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Original Article

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ABSTRACT

Purpose: To compare the cost-effectiveness of a nurse-led sexual rehabilitation intervention with standard care in women treated with external beam radiotherapy, with or without brachytherapy, for gynaecological cancers.
Methods: Eligible women were randomly assigned to the intervention (n = 112) or standard care (n = 117). Primary endpoint was sexual functioning at 12-months post-radiotherapy, assessed by the Female Sexual Function Index (FSFI). Nurses documented frequency and duration of intervention sessions, patients reported sexual healthcare and functioning at 1, 3, 6, and 12-months. Costs were related to quality-adjusted-life-years (QALYs) using the EuroQol-5 Dimensions and visual analogue scale, and to sexual functioning improvement at 12-months. T-tests compared mean QALYs and costs, with multiple imputation for missing data.
Results: The nurse-led intervention added €172 per patient, including training costs and 4–5 sessions. Other sexual rehabilitation costs were higher in the standard care group (€107 versus €141, p = 0.02). Total costs were €478 for the intervention group and €357 for standard care (p = 0.03). Valued at €20.000 per QALY, the intervention was 60 %–70 % likely to be cost-effective and less than 50 % likely to be cost-effective in terms of improved sexual functioning.
Conclusion: The nurse-led sexual rehabilitation intervention is not more cost-effective than standard care, however with low costs in both groups. Since costs for standard care were slightly lower, it is preferred from a health-economic perspective. It includes detailed patient education and a dedicated sexual rehabilitation session within the first three months post-radiotherapy, which is better provided at lower cost by a trained nurse.

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Introduction

Gynaecological cancer treatment, especially treatment involving intensive combined external beam (chemo)radiotherapy (EBRT) and brachytherapy, is associated with sexual problems, particularly pain during intercourse and vaginal symptoms such as dryness, shortness, and/or tightening [1–3]. Women who receive EBRT and brachytherapy have a higher risk of radiotherapy-induced vaginal stenosis than women receiving EBRT alone [4]. To prevent stenosis, regular vaginal dilation is recommended, however, many women (75 %) fail to use dilators regularly, even with specific instructions [5].

Randomized trials targeting dilator use and psychosexual consequences after radiotherapy for gynaecological cancer are rare. Therefore, we developed and pilot tested a nurse-led sexual rehabilitation intervention that includes psycho-education combined with elements of psychosexual-based cognitive-behavioural therapy for gynaecological cancer patients and their partners after radiotherapy, which seemed promising [6,7]. We set up a multicentre randomized trial to evaluate the effectiveness of this intervention [7,8].

Besides evaluation of effectiveness, the implementation of a new intervention requires an economic evaluation to determine whether the clinical benefits are gained at reasonable cost. Up to date, randomized trials and studies of sexual rehabilitation programmes after radiotherapy for gynaecological cancer have not involved explicit cost comparisons. Therefore, the purpose of the present study was to estimate, from a societal perspective, the cost-effectiveness and cost-utility of the nurse-led sexual rehabilitation intervention, compared to standard care.

Materials and methods

The cost-effectiveness analysis (CEA) and cost-utility analysis (CUA) were part of the multicentre randomized SPARC-trial (NCT03611517), involving 10 Dutch gynaecologic oncology centres. This trial has been described in detail elsewhere [7,8]. The SPARC-trial was approved by the Scientific Review Board of the Dutch Cancer Society, the Medical Ethics Committee Leiden-Den Haag-Delft (number NL62767.058.17), and the Institutional Review Boards and/or Ethics Committees of the participating centres. Participants were randomly assigned (1:1) to standard care or the nurse-led sexual rehabilitation intervention, stratified by radiotherapy type (brachytherapy yes/no) and partner status (yes/no).

Participants

Women treated for cervical, endometrial or vaginal cancers with primary or postoperative EBRT with or without concurrent chemotherapy and brachytherapy, or postoperative radiotherapy alone, were eligible for the trial. They had to be 18 years or older, intend to engage in sexual activity, possessed sufficient Dutch language proficiency, and had no major affective psychotic or substance abuse disorder, or post-traumatic stress disorder related to pelvic floor/genital abuse. Both single and partnered women, regardless of their sexual orientation, could participate. Women were informed and included after eligibility screening by their radiation oncologist [7,8].

