Supplementary Material 1: MEDLINE search strategy

Search strategy run 14 October 2020

Concept 1: Cervical cancer	Synonyms to be searched (MeSH OR textwords)
PubMed (results = 108,488) "uterine cervical neoplasms"[MeSH Terms] OR ("uterine"[All Fields] AND "cervical"[All Fields] AND "neoplasms"[All Fields]) OR "uterine cervical neoplasms"[All Fields] OR ("cervical"[All Fields] AND "cancer"[All Fields]) OR "cervical cancer"[All Fields]	Cervical cancer
	Uterine cervical neoplasms
Concept 2: Chemoradiotherapy	**Synonyms to be searched (MeSH OR textwords)**
PubMed (results = 139,771) ("chemoradiotherapy"[MeSH Terms] OR "chemoradiotherapy"[All Fields] OR "chemoradiotherapies"[All Fields] OR (("chemotherapy s"[All Fields] OR "drug therapy"[MeSH Terms] OR ("drug"[All Fields] AND "therapy"[All Fields]) OR "drug therapy"[All Fields] OR "chemotherapies"[All Fields] OR "drug therapy"[MeSH Subheading] OR "chemotherapy"[All Fields]) AND ("radiotherapy"[MeSH Terms] OR "radiotherapy"[All Fields] OR "radiotherapies"[All Fields] OR "radiotherapy"[MeSH Subheading] OR "radiotherapy s"[All Fields])) OR ("chemoradiotherapy"[MeSH Terms] OR "chemoradiotherapy"[All Fields] OR "radiochemotherapy"[All Fields]))	Chemoradiotherapy
	Radiochemotherapy
	Chemotherapy
	Drug therapy
	Radiotherapy
Concept 3: Quality of life	**Synonyms to be searched (MeSH OR textwords)**
PubMed (results = 410,848) "quality of life"[MeSH Terms] OR ("quality"[All Fields] AND "life"[All Fields]) OR "quality of life"[All Fields]	Quality of life

Note: Combine Concept 1 AND Concept 2 AND Concept 3 (PubMed results = 252); Apply Year 2010 to 2020 filter (PubMed results = 166).

Supplementary Material 2: Detailed search strategy for included databases

All databases searched on October 15, 2020

Limiter applied to all databases: Year 2010 to 2020

No.	Databases (Total = 3)	Search terms	Results (Total = 2,025)
1	PubMed	("uterine cervical neoplasms"[MeSH Terms] OR ("uterine"[All Fields] AND "cervical"[All Fields] AND "neoplasms"[All Fields]) OR "uterine cervical neoplasms"[All Fields] OR ("cervical"[All Fields] AND "cancer"[All Fields]) OR "cervical cancer"[All Fields]) AND ("chemoradiotherapy"[MeSH Terms] OR "chemoradiotherapy"[All Fields] OR "chemoradiotherapies"[All Fields] OR (("chemotherapy s"[All Fields] OR "drug therapy"[MeSH Terms] OR ("drug"[All Fields] AND "therapy"[All Fields]) OR "drug therapy"[All Fields] OR "chemotherapies"[All Fields] OR "drug therapy"[MeSH Subheading] OR "chemotherapy"[All Fields]) AND ("radiotherapy"[MeSH Terms] OR "radiotherapy"[All Fields] OR "radiotherapies"[All Fields] OR "radiotherapy"[MeSH Subheading] OR "radiotherapy s"[All Fields])) OR ("chemoradiotherapy"[MeSH Terms] OR "chemoradiotherapy"[All Fields] OR "radiochemotherapy"[All Fields])) AND ("quality of life"[MeSH Terms] OR ("quality"[All Fields] AND "life"[All Fields]) OR "quality of life"[All Fields])	166

(*Continued*)

