Study Protocol

Patient decision aid for chemotherapy or exclusion in cisplatin-intolerant patients with locally-advanced cervical cancer (CECIL): protocol for development, validation and clinical testing

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Background: In locally-advanced cervical cancer (LACC), adding chemotherapy (ChT) to radiotherapy (RT) improves survival at the cost of increased toxicity. Among patients with cisplatin contraindications, compliance to RT may be compromised. Shared decision-making (SDM) allows for more patient engagement in the decision-making process and decision implementation planning. In cancer-related decision-making, patient decision aids (PtDA) facilitate the SDM process and have increased patient knowledge and satisfaction and decreased decisional conflict and attitudinal barriers improved patient satisfaction and treatment compliance.

Methods: This is a two-phase study to develop, validate and test the effectiveness of a PtDA for cisplatin-intolerant LACC patients faced with the decision of adding ChT to RT. The phase 1 is a mixed-methods study to develop a PtDA prototype and determine its content validity and user acceptability. The phase 2 is a nonrandomized sequential comparison group pretest-post-test trial to determine its effectiveness in reducing decisional conflict and its utility in preparing for decision-making. Adult women with biopsy-proven, untreated LACC, with cisplatin contraindications will be included in this trial.

Discussion: The Interprofessional Shared Decision-Making Model is used as a conceptual framework. The PtDA defines the index decision, facilitates information exchange and examination of values and preferences, towards the determination of a practicable choice. The PtDA will be developed according to the International Patient Decision Aid Standards (IPDAS) Collaboration group consensus model and validated using the IPDAS instrument. The phase 2 design avoids contamination bias while allowing to account for biases that could arise from a non-randomized design. Patient factors that will be identified to be predictive of PtDA effectiveness could guide further research or implementation.

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Introduction

Cervical cancer remains one of the top causes of cancer morbidity and mortality in women (1). Worldwide, the annual incidence is 13.6 in 100,000 women with 30% diagnosed at an advanced stage. In the Philippines, where it is the second most common cancer in women, the annual incidence is 14.5, with 7,900 new cases in 2020 (2).

The standard treatment for locally-advanced cervical cancer (LACC) is concurrent chemoradiation (CRT) (3). A 2008 meta-analysis of 13 randomized controlled trials (RCTs) showed that adding concurrent chemotherapy (ChT) to radiotherapy (RT) was associated with a 6% 5-year overall survival (OS) benefit, which decreased with more advanced stages (from 7% in stage IIB to 3% in IVA) (4). This meta-analysis included trials with co-interventions, such as surgery and neoadjuvant or adjuvant ChT. A 2017 meta-analysis of 14 RCTs that compared definitive RT with and without concurrent ChT confirmed a 7.5% OS benefit but with an 11.5% increase in grade 3–4 toxicity (4). Cisplatin is the standard ChT agent; carboplatin is the recommended alternative (5).

Patients with cisplatin contraindications are underrepresented in the above studies. We conducted a meta-analysis of mostly observational studies outcomes in these patients (6). The most cited contraindications were advanced age, renal dysfunction, poor performance status and high-risk comorbidities. In patients with relative contraindications, cisplatin is effective and well-tolerated. In those with absolute contraindications, carboplatin is well-tolerated but with unclear effectiveness. Finally, adding ChT was associated with better survival but may compromise RT compliance. This is important to recognize because RT is the primary treatment and any expected gain with ChT may be offset by RT interruptions or delays.

In the Philippines, about 33% of cervical cancers are diagnosed in the elderly (2) and about 36% present with ureteral obstruction, which requires timely intervention to preserve renal function (7). Compliance could be difficult due to inadequate RT facilities, protracted treatment schedule, and prohibitive ChT costs (8). At our institute, about 20% are unable to complete the prescribed ChT cycles or have significant RT interruptions due to tumor complications, treatment toxicity, or resource constraints. Compliance could be improved by patient and family engagement in the decision-making process and decision implementation planning.

Shared decision-making (SDM) allows for evaluation of treatment options according to patient values and preferences (9) and could be facilitated by a patient decision aid (PtDA). A PtDA is a decision support intervention (DSI) that describes the index condition or problem, explicitly states the index decision, describes the options, and describes the pros and cons, and the physical, psychological, and social consequences of each option (10).