Standard care

Both the intervention and standard care groups had a follow-up session 4–5 weeks after radiotherapy with their radiation oncologist (or gynaecologist), to evaluate recovery, tumour regression and vaginal healing, and to assess symptoms. All women received a specially developed information booklet based on the pilot study [6]. Those who had received brachytherapy also received a vaginal dilator set (Amielle Comfort®; Owen Mumford) and two tubes of lubrication gel (K-Y Jelly; Johnson & Johnsen). Women under 50 with cervical or vaginal cancers were recommended hormone replacement therapy until age of about 50. If they received brachytherapy, they were also advised to use vaginal estriol ovules for 5–6 weeks during recovery.

Nurse-led sexual rehabilitation intervention

Before initiation of the trial, a study-specific 50-hour training programme was held, to which each participating centre sent at least two designated nurses. Only after completing this programme nurses were allowed to conduct the intervention. In the intervention group, all women were counselled and followed by these nurses. The intervention comprised four one-hour face-to-face sessions at 1, 3, 6, and 12-months post-radiotherapy, synchronized with visits to the radiation oncologist, with an extra session at 2-months for women who received brachytherapy. Optionally, a 30-minute follow-up session/phone call was offered between 6 and 12-months after radiotherapy. The intervention consisted of 11 modules, personalized based on individual psychological, relational, and somatic factors, with modules selected during each session to meet each woman's specific needs [7,8]. Partners were welcome to participate in the sessions.

Measurements

Patient and disease characteristics, as well as sexual functioning before the cancer diagnosis, were reported by patients before radiotherapy. Details regarding the nurse-led sexual rehabilitation intervention sessions (such as duration) were documented in Case Report Forms (CRFs) by the trained nurses after each session. Additionally, sexuality-related healthcare and sexual functioning were reported by the patients at 1, 3, 6, and 12-months after radiotherapy. Sexual function was measured by the Female Sexual Functioning Index (FSFI), a validated 19-item scale with total scores ranging from 2 to 36, where higher scores indicate better sexual functioning [9].

Costs and cost-effectiveness analysis

An economic evaluation was conducted, relating the difference in sexuality-related healthcare costs to the impact on patient-reported outcomes. Costs are reported in euros (€) at price level 2023. Costs for the nurse-led sexual rehabilitation intervention included nurse training (€1000/nurse – covering materials, one trainer, location, and food and beverage expenses), recorded direct nurse time with patients (max 60 min/session), and indirect nurse time (5 min/session). Other included healthcare utilization was limited to sexuality-related healthcare and valued using Dutch reference prices or market prices [10].

For the CEA, the estimated costs were related to the intervention's impact on the number of women with sexual improvement, measured by the FSFI (costs-per-improved-patient), defined as a Reliable Change Index (RCI) > 1.96 on the FSFI total score between 1 and 12-months after radiotherapy [9,11]. The RCI is calculated by subtracting the FSFI total score at 1-month from the score at 12-months, then dividing by the Standard error of difference (Sdiff) [11]. The Sdiff was computed from the standard error of measurement using the formula $\sqrt{2(SE)^2}$, with the SE calculated from the Dutch population's standard deviation ($SD = 3.9$) and the FSFI test–retest reliability (=.93) [12].

For the CUA, estimated costs were related to the impact on quality-adjusted-life-years (QALYs). In the primary analysis, following Dutch guidelines, QALYs were calculated as the area under the curve of the Dutch tariff for the 5-level EuroQol-5D (EQ-5D) [13,14], consisting of 5 questions on mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. From the EQ-5D classification system, the EQ-5D utility index was calculated, which is anchored at 1 (full health) and 0 (as bad as dead) [15]. This measure reflects how the general public values the health status described by the patient, which is preferred for economic evaluations from a societal perspective [10].

As the EQ-5D does not explicitly value sexuality, QALYs were also estimated using the EuroQol visual analogue scale (EQ-VAS), where

Table 1
Patient, disease and treatment characteristics.

