which urinary diversion is superior in terms of HRQOL.

Recent studies tend to favor the orthotopic neobladder over the ileal conduit but overall quality of these studies is poor.

Independent factors, such as age, comorbidities and sex might play a more important role in HRQOL after cystectomy than the type of urinary diversion.

Sexual function can play an important role in HRQOL but urologists do not routinely discuss options for sexual-preserving radical cystectomy.

Thorough preoperative counselling on different types of urinary diversion and sexual-preserving techniques decreases decision regret and increases HRQOL in patients after radical cystectomy.

factors than the type of urinary diversion, which can affect HRQOL in these patients.

ORTHOTOPIC NEOBLADDER AND ILEAL CONDUIT

The ileal conduit and ONB are the two most commonly performed types of urinary diversion after radical cystectomy. Neither urinary diversion has consequences for oncological outcomes but they bring their own advantages and disadvantages. With the ONB – being a continent diversion – patients can keep the ability to void via the urethra. However, as the neobladder is lacking muscles and innervation, it requires extensive bladder-training and lifestyle changes in order to adapt to the new bladder.

Studies report long-term complications like diurnal and nocturnal incontinence in 8–10 and 20–30%, respectively [5,6]. In some cases, there is need for clean intermittent self-catheterization (CISC) because of hyper continence. On the other hand, the ileal conduit – an incontinent diversion – comes with a urostomy, which can affect body image and comes with specific problems. Early complications like urinary tract infections (UTI), pyelonephritis and stenosis appear in about 45% of patients with an ileal conduit. With longer follow-up, complication rates can increase to up to 94% [7,8]. After a follow-up of 15 years, upper urothelial tract (UTI) changes and urolithiasis are seen in 50 and 38% of the patients, respectively [7,8].

Therefore, ONB is often performed on the younger and fitter patients, although Cerruto et al. [9] observed in 2018 that ONB might be a good option in the elderly patient as well. Comparing ONB and ileal conduit after radical cystectomy in patients over 75 years of age, no significant difference was found regarding HRQOL. Moreover, ONB had better results in other aspects like cognitive functioning and bowel function.

In general, consensus on which urinary diversion is superior in terms of HRQOL has not been reached. Some recent studies tend to lean towards the ONB, as shown in a systematic review performed by Ghosh and Somani [10]. In this study a trend was noticed favoring ONB when looking at studies from the last 5 years. More recently, an umbrella review by Rammant et al. found six systematic reviews, including three meta-analysis that showed a higher HRQOL in patients with ONB compared with ileal conduit.

Benefits for neobladder patients were reported for overall HRQOL, physical functioning, sexual functioning, social functioning and self-image. However, age, gender, type of questionnaire and follow-up time were important factors when interpreting the results.

Strikingly, in the same study, six other systematic reviews did not find a difference in HRQOL between diversions. Rammant et al. [4*] also noticed that most recent reviews showed better overall and physical HRQOL outcomes in patients with ONB, whereas ileal conduit patients showed better urinary function in comparison with ONB patients. Nevertheless, the quality assessment – using the AMSTAR 2 tool [10] – showed an overall poor quality of the included reviews.

As mentioned before, studies regarding HRQOL after radical cystectomy often have methodological limitations. Examples of these are a small sample size, a cross-sectional design and poor confounding control. In retrospective studies, there is no data on the preoperative HRQOL status of the patient. As the preoperative status of the patients affects the choice for diversions – for example, ileal conduit is more often performed in patients with comorbidities and lower life expectancy – baseline HRQOL between diversion groups can differ greatly. This affects HRQOL outcomes after urinary diversion and as a result, these studies are prone to selection bias. Also, cross-sectional studies only measure HRQOL at one point in time at unequal intervals from the date of operation. As HRQOL after radical cystectomy in ileal conduit and ONB patients gradually increases in the first year postoperative, measuring at unequal intervals can give different results in the same patient [11,12*]. Finally, studies comparing outcomes of different urinary diversions are nonrandomized. Consequently, the quality of the evidence
is insufficient to draw firm conclusions on which urinary diversion is the best in terms of HRQOL.

Interestingly, in a prospective longitudinal study on 146 patients with ileal conduit, ONB or Indiana pouch by Kern et al. [12*], similar improvements in HRQOL across all diversion cohorts were found, even though patients who received an ileal conduit had a higher morbidity index score and a lower baseline HRQOL. This shows that, in these patients, the type of urinary diversion is not necessarily important for their HRQOL status but there are other factors that play a more important role.