A systematic review of PtDAs found that PtDAs improve the attributes of the choices made and the decision-making process for patients who face cancer-related decisions (11). Studies on cancer treatment decisions for breast, prostate, colon, and thyroid were included. PtDA decreased decisional conflict, the proportion of clinician-controlled decisions, and indecision. A systematic review on PtDA use in hematologic malignancies showed that PtDAs increased patient knowledge and patient satisfaction, and decreased decisional conflict and attitudinal barriers (12).

Objectives

General objective

We aim to develop, validate and test a PtDA for cisplatin-intolerant LACC patients faced with the decision of adding ChT to RT.

Specific objectives

(I) To develop a PtDA prototype and determine its pre-clinical acceptability by alpha-testing, content validity by peer validation, and its patient and practitioner user acceptability by beta testing (phase 1);

(II) To determine the effectiveness of the beta-tested prototype in terms of decisional conflict reduction (primary outcome measure) and utility in preparation for decision-making (secondary outcome measure) (phase 2).

Exploratory objective

To investigate patient determinants to decisional conflict reduction and PtDA utility (phase 2).

Methods

Study design

This is a two-phase clinical trial consisting of a phase 1 mixed-methods study and a phase 2 non-randomized sequential comparison-group pretest-post-test study.

Phase 1

The phase 1 will employ a mixed-methods design. It will encompass prototype development, alpha testing, peer validation and beta testing, per the International Patient Decision Aid Standards (IPDAS) Collaboration consensus model development process for PtDA (13).

Prototype development

The steering group will include healthcare providers involved in managing LACC patients (gynecologic oncologist, radiation oncologist, oncology nurse), an expert in patient counselling, an LACC survivor with contraindications to ChT who has previously undergone CRT, and a caregiver for an LACC patient who has completed treatment. The elements of the prototype will be based on the Decision Support Framework (14). The patient summary will be based on the National Comprehensive Cancer Network guidelines (3), local guidelines (15), current synthesis of evidence (6), and inputs from the steering committee.

Alpha testing

Acceptability encompasses comprehensibility, length, amount of information, neutrality, and overall suitability for decision-making. The acceptability of the prototype will be evaluated by the Steering Committee members using the Patient and Practitioner Versions PtDA-Research Group-Ottawa-Acceptability Questionnaire (PtDA-RG-O-AQ) (16).

The practitioner version of the instrument consists of five-point Likert type questions with 1 being very unsatisfactory, and 5, very satisfactory. The patient version consists of questions that could be answered by "very poor" to "excellent", by "just right" or "too long", "too short", too much" or "too little", by "balanced" or "slanted", by "easy to understand" or "difficult to understand", by "easier", "same" or more difficult", or by "yes" or "no".

Whenever a response indicates that or that an item is unsatisfactory (less than 4), or that a criterion has not been achieved ("very poor" or "poor", "slanted", "too much", "too little", "too long", "too short", "slanted", "more difficult", or "no"), the respondent will be asked for a suggested improvement. The Steering Committee will discuss all suggestions to guide the next iteration of the prototype.

Peer review

Three independent reviewers will evaluate the prototype: an internal reviewer with knowledge of our center's patient demographics and internal workflow, an external local reviewer with knowledge of local patient demographics and prevalent local practices and culture, and an external international reviewer with knowledge of international standards and guidelines.

The reviewers will use the IPDAS Checklist version 4 (10), which consists of 44 items covering ten domains (information, probabilities, values, guidance, development, evidence, disclosure, plain language, evaluation, and test). Qualifying criteria will be evaluated on a binary (yes or no) scale; certification criteria and quality criteria will be scored on a 1–4 scale (strongly disagree to strongly agree).

If a reviewer indicates that a criterion is not met ("no", or scored less than 3), they will be asked for a suggested improvement. Iterations will be done until all qualifying criteria have been met and the certification criteria scored ≥3. Preferable, all quality criteria will have been scored ≥3.

Beta testing

The validated prototype will be beta-tested to 3–6 patients and their caregivers, who are faced with the decision and seen by the same gynecologic oncologist. The latter will not be directly involved in the prototype development.