		Intervention group n = 112 (48.9 %)	Standard care group n = 117 (51.1 %)	p Value (X^2 or *t*-test)
	Patient characteristics			
Age	Mean in years (SD)	43 (10.3)	44 (11.7)	0.06
Partner	Yes	88 (78.6 %)	90 (76.9 %)	0.75
	No	24 (21.4 %)	27 (23.1 %)	
Menopausal status before diagnosis	Premenopausal	75 (67.0 %)	75 (64.1 %)	0.12
	Perimenopausal	10 (8.9 %)	3 (2.6 %)	
	Postmenopausal	23 (20.5 %)	33 (28.2 %)	
	Unknown	4 (3.6 %)	6 (5.1 %)	
World Health Organization performance score	0	85 (75.9 %)	89 (76.1 %)	0.57
	1	24 (21.4 %)	25 (21.4 %)	
	2	2 (1.8 %)	3 (2.6 %)	
	Unknown	1 (0.9 %)	0	
Incapacitated for work	Yes	25 (22.3 %)	19 (16.4 %)	0.26
	No	87 (77.7 %)	97 (82.9 %)	
	Unknown	0	1 (0.9 %)	
	Disease characteristics			
Type of carcinoma	Cervical carcinoma	98 (87.5 %)	104 (88.9 %)	0.79
	Endometrial carcinoma	7 (6.3 %)	8 (6.8 %)	
	Vaginal carcinoma	7 (6.3 %)	5 (4.3 %)	
Histological type	Cervical			0.99
	- Squamous cell	80 (81.6 %)	85 (81.7 %)	
	- Other	18 (18.4 %)	19 (18.3 %)	
	Endometrial			0.62
	- Endometrioid carcinoma	5 (71.4 %)	5 (62.5 %)	
	- Serous carcinoma	0	1 (12.5 %)	
	- Mixed or other	2 (28.6 %)	2 (25.0 %)	
	Vaginal			0.79
	- Squamous cell	6 (85.7 %)	4 (80.0 %)	
	- Other	1 (14.3 %)	1 (20.0 %)	
FIGO stage (2009)	Cervical			0.99
	- IB	29 (29.6 %)	32 (30.8 %)	
	- IIA/B	52 (53.1 %)	56 (53.8 %)	
	- IIIA/B	11 (11.2 %)	11 (10.6 %)	
	- IVA	1 (1.0 %)	1 (1.0 %)	
	- Not applicable (if recurrence)	5 (5.1 %)	4 (3.8 %)	
	Endometrial			
	- IA/B	3 (42.9 %)	2 (25.0 %)	0.57
	- II	1 (14.3 %)	3 (37.5 %)	
	- IIIA-C	3 (42.9 %)	3 (37.5 %)	
	Vaginal			
	- I	4 (51.7 %)	2 (40.0 %)	0.18
	- II	3 (42.9 %)	1 (20.0 %)	
	- III	0	0	
	- IVA	0	2 (40.0 %)	
	Treatment characteristics			
Chemotherapy (concurrent)	Yes	90 (80.4 %)	87 (74.4 %)	0.28
	No	22 (19.6 %)	30 (25.6 %)	
Hyperthermia[#]	Yes	4 (3.8 %)	15 (13.8 %)	**0.01**
	No	101 (96.2 %)	94 (86.2 %)	
Type of Radiotherapy	Primary EBRT + BT	80 (71.4 %)	82 (70.1 %)	0.79
	Postoperative EBRT + BT	16 (14.3 %)	15 (12.8 %)	
	External Beam Radiotherapy only	14 (12.5 %)*	19 (16.2 %)	
	EBRT with EBRT boost	2 (1.8 %)[x]	1 (0.9 %)	
Target area External Beam Radiotherapy	Pelvic region	84 (75.0 %)	89 (76.1 %)	0.49
	Pelvic and *para*-aortal regions	22 (19.6 %)	22 (18.8 %)	
	Pelvic and inguinal regions	6 (5.4 %)	4 (3.4 %)	
	Pelvic, *para*-aortal, and inguinal regions	0	2 (1.7 %)	
External Beam Radiotherapy total dose	Median dose in Gy (±IQR)	45 (0)	45 (0)	0.09
Brachytherapy	Yes	96 (85.7 %)	97 (82.9 %)	0.56
	No	16 (14.3 %)	20 (17.1 %)	
Target area Brachytherapy	Intrauterine/vaginal Brachytherapy primary	80 (83.3 %)	87 (89.7 %)	0.34
	Vaginal vault boost postoperative	9 (9.4 %)	8 (8.2 %)	
	Vaginal intracavitary and interstitial (primary or recurrence)	6 (6.3 %)	2 (2.1 %)	
	Vaginal intracavitary primary	1 (1.0)	0	