No.	Databases (Total = 3)	Search terms	Results (Total = 2,025)
2	EBSCOhost Medical Databases (includes Biomedical Reference Collection: Basic, CINAHL Plus with Full Text, eBook Collection (EBSCOhost), MEDLINE Complete, and Psychology and Behavioral Sciences Collection)	("uterine cervical neoplasms" OR ("uterine" AND "cervical" AND "neoplasms") OR ("cervical" AND "cancer") OR "cervical cancer") AND ("chemoradiotherapy" OR "chemoradiotherapies" OR (("chemotherapy s" OR "drug therapy" OR ("drug" AND "therapy") OR "drug therapy" OR "chemotherapies" OR "drug therapy" OR "chemotherapy") AND ("radiotherapy" OR "radiotherapies")) OR ("chemoradiotherapy" OR "radiochemotherapy")) AND ("quality of life" OR ("quality" AND "life"))	96
3	ScienceDirect	("uterine cervical neoplasms" OR "cervical cancer") AND ("chemoradiotherapy" OR ("drug therapy" OR ("chemotherapy" AND "radiotherapy") OR ("radiochemotherapy")) AND ("quality of life")	1,763

Note: Manual Search Strategies

Reference checking of:

1. Initial list of included papers (results = 28).
2. Systematic reviews accepted for full text screening (results = 4).

Total = 32

Citation tracking of included studies*, performed via Google Scholar on October 26, 2020

Total = 274

Related articles checking of included studies*, performed via Google Scholar on October 26, 2020

Total = 909

Total added papers for screening after manual search strategies = 1,215

*Nine potentially eligible papers were identified by manual search. Of these, five were removed, being outcome-specific analyses of updated cohorts of an already included paper. The remaining four were included in the systematic review.

Supplementary Table S1 Risk of bias assessments of included cohort and cross sectional studies[a]

	Conway et al, 2020	Gargiulo et al, 2016	Rai et al, 2014	Ljuca et al, 2011	Kirchhneiner et al, 2016	Daga et al, 2017	Prasongvej et al, 2017	Katepratoom et al, 2014
Study type	Retrospective Cohort	Prospective Cohort	Prospective Cohort	Prospective Cohort[b]	Prospective Cohort	Cross-sectional	Cross-sectional	Cross-sectional
Research question or objective clearly stated	Yes, the objective was clearly defined and easy to understand "To evaluate the longitudinal patient reported distress in cervical cancer patients treated with CRT."	Yes, the objective was clearly defined and easy to understand "To analyze the long-term toxicity and quality of life in patients with locally advanced cervical cancer treated with chemoradiation or neoadjuvant CT followed by radical surgery."	Yes, the objective was clearly defined and easy to understand "To evaluate the vaginal dose and toxicity in patients of cervical cancer treated with image guided brachytherapy at our institute."	Yes, the objectives were clearly defined and easy to understand "The aim of this study is to, by means of interview, evaluate the vaginal and sexual function of patients with advanced cervical cancer before and after CRT and compare the results."	Yes, the objectives were clearly defined and easy to understand "The objective of this analysis is to evaluate longitudinal health-related QoL regarding functioning and symptom scores after definitive radio(chemo)therapy with IGABT in a large and homogeneously treated cohort of LACC patients and to compare these outcomes to those of a previously published age-matched female reference population."	