

Critical Review

Global Review of Tools Evaluating Quality of Life in Cervical Cancer Survivors Treated With Chemoradiation Therapy



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Purpose: This systematic review aimed to identify and compare tools used to evaluate quality of life (QoL) after pelvic radiation for cervical cancer and to describe variations in results within commonly used instruments. This review hypothesized regional preferences in the selection of these tools and an absence of uniformity in their application globally.

Methods and Materials: A comprehensive search of 6 databases was conducted between the inception of each included database and June 14, 2023, focusing on studies evaluating the QoL of patients with cervical cancer during and after radiation. Excluded were studies involving cancers originating outside the cervix, those not exclusively undergoing radiation or chemoradiation therapy, such as patients who have undergone surgery, and non-English studies.

Results: Ultimately, 229 studies covering 25,693 patients and 51 countries were identified. Most studies were conducted in Asia (35.6%) and Europe (32.9%). Ninety-nine QoL instruments were identified, not including those that were specific to a single study. The European Organisation for Research and Treatment of Cancer QoL Questionnaire Core 30 (20.5%) and the European Organization for Research and Treatment of Cancer (EORTC) QoL questionnaire cervical cancer module (16.0%) were the most commonly used; however, US-based studies primarily used the Functional Assessment of Cancer Therapy-General surveys. Furthermore, there was significant variability in the timelines of survey usage in relation to when treatment was completed, further limiting the comparisons that can be made. Of the 127 studies that reported data on the time points after completion of treatment at which QoL was measured, 72.4% measured QoL within 1 year of treatment completion, and 48.8% measured QoL >1 year after treatment completion, with some studies using multiple time points for their research.

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The data that support the findings of this study are available from the author responsible for statistical analysis, christian.lumley@utsouthwestern.edu, upon reasonable request.

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Conclusions: This study revealed a fragmented landscape with significant variability in QoL survey use, limiting the generalizability and usefulness of these results to drive meaningful change. There is a need for a global standardized method to evaluate QoL after treatment of cervical cancer with radiation therapy for comparison across regions. Simplified tools may assist with the broader collection of data, which may lead to advancements for improvement of the QoL of these patients.

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Introduction

Cervical cancer is one of the most common cancers for women worldwide, with around 604,000 new cases reported in 2020.¹ Recent advancements in radiation therapy (RT) have been instrumental in enhancing the 5-year survival rates for patients diagnosed with this condition, with remission rates as high as 97% following RT treatment.^{2,3} While the advancements in RT represent a significant milestone for cervical cancer treatment, it is important to acknowledge the adverse treatment-related side effects that may arise. Patients with gynecologic cancer and survivors treated with RT report many treatment-related symptoms, such as urinary and gastrointestinal tract symptoms, sexual dysfunction, lymph edema, and pelvic pain.⁴ These symptoms can interfere with daily activities and negatively impact patients' well-being. Because patients live longer posttreatment, it becomes critical to understand and address the impact these symptoms have on quality of life (QoL).

Assessment of health-related QoL in patients with cervical cancer following RT is a complex and multifaceted process. It varies significantly globally because of differences in health care systems, cultural perspectives, and the availability of resources.⁵ Currently, there is no standardized way for providers to evaluate QoL, leading to the utilization of various standardized questionnaires and patient-reported outcomes to assess the wide array of physical, psychological, and social aspects that contribute to QoL.⁶ These tools are designed to evaluate the extent to which symptoms affect daily living and overall health satisfaction. However, the implementation and interpretation of these measures can differ significantly across different regions and health care settings.⁷ Some countries have a stronger emphasis on patient-centered care, which increases the availability of more rigorous and regular QoL evaluations, while others are limited in resources or have differing medical priorities, which tends to result in less frequent or thorough evaluations.^{8,9} This lack of standardization limits the ability to systematically understand and enhance the QoL for patients with cervical cancer. To bridge this gap, a better understanding of how QoL in patients with cervical cancer is currently evaluated globally is necessary.

This study aimed to systematically review the tools frequently employed to assess QoL and to determine which countries have collected this type of data the most. The

hypothesis was that despite the high prevalence and significant advancements in the treatment of cervical cancer, the lack of a standardized QoL assessment method leads to varied approaches internationally. This variation may result in gaps in patient care, and it limits our ability to compare QoL. By highlighting this, the study aimed to encourage the development of a more standardized approach that can be adopted globally.

Methods and Materials

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. The complete checklist is included in [Supplementary Table E1](#).

Search strategy

PubMed, Embase, Global Health, Global Index Medicus, and Scopus were used to find eligible studies. These searches were done on November 22, and then again on June 14, to look for any publications that had occurred after the original search date. These searches were focused on material published at any point in time for the topic at hand. The search terms not only included surveys that are commonly used to study QoL in this patient population but also included terms that were broad enough to find surveys that are not as well known. The concepts searched include "cervical cancer," "cervical neoplasms," "quality of life," "QoL," "QLQ-CX24," "QLQ-C30," "FACT-Cx" OR "FACT-G," "sexual dysfunction" and others. For more details on the search strategy used, please refer to [Supplementary Figure E2](#).