Recently Catto et al. conducted a study with 1796 patients with bladder cancer, including 705 patients who received radical cystectomy with or without other treatments (chemotherapy, immunotherapy, radiotherapy).

This study reported large variations in HRQOL in bladder cancer patients, according to patient age and co-existing long-term conditions, rather than disease stage, treatment type or time since diagnosis [13*].

Likewise, in a study from Allareddy et al. on HRQOL, no major differences in long-term survivors of bladder cancer between patients after radical cystectomy and patients who still had their bladder intact, or between continent and conduit diversion groups were found. However, the presence of comorbid conditions lowered HRQOL independent of treatment [14]. In the earlier mentioned study of Cerruto et al. regarding urinary diversion in elderly patients, there was no difference in HRQOL between the urinary diversion subgroups. However, they did find that occurrence of long-term complications was an independent predictor of impaired emotional functioning, thus affecting HRQOL. Furthermore, Miyake et al. [15] and Autorino et al. [16] observed similar HRQOL outcomes in different ONB subgroups but both studies found older age being associated with worse HRQOL scores. These results suggest that factors, such as age and co-existing morbidities are more important factors regarding HRQOL than the type of urinary diversion a patient has undergone.

However, even when one type of urinary diversion is not necessarily superior in term of HRQOL in all patients, this does not mean that the type of urinary diversion an individual patient receives is irrelevant.

As choosing the right diversion for any one patient strongly depends on the values and preferences of that patient, proper preoperative counselling on the various types of urinary diversions is important. Yang et al. performed a systematic review and meta-analysis on QOL outcomes after radical cystectomy for MIBC, including 29 studies and 3754 patients. They found that HRQOL was comparable between continent and incontinent diversions and concluded that patient’s choice, in consultation with the treating surgeon, should be the determinant of urinary diversions. Other studies come to the same conclusion [3,16–19]. Unfortunately, as shown by McMullen et al. [20] in a qualitative study on patients after radical cystectomy, proper preoperative and postoperative counselling is not always self-evident. They found that patient perceptions about the benefits and disadvantages of different diversion types were not consistent. Moreover, they found that patients were often unaware of potential issues they might encounter with bowel function or other complications that can arise after surgery.

Furthermore, a recent longitudinal study regarding informed decision-making in patients who underwent radical cystectomy was performed by Check et al. This study showed that patients who believed that they are better informed preoperatively, experienced less regret of their decision both at 6 and 18 months after operation, independent of the selected bladder reconstruction method. In addition, they observed no independent association between occurrence of complications and decision regret in patients [21*]. It is known that decision regret is associated with poorer physical and psychological health and lower overall QOL [22]. Thus, showing that thorough preoperative counselling and shared decision-making are important factors that can influence HRQOL in patients after radical cystectomy.

**SEXUAL FUNCTION**

Sexual function can also play an important role in HRQOL in patients. While high-quality studies specifically comparing sexual function in different types of urinary diversion are lacking, radical cystectomy prior to urinary diversion is known to negatively affect sexual function in both men and women. Anatomical changes during surgery, such as partial vaginectomy and damaging of the neurovascular bundles or cavernous nerve can cause severe sexual disfunction [23]. Zippe et al. examined sexual function after radical cystectomy in 27 female patients and found that only 48% of the patients were able to have successful vaginal intercourse, with 52% reporting decrease in desire for sexual activity. The most common reported symptoms included inability to achieve orgasm in 45%, decreased lubrication in 41%, decreased sexual desire in 37% and dyspareunia in 22% [24]. Likewise, erectile dysfunction in men after radical cystectomy is reported in up to 89% of respondents [14].

However, in studies regarding HRQOL after radical cystectomy, problems in sexual function are often under-reported. In a study from Normann
et al. [25] questions regarding sexual functioning of men and women were answered in only 23 and 16%, respectively, thus the variable was not included in the analysis. Likewise, the above-mentioned study from Catto et al. [13] reported that question completeness was more than 95% except for items relating to sexual intimacy (39%), sexual enjoyment (36%) and female sexual problems (28%). Unfortunately, studies struggle with lack of reporting on sexual health after radical cystectomy [3,19,21,25].