Yes, the objectives were clearly defined and easy to understand "This study evaluated sexual function in cervical cancer survivors after concurrent CRT."	Yes, the objective was clearly defined and easy to understand "The purpose of this study is to get a baseline QoL in cervical cancer survivors compared to that of healthy subjects in our tertiary Thammasat University Hospital."	Yes, the objectives were clearly defined and easy to understand "This study explored the rate of LUTD in cervical cancer survivors. Due to the different pathophysiology of LUT injury from various treatment modalities, LUTD and QoL between patients who received CCRT and RH were compared."
Study population clearly specified and defined	Yes, the study population was identified as patients treated for cervical cancer FIGO IB-IVA treated with definitive CRT with concomitant MR guided brachytherapy.	Yes, the population was identified as patients diagnosed with locally advanced cervical cancer FIGO IB2-IVA with complete response following locoregional treatment lasting at least 18 mo.	*No, the study only mentioned that the population was composed of 35 patients who underwent MRI guided image brachytherapy from March 2011 to July 2013*	Yes, the study population was identified as patients treated against cervical cancer FIGO IIb stage by concomitant CRT	Yes. The study population was identified as patients with primary biopsy-proven squamous-, adeno- or adenosquamous carcinoma of the uterine cervix, FIGO stage IB-IVA (and stage IVB with para-aortic metastatic nodes below L1-L2 only) treated in curative intent with definitive radio(chemo)therapy, including IGABT	Yes, the study population was identified as those previously treated for cervical cancer and who satisfied the following criteria: older than 18 y, diagnosis of stages IIB-IVA cervical cancer, treatments in the form of concurrent CRT that finished at least 2 y prior to study entry, and able and willing to sign the informed consent form. Excluded were those whose tumor had recurred, or who had mental illness or cognitive impairment	Yes, the study population was identified as those with a history of treatment cervical carcinoma between 1996 and 2015 with no evidence of other malignancies, age between 30 and 70 y old, Thai nationality, and agreement to participate in the study by signing informed consent. Excluded were those in disagreement to participate in the study, language barrier, severe medical condition, severe psychological disease, and nursing home residence	Yes. The study population was identified as patients who had received primary treatment, either CCRT or RH, before June 2008. Survivors were defined as those who received treatment at least 3 y previously and had no disease recurrence. Cross-sectional analysis was done on 70 cervical cancer survivors between June 2011 and May 2012.
At least 50% participation rate of eligible persons	Yes 67 out of 67 eligible patients were included in the analysis	Cannot be determined, the authors did not state how many eligible participants they had identified	Cannot be determined, the authors did not state how many eligible participants they had identified	Yes, 35 out of 35 eligible patients were included in the analysis	Yes, 744 out of 1250 eligible patients were included in the analysis	Cannot be determined, the authors did not state how many	Yes, 192 out of 192 women met the criteria of the study and were included in the analysis	Cannot be determined, the authors did not state how many