The gynecologic oncologist will refer an eligible patient and her nominated caregiver upon diagnosis of LACC, identification of contraindication to ChT, completion of the usual patient encounter, and grant of patient and caregiver verbal consent. The primary investigator will then confirm eligibility and proceed with the informed consent procedure. The investigator will provide the PtDA to the patient and her caregiver and orient them to its use. They may bring the PtDA home and use it in their decision-making process however they want.

Each patient will evaluate the acceptability using the PtDA-RG-O-AQ Patient Version (16) after using the PtDA and following up with the gynecologic oncologist.

After encounters with three patient-caregiver dyads, the gynecologic oncologist will evaluate the acceptability of the validated prototype using the PtDA-RG-O-AQ Practitioner Version (16), based on the collective experience from these encounters. Gathering feedback from a single gynecologic oncologist limits the variation to patient factors.

The same rules for the alpha testing will apply.

Phase 2

The non-randomized sequential comparison-group pretest-

post-test design will be employed to evaluate decisional conflict reduction, utility in preparation for decision-making, and patient determinants of these outcomes.

Clinical testing

The gynecologic oncologist will refer an eligible patient upon diagnosis of LACC, identification of contraindication to ChT, completion of the usual patient encounter, and grant of verbal consent. The primary investigator will then confirm eligibility and proceed with the informed consent procedure.

Eighteen and 27 patients will be consecutively recruited into the control and experimental groups. The groups will be recruited sequentially. In both groups, the investigator will ask the patient to evaluate her decision self-efficacy using the Decision Self-Efficacy Scale (DSES) (17) and baseline decisional conflict (pretest) using the Decisional Conflict Scale (DCS) (18). The experimental group will be provided the PtDA and oriented to its use. The participant may bring the PtDA home and use it in the decision-making process however she wants.

On follow-up, in both groups, the patient will be asked to evaluate her decisional conflict (post-test) using the DCS. The experimental group will also be asked to evaluate the utility of the PtDA using the Preparation for Decision-Making Scale (PDMS) (19) after using the PtDA and before following up with the gynecologic oncologist.

Study setting

The study will be conducted at the University of Santo Tomas Hospital-Benavides Cancer Institute (USTH-BCI), by the Gynecologic Oncology Unit. The Unit consists of two in-house and three visiting gynecologic oncologists, three in-house radiation oncologists specializing in gynecologic malignancies and a brachytherapy nurse. One of the radiation oncologists is a brachytherapy specialist. The Unit conducts monthly Tumor Boards for the mandatory institutional review of service cases, requested review of private cases, and follow-ups and updates of previous cases. The Tumor Boards are attended by radiologists with training in ultrasound (US), computed tomography (CT) and magnetic resonance (MR) imaging, pathologists, trainees in radiation oncology, gynecology, radiology, pathology departments, and per invitation, interventional radiologists, and urologists.

The Unit uses a dedicated clinic for regular consultations and procedures and a separate clinic for multi-disciplinary consultations with patients and their families. Both clinics are on the second floor of the Institute.

Trial organization and coordination

The CECIL trial was developed by the study proponents at the Department of Radiation Oncology and the Gynecologic Oncology Unit of the USTH-BCI, in cooperation with the University of Santo Tomas-Research Center for Health Sciences. The overall coordination will be performed by the Department of Radiation Oncology, which will also be responsible for the overall trial management, database management, and quality assurance.

Investigators

The study investigators are health care professional involved in the treatment and care of LACC patients. Patients will be recruited by the physicians of the Department of Radiation Oncology and the Gynecologic Oncology Unit of the USTH-BCI.

Ethics, informed consent, and safety

This study will be conducted according to the National Ethical Guidelines on Health Research (Philippine Health Research Ethics Board) (20), the principles laid down by the World Medical Assembly in the Declaration of Helsinki (as revised in 2013) and other relevant local and international guidelines in health research.

This protocol has been reviewed and approved by the Technical Review Board of the University of Santo Tomas-Graduate School (UST-GS) and by the Research Ethics Committee of the University of Santo Tomas Hospital (USTH-REC) (No. REC-2023-02-003-MD). No patient will be recruited until all the necessary approvals have been obtained and the patient has provided written informed consent.