Note. EBRT + BT = External Beam Radiotherapy combined with Brachytherapy; FIGO = Fédération Internationale de Gynécologie et d'Obstétrique; IQR = interquartile range; N = total sample; n = subgroup sample; SD = standard deviation.
= Only applicable for cervical and vaginal carcinoma.
* = One participant was stratified as EBRT + BT radiotherapy, however she was treated with EBRT only. Her rehabilitation trajectory was according to EBRT alone; therefore she was moved to EBRT alone.
[x] = One participant was stratified as EBRT alone, however she received an additional EBRT boost. Her rehabilitation trajectory was according to EBRT + BT; therefore she was moved to EBRT + BT.

patients rated their personal health ranging from worst imaginable health (0) to best imaginable health (100). The EQ-VAS was transformed to a utility scale, using the power transformation $1–(1–EQ–VAS/100)^{1.61}$ [16]. Instead of using individually observed EQ-VAS scores, we used a mapping to predict the EQ-VAS from the individually observed FSFI, estimated from our own trial data using linear regression, to make the QALY as sensitive to change as possible.

The cost-effectiveness of the sexual rehabilitation intervention compared to standard care depends on the difference in costs and QALYs, and the willingness-to-pay (WTP) per QALY. Statistical uncertainty was analysed using the net benefit approach, using a cost-effectiveness acceptability curve to graph the probability that the intervention was cost-effective (i.e. had higher net benefit) compared with standard care [17]. Based on the 5-year survival rate of 68 % of women with cervical cancer who received EBRT with brachytherapy [18], the relevant Dutch WTP threshold for our study population is €20.000 per QALY [10].

All analyses used data collected during the 12-months follow up, according to intention-to-treat as initially assigned. Multiple imputation with predictive mean matching accounted for missing data. We imputed 100 data sets, using randomization group, type of radiotherapy, partner status (yes/no), type of gynaecological cancer, age at diagnosis, sexual functioning (FSFI scores [9]) and sexual distress (Female Sexual Distress Scale (FSDS) scores [19]), sexuality-related healthcare use, costs, and utilities as predictors. To investigate changes in sexual functioning from 1 to 12-months between groups, a 2 Group (intervention, standard care) by 2 Time (1-month, 12-months) repeated measures analyses of variance (ANOVAs) were applied, with FSFI scores as within-subject factors. T-tests assessed differences in mean 1-year QALYs and costs. Analyses were conducted with the Statistical Package for Social Scientists (SPSS, version 29).

Results

Between August 7, 2018, and December 31, 2021, 229 women were enrolled [8]. Patient, disease, and treatment characteristics were well balanced between the study groups (Table 1). Women in the intervention group and standard care group were, on average, respectively 43 and 44 years old. Most were treated with primary or postoperative EBRT combined with brachytherapy (80 (71 %) in the intervention group; 82 (70 %) in the standard care group) and for cervical cancer (98 (87.5 %) for the intervention group; 104 (89 %) for the standard care group).

Table 2 shows the mean one-year sexual healthcare use and costs per patient. Women in the sexual rehabilitation intervention attended an average of 4.5 sessions. The total average time spent for all sessions per patient was 162 min, including 22 min indirect time for preparing the sessions. The total costs of the nurse-led intervention, including the training course for the nurse, were estimated at €172 per participant. Total costs of standard healthcare regarding sexual rehabilitation were estimated at €107 for the intervention group and €141 for the standard care group (see Table 2). These costs were significantly higher in the standard care group ($p = 0.02$), mostly because women in the standard care group consulted their radiation oncologist regarding sexual issues more frequently in the first three months after radiotherapy. Other or additional sexual healthcare use and costs were similar between the study groups. No statistically significant differences in total non-intervention standard sexual rehabilitation costs were found between the groups at 12-months. Total sexual rehabilitation costs over the one-year follow-up period, including intervention costs, were significantly higher for the intervention group (€478) compared to the standard care group (€357; $p = 0.03$).