Supplementary Table S1 (*Continued*)

	Conway et al, 2020	Gargiulo et al, 2016	Rai et al, 2014	Ljuca et al, 2011	Kirchhneiner et al, 2016	Daga et al, 2017	Prasongvej et al, 2017	Katepratoom et al, 2014
Study type	Retrospective Cohort	Prospective Cohort	Prospective Cohort	Prospective Cohort[b]	Prospective Cohort	Cross-sectional	Cross-sectional	Cross-sectional
						eligible participants they had identified		eligible participants they had identified
Subjects from same population and eligibility criteria prespecified and uniformly applied	Yes, all patients were included in accordance to a prespecified inclusion and exclusion criteria in a similar population in the same time period. *Unclear whether patients with disease recurrence were excluded from the QoL analysis.*	Yes, all patients were included in accordance to a prespecified inclusion and exclusion criteria in a similar population in the same time period. *Unclear whether patients with disease recurrence were excluded from the QoL analysis.*	*No, the eligibility criteria were not elaborated on in the study. Unclear whether patients with disease recurrence were excluded from the QoL analysis.*	Yes, all patients were included in accordance to a prespecified inclusion and exclusion criteria in a similar population in the same time period. *Unclear whether patients with disease recurrence were excluded from the QoL analysis.*	Yes, all patient were included in accordance to a prespecified inclusion and exclusion criteria in a similar population in the same time period (October 31, 2014). *Patients with disease recurrence were censored from QoL analysis from time of disease recurrence.*	Yes, all patients were included in accordance to a prespecified inclusion and exclusion criteria in a similar population. *Patients with disease recurrence were excluded.*	Yes, all patients were included in accordance to a prespecified inclusion and exclusion criteria in a similar population in the same time period. *Unclear whether patients with disease recurrence were excluded.*	Yes, all patients were included in accordance to a prespecified inclusion and exclusion criteria in a similar population in the same time period. *Patients with disease recurrence were excluded.*
Sample size justification, power description, or variance and effect estimates provided	No, different statistical tests were used to achieve the objective of the study	No, different statistical tests were used to achieve the objective of the study	No, different statistical tests were used to achieve the objective of the study	No, different statistical tests were used to achieve the objective of the study	No, study used a common rule and different statistical test to test for difference between two groups	Not reported	Yes, sample size was assessed based on Kimlin's work	No, different statistical tests were used to achieve the objective of the study
Exposure measured prior to outcome	Yes. all patients underwent CRT before QoL was measured	Yes, all patients underwent CRT before QoL was measured	Yes, all patients underwent CRT before QoL was measured	Yes, all patients underwent CRT before QoL was measured	Yes, all patients underwent CRT before QoL was measured	Yes, all patients underwent CRT before QoL was measured	Yes, all patients underwent CRT before QoL was measured	Yes, all patients underwent CRT before QoL was measured
Time-frame sufficient to observe for association	Yes, the time frame was sufficient since a period of 24 mo median range, with at least 60% compliant after 12 mo after the completion of treatment was given to assess QoL.	Yes, the time frame was sufficient since follow-up was done 3.1 y after the end of therapy	Yes, after the completion of treatment, the patients were followed up every 3 mo for the first year and every 6 mo thereafter	Yes, the time frame was sufficient since a period of 12 mo after the completion of treatment was given to assess QoL	Yes, the time frame was sufficient to measure for the acute and late effects of RT (up to 3 y follow-up)	Yes, the time frame was sufficient since a period of at least 2 y was given prior to study entry and assessment of FSFI	Yes, the time frame was sufficient since a period of 4.1 y $\pm$ 3.8 (Mean $\pm$ SD) after treatment was given to assess QoL	Yes, the time frame was sufficient to measure for the acute and late effects of RT (up to 3 y follow-up)
If applicable, different levels of exposure measured	NA	NA	NA	NA	NA	NA	NA	NA
Exposure measures clearly defined, valid, reliable, and implemented consistently	No, patients underwent concurrent CRT, but the regiment was not specified.	Yes, the CT/RT group was given radiotherapy and brachytherapy >80 Gy concurrent with cisplatin 40 mg/m^2 weekly. Surgery consisted of type C radical hysterectomy with or without bilateral salpingo-	Yes, all patients underwent external radiotherapy (EBRT) 46Gy in 23 fractions over four and a half weeks with concurrent weekly cisplatin (40 mg/m^2) and brachytherapy was performed toward the last	Yes, patients were irradiated to 40–46 Gy to the pelvis by the linear accelerator Siemens Primus with the irradiation energy of 6 MV and 18 MV and received intracavitary brachytherapy dosage of 20–24 Gy.	Yes, patients were treated by a combination of 45–50 Gy pelvic external beam radiotherapy (EBRT), either 3D conformal or IMRT and concomitant chemotherapy (Cisplatin 5–6 cycles 40 mg/m^2 body surface) and	No, patients underwent concurrent CRT, but the regimen was not specified	No, patients underwent concurrent CRT, but the regimen was not specified	Yes, the CCRT group received external pelvic radiation and brachytherapy. The total dose was 54 Gy, given as 2 Gy per fraction and five fractions per week,

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Supplementary Table S1 (*Continued*)