Throughout the conduct of the trial, strict compliance with existing local, hospital and department policies regarding coronavirus disease 2019 (COVID-19) screening and triage will be observed.

Data handling, storage and archiving of data

The study will be conducted in accordance with applicable Privacy Acts and Regulations including the Data Privacy Act of 2012 (21) and its implementing rules and regulations in 2021 (22). All data generated in this study will remain

confidential and will be stored securely at the USTH-BCI and will only be available to people directly involved with the study and who have signed a Confidentiality Agreement.

Participant selection

Participants must meet all the inclusion criteria and none of the exclusion criteria to be eligible for the phase 1 beta-testing and phase 2 clinical testing.

Patient eligibility

Inclusion criteria

(I) Squamous, adeno- or adenosquamous histology;
(II) International Federation of Gynecology and Obstetrics (FIGO) stage IB3, IIA2, IIB–IVA;
(III) Contraindication to ChT, such as hydronephrosis, renal or cardiac dysfunction, advanced age, or frailty;
(IV) Grade 6 level English literacy (finished grade 6 level, or self-assessed);
(V) Informed consent.

Exclusion criteria

(I) Other histologies.
(II) Metastatic disease;
(III) Other active cancers;
(IV) Prior cancer except for a cancer treated curatively, in remission for ≥5 years, with low recurrence risk; adequately treated carcinoma-*in-situ*, lentigo maligna or non-melanoma skin cancer in remission;
(V) Prior pelvic radiation, or ChT;
(VI) Pregnancy;
(VII) Cognitive impairment or psychological disturbance limiting study compliance.

Caregiver eligibility (for the beta-testing)

Inclusion criteria

(I) Nominated by an eligible and consenting patient as the primary provider of care for most of her treatment;
(II) Grade 6 level English literacy;
(III) Informed consent.

Exclusion criteria

(I) Cognitive impairment or psychological disturbance limiting study compliance.

Sample size calculation

Minimum sample sizes of 16 and 24 for the control and experimental groups, respectively, are required based on the following assumptions.

Given that this study is exploratory, a bigger two-sided alpha error (0.10) is accepted, and a higher power (0.90) used to maximize the detection of the outcome (23). The calculation assumes that 50% and 90% (a 40% difference) of the control and experimental groups will have post-test DCS scores <25.

The 40:60 proportion, favoring the experimental group, limits the impact of history during the recruitment of the control group. Further, this allows recruiting more participants into the experimental group. For the experimental group, a sample size of 24 allows for a power of 0.90 to detect the outcome of utility (≥75% reporting utility; versus non-utility, ≤50% reporting utility), given a one-sided alpha error of 0.10

Assuming an attrition rate of 10%, we will target to recruit 18 and 27 participants into the control and experimental groups.

Investigation schedule

Indication

The gynecologic oncologist will confirm the diagnosis, stage, and cisplatin contraindication. The primary investigator will confirm final eligibility and perform the informed consent process.

Intervention

The development, validation, and testing of the PtDA will be guided by the Decision Support Framework (14). The intervention will be limited to the PtDA, without specifications for the clinical patient encounter or decision coaching. The primary user will be the patient-caregiver dyad. The PtDA will be in the English language and will be in print or in a portable document format (PDF). Its specifications and elements are summarized in *Table 1* and *Table 2*, respectively.

Administration

After the investigator has confirmed patient eligibility and secured the signed written informed consent, they will ask the patient to accomplish the DSES (17) and DCS (18).

For the experimental group, the investigator will provide the PtDA and orient the patient to its use. The investigator may not offer counselling regarding the decision-making. The patient may bring the PtDA home and use it in the

Table 1 Decision aid specifications

Parameter	Specification
Problem	Locally advanced cervical cancer with contraindications to cisplatin
Decision to be made	Addition or non-addition of concurrent chemotherapy (cisplatin or alternative agent/s) to definitive radiotherapy
Target audience	Patients and their primary caregivers
Theoretical framework	Decision Support Framework (14)
Language	English
Format	Paper; Web, without enhanced material
Setting	Pre-treatment
Patient pathway	Once with confirmation of LACC diagnosis and identification of contraindication/s to cisplatin, and before decision-making or any treatment
Evidence	NCCN Guidelines for Cervical Cancer
	SGOP Guidelines
	Evidence Synthesis (Systematic Review and Meta-Analysis of Outcomes with Definitive Radiotherapy with and without Chemotherapy) (6)
Elements	Patient information
	Summary of treatment outcomes, processes, and costs
	Guidance on examining personal values/preferences and resources
	Guidance for discussion with attending on follow-up

LACC, locally advanced cervical cancer; NCCN, National Comprehensive Cancer Network; SGOP, Society of Gynecologic Oncologists of the Philippines.

decision-making process however she wants.