Studies that do report on sexual functioning find that it plays an important role in HRQOL. Tostivint et al. showed that in patients with ONB, sexual dysfunction were the most frequently reported symptoms – determined only for patients who were sexually active – while urinary symptoms were the least reported. They also found that sexually active patients showed a significantly better QOL score compared with those being sexually inactive, also sexuality was the only independent factor related to QOL in the multivariate analysis [26]. Similarly Kretschmer et al. [27] showed that a high erectile function score and nerve-sparing were associated with better QOL in patients with ONB after radical cystectomy.

Nerve-sparing techniques have been shown to result in better preservation of sexual function after cystectomy than nonnerve-sparing techniques [28–31]. Additionally, last year, Westerman et al. [32] found that 53% of patients who underwent radical cystectomy still have interest in sexual activity. Unfortunately, 71 and 36% of urologists do not routinely discuss the potential for nerve-sparing cystectomy with female and male patients, respectively, shown by a recent study from Gupta et al. Also, they reported that 41.2% of providers did not routinely discuss the potential for pelvic organ-preserving radical cystectomy with sexually active female patients [33*]. Similarly, in a review by Voigt et al. on the influence of cystectomy on sexual function in female patients, multiple studies reported generally poor counselling on sex-sparing techniques. They also found that information regarding sexual side effects of the patients’ cancer and treatment was seriously lacking [34]. Although the American and European guidelines for MIBC recommend to offer sexual-preserving techniques to men and women [35,36], practice shows that this is still not implemented in routine clinical practice.

**HEALTH-RELATED QUALITY-OF-LIFE IN MALE AND FEMALE INDIVIDUALS**

Although high-quality studies regarding HRQOL after urinary diversion are lacking, this is especially true for studies regarding HRQOL in female individuals. It is known that complications, oncological outcomes and mortality are worse in female patients treated with radical cystectomy and one can imagine that these results also reflect on the HRQOL of female patients [37–39]. Nonetheless, as the majority of the bladder cancer patients is male, female individuals are often underrepresented, or left out entirely in studies on HRQOL after radical cystectomy [40–42]. Fortunately, in recent years, there is an increase in studies on HRQOL with more emphasis on the female patient.

In 2018, Siracusano compared HRQOL after radical cystectomy with ileal conduit in 112 male and 33 female patients and found that women scored significantly worse than men in questions regarding their cognitive functioning and future perspective. On the other hand, less problems in sexual functioning were reported, although the study did not report if any sex-sparing techniques were used [42]. In contrast, Westerman et al. [32] found that the female gender was independently associated with worse scores in sexual function. Likewise, in the earlier mentioned study on elderly patients from Cerruto et al. [9] being female was independently associated with lower HRQOL after radical cystectomy.

Regarding different types of urinary diversion, another study from Siracusano et al. compared HRQOL in ONB and ileal conduit for long-term female BC survivors. They found no significant differences between both groups, except for more financial difficulties in patients with ONB, for which there was no evident explanation [43]. Although there is a positive trend in studies with emphasis on HRQOL in female bladder cancer patients, the overall quality of the evidence is poor [44], and there is a need for more high-quality studies on the subject.

**CONCLUSION**

General consensus on which type of urinary diversion is superior in term of HRQOL has not been reached. Although some recent studies favor the ONB, other studies suggest effects of different urinary diversion types on HRQOL are similar. However, they argue that independent factors, such as age, comorbidities and sex are more important, instead. For the individual patient, choice on which urinary diversion is applied after radical cystectomy is still of very importance. Thorough preoperative counselling and shared decision-making affect patient satisfaction and decrease decision regret, thus increasing HRQOL. This counselling should not be limited to the type of urinary diversion but should also include preoperative sexual function, the effects of the procedure on sexual health and the
possibility of nerve-sparing or organ-sparing cystectomy with patients whenever applicable. Studies have shown that there is still much to gain in the field of preoperative counselling of the individual patient. To further improve the quality of this counselling, future prospective, longitudinal studies regarding HRQOL in ONB and ileal conduit in men and specifically women are needed.

Furthermore, information on HRQOL in patients who underwent urinary diversion following cystectomy for functional disorders and/or congenital anomalies is lacking. Although the tendency is to perform procedures for these indications to a lower extent, it is in the interest of these patients that studies regarding HRQOL in this specific group of patients will be performed in the future.

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Papers of particular interest, published within the annual period of review, have been highlighted as:

• of special interest

• of outstanding interest

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