Fig. 1 shows participants' utility scores, mean QALYs and RCI scores above 1.96 over the 12-months follow-up. Utilities according to the EQ-5D and the EQ-VAS were similar between the study groups throughout

Table 2
Mean one-year healthcare use and costs per patient, by randomization group.

	Intervention group (N = 112)		Standard care group (N = 117)		Difference in costs (€)	p Value difference in Costs
	Use	Cost (€)	Use	Cost (€)		
Sexual rehabilitation intervention						
Direct patient contact (sessions and total minutes)	4.49; 140	119	–	–		
Indirect time (minutes)	min	19	–	–		
Training costs	22 min	33		–		
Total intervention costs		*172*		–	*172*	***<.001***
Standard sexual rehabilitation healthcare						
Gynaecologist (visits 1–3 months)	0.13	12	0.18	18	−6	0.37
Radiation oncologist (visits 1–3 months)	0.30	31	0.59	59	−28	**0.01**
Materials:						
• Dilator set*	0.88	39	0.84	38	1	0.42
• Lubrication jelly*	1.75	12	1.68	12	0	0.42
• Patient information brochure	1	8	1	8	0	1.00
• Local oestrogens (days)	5.74	1	7.04	1	0	0.42
• Other out of pocket expenses (e.g. dildo, Vaseline tampons) (days)	2.70	3	4.47	6	−3	0.17
Total non-intervention standard sexual rehabilitation costs		*107*		*141*	*−34*	***0.02***
Other sexuality-related healthcare						
General practitioner (visits)	0.38	12	0.38	12	0	0.97
Sexologist/psychologist/psychotherapist (visits)	0.30	37	0.30	38	−1	0.97
Gynaecologist (visits 4–12 months)	0.44	44	0.46	46	−2	0.86
Radiation oncologist (visits 4–12 months)	0.57	57	0.56	56	1	0.94
Pelvic floor therapist (visits)	0.78	32	0.92	37	−5	0.76
Other healthcare providers (e.g. nurse, case manager, urologist, physiotherapist) (visits)	0.27	13	0.36	19	−6	0.35
Other materials:						
• Moistening gel/cream (e.g. premeno Duo ovules) (days)	5.13	4	7.45	5	−1	0.45
• Anaesthetic ointment (Lidocaine) (days)	0.56	1	1.36	2	−1	0.07
Total other sexuality-related costs		*200*		*216*	*−16*	*0.73*
Total sexuality-related healthcare costs		*478*		*357*	*121*	***0.03***

Note. N = sample size; € = Euro.* = Every participant treated with External Beam Radiotherapy combined with Brachytherapy received 1 dilator set and 2 lubrication jelly (82 g per tube).

the follow-up period. At 12-months, the results show utilities of 0.82 for both groups according to the EQ-5D and of 0.88 and 0.87 for the intervention group and the standard care group, respectively, according to the EQ-VAS. Over the full year, the QALYs according to the EQ-5D the EQ-VAS did not statistically significantly differ between the intervention group and standard care group ($p = 0.43$ and 0.39, respectively).

The total FSFI score increased significantly between 1 and 12-months after radiotherapy ($F(1, 227) = 30.09$, $p < 0.001$, $\eta_p^2 = 0.12$). In the total group, 94 of 229 women (41 %; n = 46 (41 %) intervention group, n = 48 (41 %) standard care group) had a RCI score above 1.96, meaning a clinically relevant improvement in sexual functioning at 12-months. No significant differences in Time X Group interaction, and RCI scores above 1.96 between the intervention group and standard care group were found ($p = 0.77$ and 0.97, respectively).

Fig. 2 shows the cost-effective acceptability curves. In the base-case analysis comparing societal costs to EQ-5D QALYs, the probability that the intervention was cost-effective ranged from 3 % for low WTP/QALY to about 70 % at €20.000 and higher WTP/QALY. Taking only the intervention costs into account, the probability that the intervention was cost-effective ranged from 0 % for low WTP/QALY to about 68 % at €20.000 and higher WTP/QALY. The probability that the sexual rehabilitation intervention is cost-effective based on the EQ-VAS ranged from 3 % for low WTP/QALY to 68 % at €20.000 WTP/QALY from a societal perspective and to 60 % from a narrower interventional cost perspective. Based on the FSFI RCI above 1.96, the probability that the sexual rehabilitation intervention is cost-effective ranged from 3 % for low WTP/QALY to about 45 % at €20.000 and higher WTP/QALY, also when taking only the intervention costs into account.