During the follow-up visit, the investigator will ask the patient to accomplish the PDMS (19) after confirming PtDA use and before following up with the gynecologic oncologist.

Loss to follow-up and withdrawal from the study

A patient will be considered lost to follow-up only if no contact has been established, such that neither the post-test DCS nor the PDMS could be reasonable accomplished given time passage considerations. A patient may withdraw from the study at any time without prejudice to further treatment and care.

Assessment plan

Assessment tools

Decision Self-Efficacy Scale

The DSES was developed to measure self-confidence in decision-making, including SDM. It has two versions, with three- and five-response categories. The latter will be used as it has a better alpha coefficient (0.92) (17).

Decisional Conflict Scale

The DCS was developed to measure perceptions of uncertainty with regards to the decision, modifiable factors that contribute to the uncertainty (information, clarity of personal values, support), and effective decision-making (feeling that the decision is informed, values-based, practicable, and satisfactory) (18). It has a good correlation to constructs of knowledge, regret, and discontinuance, test-retest correlations (>0.78), alpha coefficients (>0.78), and discrimination (effect sizes of 0.2 to 0.3).

Scores <25 are associated with implementation; scores >37.5, with uncertainty resulting in deferral or non-implementation. For this study, DCS <25 and ≥25 will indicate the absence or presence of decisional conflict, respectively.

Preparation for Decision-Making Scale

The PDMS was developed to measure patient perception of how useful a DSI is in preparing the respondent to communicate with their health provider during a consultation and in making a health decision. It has good

Table 2 Elements of the prototype

Patient information
1. Sociodemographic: age, marital and family status, educational attainment
2. Clinical: stage
Patient summary: options and outcomes
1. Present current recommendations and extent of applicability
2. Present standard and non-standard options
3. Summarize outcomes for each option (e.g., disease control, survival, toxicity, quality-of-life)
4. Summarize procedures and costs for each option
Personal worksheet: perceptions, preferences, and resources (weigh scales)
1. Evaluate the current state of health compared to peers of the same age (e.g., overall, physical, emotional, social, cognitive)
2. Evaluate the perceived importance of each outcome and acceptability of each risk
3. Evaluate predisposition towards chemotherapy (decisional conflict)
4. Evaluate the perceived predisposition of important others towards chemotherapy
5. Evaluate perceived internal pressure (influence) and external pressure (persuasion) from important others towards a choice
6. Evaluate confidence, interest, and preference for decision-making (i.e., active, passive, or shared)
7. In case of deference of decision, identify preference to the physician or important others
8. Evaluate personal capability (e.g., cognitive—knowing, understanding, remembering, and applying; instrumental—independence in daily activities; financial) to implement the decision
9. Evaluate external resources (e.g., instrumental, financial, social, and emotional support) to implement the decision
Patient guidance: preparation for decision-making
1. List questions arising from the above materials
2. Review outcomes and risks with the attending physician to verify or clarify gaps in understanding
3. Discuss personal values with the attending physician by referring to the weigh scales
4. Make a (shared) decision
5. Formulate a plan and implement it

reliability (0.944), alpha coefficient (0.92–0.96), and discrimination (effect size 1.8) (19,24).

Assessment schedule

Pretest

After the initial visit and routine care, eligibility confirmation, informed consent procedure and participant registration, the investigator will ask the patient to accomplish the DSES and DCS.

Post-test

During the follow-up visit, the investigator will ask the patient to accomplish the PDMS, after confirming PtDA use for the experimental group, and before following up with the gynecologic oncologist.

Data management and statistical analyses

Baseline demographic and clinical characteristics

Frequency distributions will be described for categorical variables such as marital and family status, educational attainment, and disease stage. Means and standard deviations or medians, interquartile ranges, and ranges will be reported for continuous variables such as age and scale scores.