	Conway et al, 2020	Gargiulo et al, 2016	Rai et al, 2014	Ljuca et al, 2011	Kirchhneiner et al, 2016	Daga et al, 2017	Prasongvej et al, 2017	Katepratoom et al, 2014
Study type	Retrospective Cohort	Prospective Cohort	Prospective Cohort	Prospective Cohort[b]	Prospective Cohort	Cross-sectional	Cross-sectional	Cross-sectional
		oophorectomy as well as systematic pelvic lymphadenectomy with or without infra-mesenteric lymphadenectomy in all cases.	week of external radiotherapy or at completion of treatment. A total four fractions of 7Gy high dose rate brachytherapy (HDR) were delivered and two applications of brachytherapy were performed one week apart.	Intracavitary brachytherapy was applied by a high dosage rate (HDR) with Ir192 by Varian GammaMed. Patients received 40 mg/m^2 of cisplatin once a week - a total of 4–6 cycles of cisplatin.	30–50 Gy IGABT, either by pulse dose rate or high dose rate with intracavitary ± interstitial technique (total dose 70–100 Gy). Dose prescription for tumor target and dose constraints for organs at risk (bladder, rectum, sigmoid and bowel) were individually applied according to the institutional practice of the participating center, but reported in a uniform way as proposed by the GEC-ESTRO recommendations.			followed by high-dose-rate brachytherapy, 7.5 Gy three times or 8.3 Gy two times, with a treatment interval of 1 week. This radiation regimen was given concomitantly with platinum-based chemotherapy Cisplatin 40 mg/m^2 weekly or 100 mg/m2 triweekly, carboplatin area under the curve 2 weekly or AUC 6 triweekly. The RH group comprised early-stage cervical cancer survivors who underwent standard type III abdominal RH with bilateral pelvic lymphadenectomy.
Exposure assessed more than once over time	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable
Outcome measures clearly defined, valid, reliable, and implemented consistently	Yes, QoL was clearly defined. Patients were assessed using the Edmonton Symptom Assessment System. Although the outcome measure couldn't be implemented at predefined and regular intervals, this was justified given the nature of the study design.	Yes, QoL was clearly defined. Patients were assessed using the EORTC QLQ-C30, EORTC QLQ-CX24 and the Incontinence Impact Questionnaire IIQ-7.	Yes, QoL was clearly defined. Patients were assessed using the Common Terminology Criteria for Adverse Events (CTCAE) Version 3 for the vaginal morbidity. Sexual function was assessed prior to treatment and at 1 y of completion using the EORTC QoL-CX24.	Yes, QoL was clearly defined. Patients were surveyed with the questionnaires for the assessment of the vaginal and sexual function (EORTC QLQ Cx24). Patients were assessed immediately before cervical cancer was diagnosed then for the period 12 mo after the completion of concomitant CRT. Although the outcome measure couldn't be implemented at pre-defined and regular intervals, this was justified given the nature of the study design.	Yes, QoL was prospectively assessed at baseline (before treatment) and every 3 mo after treatment during the first year, every 6 mo during the second third year, and yearly thereafter with the internationally established and validated questionnaires (EORTC).	Yes, QoL was clearly defined by using the FSFI to evaluate sexual function of patients with cervical cancer. Although the outcome measure couldn't be implemented at predefined and regular intervals, this was justified given the nature of the study design.	Yes, QoL was clearly defined and patients were assessed using the Thai version of EORTC QLQ C30. Although the outcome measure couldn't be implemented at predefined and regular intervals, this was justified given the nature of the study design.	Yes, lower urinary tract symptoms and QoL were evaluated by the Thai version of the Urogenital Distress Inventory (UDI) and Incontinence Impact Questionnaire (IIQ). Although the outcome measure couldn't be implemented at predefined and regular intervals, this was justified given the nature of the study design.

Supplementary Table S1 (*Continued*)