Discussion

The study aimed to estimate the cost-effectiveness of a nurse-led sexual rehabilitation intervention for women treated with radiotherapy for gynaecological cancer compared to standard care. To our knowledge, this is the first well-powered randomized trial that explored the cost-effectiveness of such a sexual rehabilitation intervention (albeit as a secondary outcome).

The costs of the nurse-led sexual rehabilitation intervention including nurse training, were estimated at €172 per patient. Total costs over the one-year follow-up period, including these intervention costs, were significantly higher for the intervention group compared to the standard care group. Of note, the cost differences were small (€478 versus €357), especially in light of overall cancer treatment costs. If the sexual rehabilitation intervention had been found more effective than standard care, it would likely be worth its cost. While 41 % of women showed reliable improvement in sexual functioning between 1 and 12-months after radiotherapy, there were no significant differences in reliable FSFI improvement between the study groups. This is in line with the results of the randomized SPARC-trial, which showed no significant benefit for the nurse-led rehabilitation intervention [8]. At 12-months post-radiotherapy, both groups reported similar improvements in sexual functioning, with relatively high sexual activity rates (71 % in the intervention group vs. 69 % in the standard care group). Moreover, dilatation compliance $\geq$ 2 times weekly after brachytherapy (dilators, vibrators, dildos, fingers or intercourse combined) was high (85 % in the intervention vs. 75 % in the standard care group). Most women had no or little physician-reported vaginal stenosis, with the majority of sexually active women reporting little to no feeling of vaginal shortness, dryness, or pain during intercourse. Similarly, the current economic evaluation showed no differences in QALYs or in the number of patients with improved sexual functioning between the groups. The lack of difference in outcomes between the study groups is likely explained by the substantial improvement and awareness of sexual rehabilitation care as a standard in the Netherlands during the initiation and course of the trial. As a result, standard care nowadays consists of thorough patient information, which includes a sexual rehabilitation appointment at 4–6 weeks post-radiotherapy, often with a trained nurse, or radiation oncologist or gynaecologist. During this appointment explicit guidance on dilator use is provided for women who underwent radiotherapy combined with brachytherapy; and coaching on sexual health in the recovery phase for all women. Additionally, there is dedicated follow-up regarding sexual functioning and dilator use over the first year after completion of treatment.

Differences in non-intervention sexual healthcare costs should be interpreted with caution, since differences in almost all specific cost categories were not statistically significant. However, we did find a significant difference in total non-intervention standard sexual rehabilitation healthcare costs between the study groups (i.e., costs incurred