Decisional conflict reduction

The proportion of participants having DCS scores of

≥25 for the following group pairs will be compared using Fisher's exact test: control group post-test and experimental group post-test, and experimental group pretest and experimental group post-test.

Utility in preparation for decision-making

The PtDA will be considered useful if ≥75% of the users report utility (mean PDMS score ≥3.5).

Predictors of DCS reduction and utility

Linear regression analyses will be performed to examine the predictive value of demographic and clinical variables with regards to DCS reduction and utility (PDMS). The differences in DCS reduction and utility between two demographic or clinical groups will be analyzed by Student's *t*-test, and by one-way analysis of variance (ANOVA) when there are more than two groups. Correlations will be analyzed by Spearman's correlation analysis. A P value less than 0.05 will be considered statistically significant.

Missing data

No imputation of missing data will be done.

Statistical software

All analyses will be performed using Stata v16.1 (StataCorp LLC, Texas, USA).

Discussion

In LACC, adding ChT to RT improves survival at the cost of increased toxicity (5). In patients with cisplatin contraindications, ChT may compromise compliance to RT (6), thereby diminishing treatment effectiveness. The patient and her family must be actively engaged in the decision-making process not only to reach a well-informed, patient-centered and practicable decision, but also to develop a decision implementation plan, optimize resource allocation, and ensure treatment compliance.

Conceptual framework

The Interprofessional Shared Decision-Making (IP-SDM) Model places the patient at the center of the process, with the family and/or the caregiver on one side, and the healthcare providers and the decision coach on the other (25,26). The initiator of the process could be anyone from the interprofessional team. The process begins with a recognition of the equipoise, followed by information exchange, examination of patient values and preferences, evaluation of feasibility, determination of the preferred choice, and formulation of a compromise leading to the actual choice. The entire process is influenced by the rapport or partnership between the patient/family/caregiver and the interprofessional team, institutional structure, organizational routines, and social norms.

We will develop a PtDA to facilitate the SDM process, specifically, to explicitly define the decision to be made and to facilitate information exchange and examination of patient values and preferences. The PtDA will be in the English language to allow for peer validation by an international reviewer. To ensure its validity and quality, we will be guided by the IPDAS Collaboration Group consensus development model (13), validate the PtDA using the IPDAS instrument version 4 (10), and subject it to preclinical and pilot testing for user acceptability prior to formal clinical testing.

Rationale for the trial design

The sequential comparison group design prevents contamination bias. In a single-center, simultaneous recruitment, controls may be inadvertently exposed to the intervention by interaction with patients in the experimental group, or healthcare providers might unconsciously integrate experimental components of the PtDA in routine care. In a simultaneous recruitment in two separate centers, the control and experimental groups might significantly differ in routine care in the two centers.

Given the sequential recruitment, history could be an issue. History refers to events during the experiment other than the intervention. Thus, a smaller proportion of participants will be recruited into the control group to shorten the recruitment, thus limiting the impact of history.

Despite non-randomization, patient baseline characteristics and the pretest would account for any group dissimilarity or selection bias. The control group and the pretest would account for maturation, testing, and regression to the mean (27). Maturation refers to any change in the participants due to time passage, and testing, to changes caused by repeated measurements, rather than the intervention itself. Regression to the mean is the tendency for extreme subjects to regress closer to the mean with time.

Given the nature of the intervention, true blinding could not be done on the participant, who is also the assessor. Blinding is necessary to control for participant expectation

bias and participant performance bias. Therefore, the control group will not be made aware of a subsequent experimental group, and the experimental group will not be made aware of a prior control group. While the routine care provider could not be entirely blinded from the allocation, the pretest, as a measure of comparability, could control for provider performance bias.

Given the nature of the measurement, the impact of instrumentation or inter-observer variability is minimized. The questionnaires will be self-administered, and the investigators will limit intervention to clarifications and will not offer interpretations. The participant will be allowed to complete the questionnaires in private and be assured of anonymity to limit the impact of social desirability bias.