	Conway et al, 2020	Gargiulo et al, 2016	Rai et al, 2014	Ljuca et al, 2011	Kirchhneiner et al, 2016	Daga et al, 2017	Prasongvej et al, 2017	Katepratoom et al, 2014
Study type	Retrospective Cohort	Prospective Cohort	Prospective Cohort	Prospective Cohort[b]	Prospective Cohort	Cross-sectional	Cross-sectional	Cross-sectional
Outcome assessors blinded to exposure status	No, due to the nature of a self-administered questionnaire, blinding cannot be done.	No, due to the nature of a self-administered questionnaire, blinding cannot be done.	No, due to the nature of a self-administered questionnaire, blinding cannot be done.	No, due to the nature of a self-administered questionnaire, blinding cannot be done.	No, due to the nature of a self-administered questionnaire, blinding cannot be done.	No, due to the nature of a self-administered questionnaire, blinding cannot be done.	No, due to the nature of a self-administered questionnaire, blinding cannot be done.	No, due to the nature of a self-administered questionnaire, blinding cannot be done.
Loss to follow-up after baseline is 20% or less	Yes, there was no loss to follow-up in the study	Yes, there was no loss to follow-up in the study	Yes, there was no loss to follow-up in the study	Yes, there was no loss to follow-up in the study	Yes, only 7%	Yes, there was no loss to follow-up in the study	Yes, there was no loss to follow-up in the study	Yes, there was no loss to follow-up in the study
Key potential confounding variables measured and adjusted statistically	*No, recurrence occurred within the study period and was not adjusted for in the analysis.*	*No, comorbidities were documented and were not adjusted for in the analysis*	*No, the researchers did not state possible confounding factors in their study*	*No, the researchers did not state possible confounding factors in their study.*	Yes, the researchers documented chronic disease. QoL measures were compared with normative data from a female general reference population.	Yes, key potential confounding factors (disease recurrence, mental illness, cognitive impairment) factored in the exclusion criteria. No statistical adjustments made for other comorbidities.	*Yes, although potential confounding factors were identified. However, there was no mention of statistical analysis to adjust for them.*	Yes key potential confounding factors (disease recurrence, mental illness, cognitive impairment, and relevant active comorbidities) factored in the exclusion criteria.
Risk of bias	High	High	High	High	Low	Low	Unclear	Low

Abbreviation: NA, not applicable.
[a]Risk of bias was assessed using the National Institutes of Health Study Quality Assessment Tools.
[b]Some retrospective cases were included in the analysis.

Supplementary Table S2 Risk of Bias Assessment of Included Randomized Trial[a]

Criteria	Nunes de Arruda et al, 2020
1. Was the study described as randomized, a randomized trial, a randomized clinical trial, or an RCT?	Yes, Randomized Phase II Trial
2. Was the method of randomization adequate (i.e., use of randomly generated assignment)?	Yes, patients were allocated, by a simple 1:1 randomization using a computer generated random list, to three cycles of neoadjuvant chemotherapy with cisplatin and gemcitabine, followed by standard CRT, followed by brachytherapy or standard CRT and brachytherapy alone
3. Was the treatment allocation concealed (so that assignments could not be predicted)?	No, trial is open label
4. Were study participants and providers blinded to treatment group assignment?	No, trial is open label
5. Were the people assessing the outcomes blinded to the participants' group assignments?	No, trial is open label
6. Were the groups similar at baseline on important characteristics that could affect outcomes (e.g., demographics, risk factors, co-morbid conditions)?	Yes, patient characteristics are balanced between both arms
7. Was the overall drop-out rate from the study at endpoint 20% or lower of the number allocated to treatment?	Yes, only 3 out of 110 withdrew consent for the study
8. Was the differential drop-out rate (between treatment groups) at endpoint 15 percentage points or lower?	None
9. Was there high adherence to the intervention protocols for each treatment group?	Yes, adherence for the CRT group is 94.2% and the NAC arm 80%
10. Were other interventions avoided or similar in the groups (e.g., similar background treatments)?	The radiotherapy was similar between two groups
11. Were outcomes assessed using valid and reliable measures, implemented consistently across all study participants?	Yes
12. Did the authors report that the sample size was sufficiently large to be able to detect a difference in the main outcome between groups with at least 80% power?	Sample size was sufficiently large to detect a difference in its primary outcome (3 y PFS); however, for QoL it was not reported
13. Were outcomes reported or subgroups analyzed prespecified (i.e., identified before analyses were conducted)?	NA
14. Were all randomized participants analyzed in the group to which they were originally assigned, i.e., did they use an intention-to-treat analysis?	Yes
Risk of bias	Low

Abbreviation: NA, not applicable.
[a]Risk of bias was assessed using the National Institutes of Health Study Quality Assessment Tools.