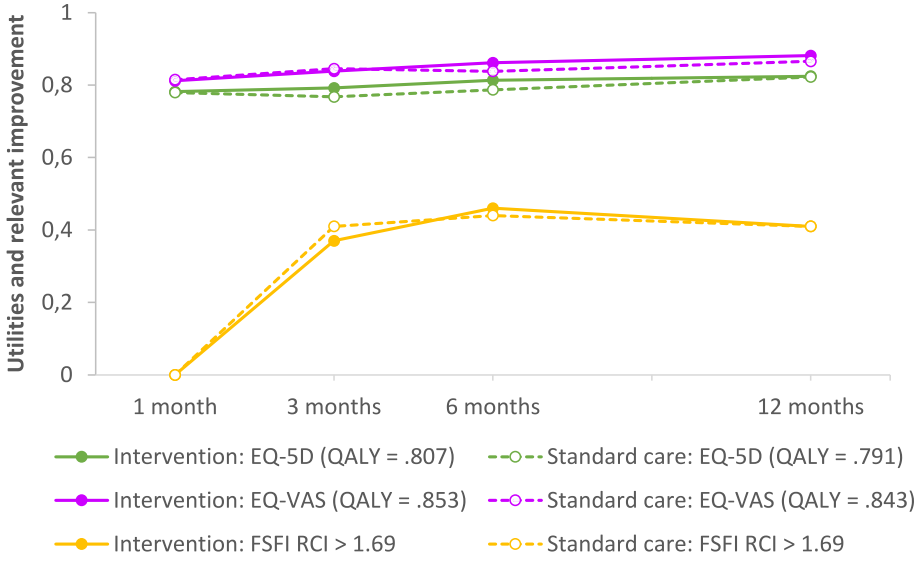

Fig. 1. Participants' utility scores, mean quality-adjusted life years (QALY) and RCI scores above 1,96 over the 12-months of follow-up. QALY was measured as the area under the curve over 12-months with the EuroQol 5 dimensions (EQ-5D) utility score (Dutch tariff) and EQ-5D visual analogue scale (EQ-VAS) ranging from 0 (worst health status) to 1 (best health status). FSFI = Female Sexual Function Index; RCI = Reliable Change Index (% reliable change compared to 1 month after radiotherapy).

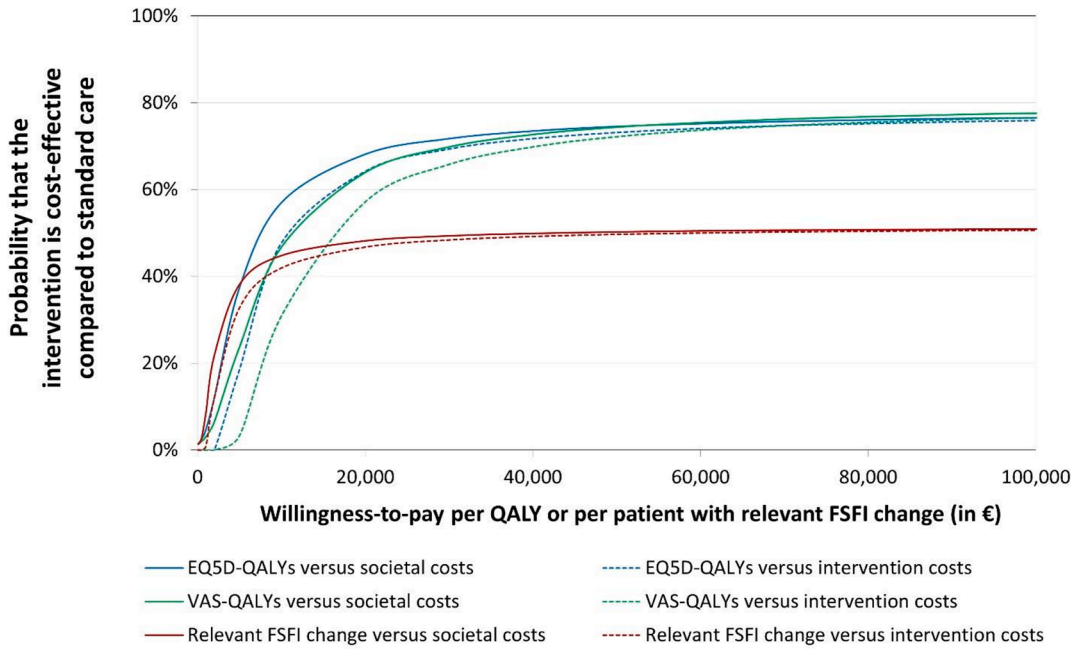

Fig. 2. Cost-effective acceptability curves from a societal perspective (solid lines) and interventional perspective (dashed lines), showing the probability that the sexual rehabilitation intervention is cost-effective compared to standard care depending on the willingness to pay for patient outcomes. EQ-5D = EuroQol-5 Dimensions 5 Levels; FSFI = Female Sexual Functioning Index; QALY = quality-adjusted life years; VAS = Visual Analogue Scale.

in the first three months after radiotherapy), with higher costs for the standard care group. Specifically, costs for radiation oncologist visits regarding sexual issues were significantly higher in the standard care group than the intervention group. During the first three months after radiotherapy, women received the most guidance and coaching regarding sexual rehabilitation. Nurses can devote more time to patient interaction than radiation oncologists, and at lower cost. A visit with a specifically trained nurse would cost only €38 per patient on average (Table 2). In addition, nurses are often easier accessible for patients and can integrate their role in information and counselling into other clinical tasks. Therefore, their involvement in standard information and coaching of these patients could still be an economically sound strategy for dedicated sexual rehabilitation.