Scope and delimitations

Our institute is a tertiary cancer care center in a private, academic, and training hospital. Among advanced cancer patients surveyed at our center, shared or active decision control preferences were more common (48.5% and 29.3%, respectively) than passive decisional control (22.2%); 75% had at least some college schooling (28). High educational attainment was a significant negative predictor for passive decision control preference. Performance status, age and religiosity were not significant factors. Cervical cancer is a disease that is more prevalent in the lower socioeconomic classes, where lower education is more prevalent (29).

Despite SDM being considered the gold standard for helping patients in clinical decision-making and being promoted by health policies, adoption and implementation remains poor and limited (30,31). Barriers and facilitators to its use for cancer-related decisions include physician perspectives, practical considerations, evidence of cost-effectiveness, and organizational- and system-level characteristics. The primary barriers are patient perception and preference for decision control, clinician perceptions and expectations, and logistic constraints due to local clinic workflows.

Given the above considerations, subsequent research may include (I) development and testing of a Filipino version or an interactive web-based version, (II) testing in other practice settings, such as in a government center, or (III) conduct of a dissemination-implementation study (scale up) at our institute. Patient determinants for decisional conflict reduction and PtDA utility that will be identified from the current study could inform subsequent research and implementation projects.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jhmhp.amegroups.com/article/view/10.21037/jhmhp-23-9/coif). WB is currently the Treasurer of the Philippine Society of Oncologists, Inc. TSO is currently the President of the Benavides Cancer Institute. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are 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 protocol has been reviewed and approved by the Technical Board of the UST-GS and by the USTH REC (No. REC-2023-02-003-MD). No patient will be recruited until all the necessary approvals have been obtained and the patient has provided written informed consent. The study will be continually reviewed by the USTH REC according to institutional protocols, to which all adverse or reportable negative events, or protocol deviations or violations will be reported. Any protocol amendment will be reviewed and approved by the USTH REC prior to implementation. This study will be conducted according to the National Ethical Guidelines on Health Research (Philippine Health Research Ethics Board), the principles laid down by the World Medical Assembly in the Declaration of Helsinki (as revised in 2013) and other relevant local and international guidelines in

health research.

References

1. World Health Organization. Cervical cancer. World Health Organization. 2022, February 22. Available online: https://www.who.int/news-room/fact-sheets/detail/cervical-cancer
2. Bruni L, Albero G, Serrano B, et al. Human Papillomavirus and Related Diseases Report. Human Papillomavirus and Related Diseases Report. ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). 2023.
3. National Cancer Comprehensive Network. NCCN Guidelines—Cervical Cancer. V1.2022. 2022. Available online: https://www.nccn.org/professionals/physician_gls/pdf/cervical_blocks.pdf
4. Reducing uncertainties about the effects of chemoradiotherapy for cervical cancer: a systematic review and meta-analysis of individual patient data from 18 randomized trials. J Clin Oncol 2008;26:5802-12.
5. Datta NR, Stutz E, Liu M, et al. Concurrent chemoradiotherapy vs. radiotherapy alone in locally advanced cervix cancer: A systematic review and meta-analysis. Gynecol Oncol 2017;145:374-85.
6. Bacorro W, Baldivia K, Yu KK, et al. Outcomes with definitive radiotherapy among patients with locally advanced cervical cancer with relative or absolute contraindications to cisplatin: A systematic review and meta-analysis. Gynecol Oncol 2022;166:614-30.
7. Ong SRK, Rivera AS, Pauig JP. Diagnosis of Hydronephrosis or Ureteral Obstruction using Renal Sonography among Patients with Cervical Cancer. Acta Med Philipp 2022;56:82-7.
8. Laudico AV, Mirasol-Lumague MR, Medina V, et al. 2015 Philippine Cancer Facts and Estimates. Philippine Cancer Society; 2015. Available online: https://www.philcancer.org.ph/wp-content/uploads/2017/07/2015-PCS-Ca-Facts-Estimates_CAN090516.pdf
9. Makoul G, Clayman ML. An integrative model of shared decision making in medical encounters. Patient Educ Couns 2006;60:301-12.
10. Joseph-Williams N, Newcombe R, Politi M, et al. Toward Minimum Standards for Certifying Patient Decision Aids: A Modified Delphi Consensus Process. Med Decis Making 2014;34:699-710.
11. McAlpine K, Lewis KB, Trevena LJ, et al. What Is the Effectiveness of Patient Decision Aids for Cancer-Related Decisions? A Systematic Review Subanalysis. JCO Clin Cancer Inform 2018;2:1-13.
12. Zhao J, Abdallah M, Sanapala C, et al. A Systematic Review of Decision Aids in Hematologic Malignancies: What Are Currently Available and What Are We Missing? Oncologist 2023;28:105-15.
13. Coulter A, Stilwell D, Kryworuchko J, et al. A systematic development process for patient decision aids. BMC Med Inform Decis Mak 2013;13 Suppl 2:S2.
14. O'Connor AM, Tugwell P, Wells GA, et al. A decision aid for women considering hormone therapy after menopause: decision support framework and evaluation. Patient Educ Couns 1998;33:267-79.
15. Society of Gynecologic Oncologists of the Philippines. Cervical Cancer. 8th ed. Society of Gynecologic Oncologists of the Philippines, Inc.; 2018:3-16.
16. O'Connor AM, Cranney A. User Manual—Acceptability. Ottawa Hospital Research Institute; 1996. Available online: http://decisionaid.ohri.ca/docs/develop/User_Manuals/UM_Acceptability.pdf
17. O'Connor AM. User Manual—Decision Self-Efficacy Scale. Ottawa Hospital Research Institute; 1995. Available online: http://decisionaid.ohri.ca/docs/develop/User_Manuals/UM_Decision_SelfEfficacy.pdf
18. O'Connor AM. Validation of a decisional conflict scale. Med Decis Making 1995;15:25-30.
19. Bennett C, Graham ID, Kristjansson E, et al. Validation of a preparation for decision making scale. Patient Educ Couns 2010;78:130-3.
20. Philippine Council for Health Research and Development. National Ethical Guidelines for Health and Health-Related Research, 2017 (V2 ed.). Department of Science and Technology, Philippine Council for Health Research and Development; 2018. Available online: https://ethics.healthresearch.ph/index.php/phoca-downloads/category/4-neg?download=151:national-ethical-guidelines-for-health-and-health-related-research-2017-new-version
21. National Privacy Commission. Republic Act 10173 – Data

Privacy Act of 2012. National Privacy Commission; 2012. Available online: https://www.privacy.gov.ph/data-privacy-act/#0
22. National Privacy Commission. NPC-Advisory-2021-01—Data Subject Rights. National Privacy Commission; 2021. Available online: https://www.privacy.gov.ph/wp-content/uploads/2021/02/NPC-Advisory-2021-01-FINAL.pdf
23. Serdar CC, Cihan M, Yücel D, et al. Sample size, power and effect size revisited: simplified and practical approaches in pre-clinical, clinical and laboratory studies. Biochem Med (Zagreb) 2021;31:010502.
24. Graham ID, O'Connor AM. Preparation for Decision Making Scale (Data set). American Psychological Association; 2014. Available online: https://doi.org/10.1037/t22758-000
25. Légaré F, Stacey D, Gagnon S, et al. Validating a conceptual model for an inter-professional approach to shared decision making: a mixed methods study. J Eval Clin Pract 2011;17:554-64.
26. Stacey D, Légaré F, Pouliot S, et al. Shared decision-making models to inform an interprofessional perspective on decision making: A theory analysis. Patient Educ Couns 2010;80:164-72.
27. Shi L. Chapter 7: Experimental Research. In: Health Services Research Methods. 1st ed. Delmar Publishers; 1997:143-64.
28. Yennurajalingam S, Rodrigues LF, Shamieh OM, et al. Decisional control preferences among patients with advanced cancer: An international multicenter cross-sectional survey. Palliat Med 2018;32:870-80.
29. Bhatla N, Aoki D, Sharma DN, et al. Cancer of the cervix uteri. Int J Gynaecol Obstet 2018;143 Suppl 2:22-36.
30. Scholl I, LaRussa A, Hahlweg P, et al. Organizational- and system-level characteristics that influence implementation of shared decision-making and strategies to address them - a scoping review. Implement Sci 2018;13:40.
31. Spiegle G, Al-Sukhni E, Schmocker S, et al. Patient decision aids for cancer treatment: are there any alternatives? Cancer 2013;119:189-200.

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