The CUA consistently estimated that the nurse-led sexual rehabilitation intervention was about 70 % likely to be the more cost-effective policy (at €20.000 WTP/QALY), regardless whether we valued health from a more societal or a more individual perspective (EQ-5D versus EQ-VAS), and regardless of the scope of the cost estimates (societal versus intervention only). While the Netherlands has thresholds for the WTP to achieve a certain QALY gain, no such thresholds exist for the WTP for improved sexual functioning.

Strengths of this study are the well-powered randomized trial design, the participation of all Dutch gynaecological oncology centres, a limited drop-out of study participants, the use of different methods to estimate QALYs, the comprehensive societal cost perspective, a net benefit approach for statistical uncertainty and multiple imputation for missing values. There are also some limitations. First, we utilized patient-reported sexual healthcare use. The primary drawback of relying on patients is that it necessitates their recall, which can be challenging and may result in inaccurate estimates [20]. Especially between 6 and 12-months after radiotherapy, recall bias may have occurred, possibly resulting in underreporting of healthcare use. It would have been beneficial if we had also included questions regarding additional sexual healthcare use to be answered by patients during each follow-up visit with the physician. Second, the costs of the nurse-led intervention included the training expenses for the nurses, but we chose not to account for their time spent away from clinical duties to enable attendance at the 50-hour training course. In the Netherlands, time spent on additional professional training is incorporated into continuous professional education, and our training was also directed at general communication skills on sexual topics for daily patient care, and was accredited for this. The costs of sexual rehabilitation healthcare were specific to the Netherlands and University Medical Centres and may not be generalizable to other, international, healthcare systems. Third, it could be argued that this study attracted relatively young and (sexually) motivated participants. Women with cervical cancer constituted the large majority (88 %) of the study population, making our findings particularly relevant for these relatively young women treated with intensive combined chemoradiotherapy and brachytherapy. Last, the FSFI which is widely employed to evaluate sexual functioning in female cancer survivors, could yield biased results for sexually inactive women due to lack of a partner, relationship quality, or reasons unrelated to cancer treatment effects [9,21]. To mitigate this, we randomized participants with stratification based on partner status, and included the response option 'not applicable, no partner' for items concerning the partner relationship, thereby minimizing potential imbalance in the study outcomes [7,8].

Conclusions

In conclusion, our study estimated that the effectiveness of the sexual rehabilitation intervention provided by trained nurses is similar to standard care, with costs that are low for both approaches to sexual rehabilitation care. However, as costs for standard care were slightly lower, the preferred treatment from a health-economic perspective is standard care. This standard approach encompasses thorough patient information, as well as a sexual rehabilitation appointment with explicit guidance on dilator use and coaching on resuming sexual activities. Instead of providing this care in additional or extended consultations with the radiation oncologist or gynaecologist, this sexual rehabilitation care is better provided at lower costs by a specifically trained dedicated nurse.

CRediT authorship contribution statement

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Author contributions

IS was the principal investigator of the study, was responsible for the conceptualization, investigation, resources, methodology, and writing of the original draft, and was involved in data curation, project administration, formal analysis, and visualization. WvdH was involved in conceptualization, methodology, formal analysis, writing the original draft, and supervision. SH was involved in data curation, project administration, and methodology, and responsible for conceptualization, investigation, and resources. JWM was involved in funding acquisition, and responsible for conceptualization, investigation, and resources. CTR was responsible for conceptualization, investigation, and resources, and involved in methodology. LV was involved in investigation and resources. HW was involved in investigation and resources. JC was involved in investigation and resources. AS was involved in investigation and resources. IJS was involved in investigation and resources. LL was involved in investigation and resources. JB was involved in investigation and resources. MH was involved in investigation and resources. MN was involved in investigation and resources. RN was involved in conceptualization. CdK was involved in conceptualization. HvD was responsible for conceptualization, investigation, and resources, and involved in methodology. CC was the principal investigator of the study, was responsible for the conceptualization, investigation, resources, methodology, writing of the original draft, and was involved in funding acquisition, and supervision. MtK was the principal investigator of the study, was responsible for the conceptualization, investigation, resources, methodology, and writing of the original draft, and was involved in the formal analysis, in funding acquisition, project administration, and supervision.

All authors were involved in writing, reviewing, and editing the manuscript.

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