Selection Criteria

Inclusion criteria for eligible studies included various research methodologies, including cross-sectional surveys, cohort studies, prospective and retrospective studies, qualitative analyses, and randomized controlled trials. The studies that were included investigated many features that may affect QoL in cervical cancer survivors who underwent RT with or without chemotherapy. In order to mitigate any confounding variables as much as possible, studies involving patients with preinvasive cancers,

cancers originating outside the cervix, those not exclusively undergoing radiation treatment or combined treatment with chemorRT, and studies whose patient demographic characteristics only included those who have received surgery were excluded from the studies. We excluded patients receiving surgery to avoid including any tools that were created to look at QoL in surgery patients, specifically. The main interest was in questionnaires used to evaluate QoL after RT. Also excluded were systematic reviews and non-English studies.

Study selection and data extraction process

The studies for this review were selected using Covidence software. Two reviewers independently screened all titles and abstracts, blinded to one another's decisions. A study was included if both reviewers independently determined fulfillment of inclusion criteria. The same process was followed for full-text review. For both of these steps, any disputes were resolved by a third author. After a paper had been approved for the data extraction phase by at least 2 authors, data collection was done using the Covidence software as well. Each approved paper was reviewed by 2 different researchers, with the first filling out a data extraction form to include quantitative data collected, patient demographic characteristics, types of surveys, and methods used for collection and data analysis. After that, a second researcher filled out the same template, once again blinded to the previous researcher's answers. After each paper had been evaluated in this manner, it moved to the data consensus stage, where a third author would assess the 2 completed templates and settle any disputes that may have occurred for questions where the data did not match. For a comprehensive list of the studies used, please refer to [Supplementary Table E3](#).

Data Items

The primary outcome of interest in this study was to identify which surveys were used to evaluate QoL after treatment with RT for cervical cancer. Meanwhile, the following secondary outcomes were also collected: which countries most of the QoL data came from, which countries used which pre-existing standardized surveys for evaluation, and what time points were typically used for the data collected from these patients.

Data analysis

Using data extracted with Covidence, analysis was completed in R Studio and Microsoft Excel.^{10,11} Data were cleaned in R and Excel. Basic descriptive analysis of

the country of origin, survey instrument, study methodology, and QoL measurement time point were conducted using R. Maps and figures were generated in R using the `ggplot2` and `maps` packages.^{12,13}

Results

This systematic review consisted of 229 studies ([Fig. 1](#)) encompassing at least 25,693 total patients. In total, 159 studies reported data on the number of patients included. A median of 66 patients were included in each study, with a range of 2 to 8917 ([Supplementary Table E4](#)). Of the studies, 63.7% were cross-sectional, 27.7% were cohort studies, 5.5% were randomized controlled trials, and the remaining 2.1% were of various other methodologies, including case-control studies ([Supplementary Figure E5](#)). In terms of methodology, 91.5% of studies used a quantitative one, 7.2% used a qualitative methodology, and 1.3% used a mixed qualitative and quantitative method.

In total, 52 countries were represented. It is important to note that naturally, publication numbers will be higher in countries that have larger populations. However, the data that has not been normalized is valuable because it shows which countries are the most influential in this research landscape. 18 studies (7.6%) were conducted in multiple countries. Of the 219 studies conducted in a single country, 8.2% were conducted in Africa, 21.9% were conducted in the Americas, 35.6% in Asia, 32.9% in Europe, and 1.4% in Oceania when stratified by continent. The most frequently represented countries, however, were the US, with representation in 13.9% of studies; China, with representation in 12.6%; and India, with representation in 9.3% of studies ([Fig. 2, Table 1](#)). A majority of studies represented high-income countries (63.4%). Upper-middle-income countries were seen in 22.9% of the studies, lower-middle-income countries appeared in 12.7% of studies, and finally, low-income countries were only represented in 0.1% of studies.

Of the 78 studies that reported the proportion of patients receiving RT only, covering a total of 17,708 patients, the overall mean percentage of patients receiving this modality was 25.6%, with a median of 47.2%. Of the 96 studies reporting patients that underwent combination chemoRT, covering a total of 9,371 patients, the overall mean percentage of patients receiving this modality was 75.0%, with a median of 87.4%. Of 30 studies reporting patients receiving any brachytherapy as part of their treatment protocol, covering 3791 patients, the overall mean percentage of patients receiving this modality was 94.3%, with a median of 100%.

Ninety-nine QoL instruments were identified, not including those that were specific to a single study. The European Organisation for Research and Treatment of

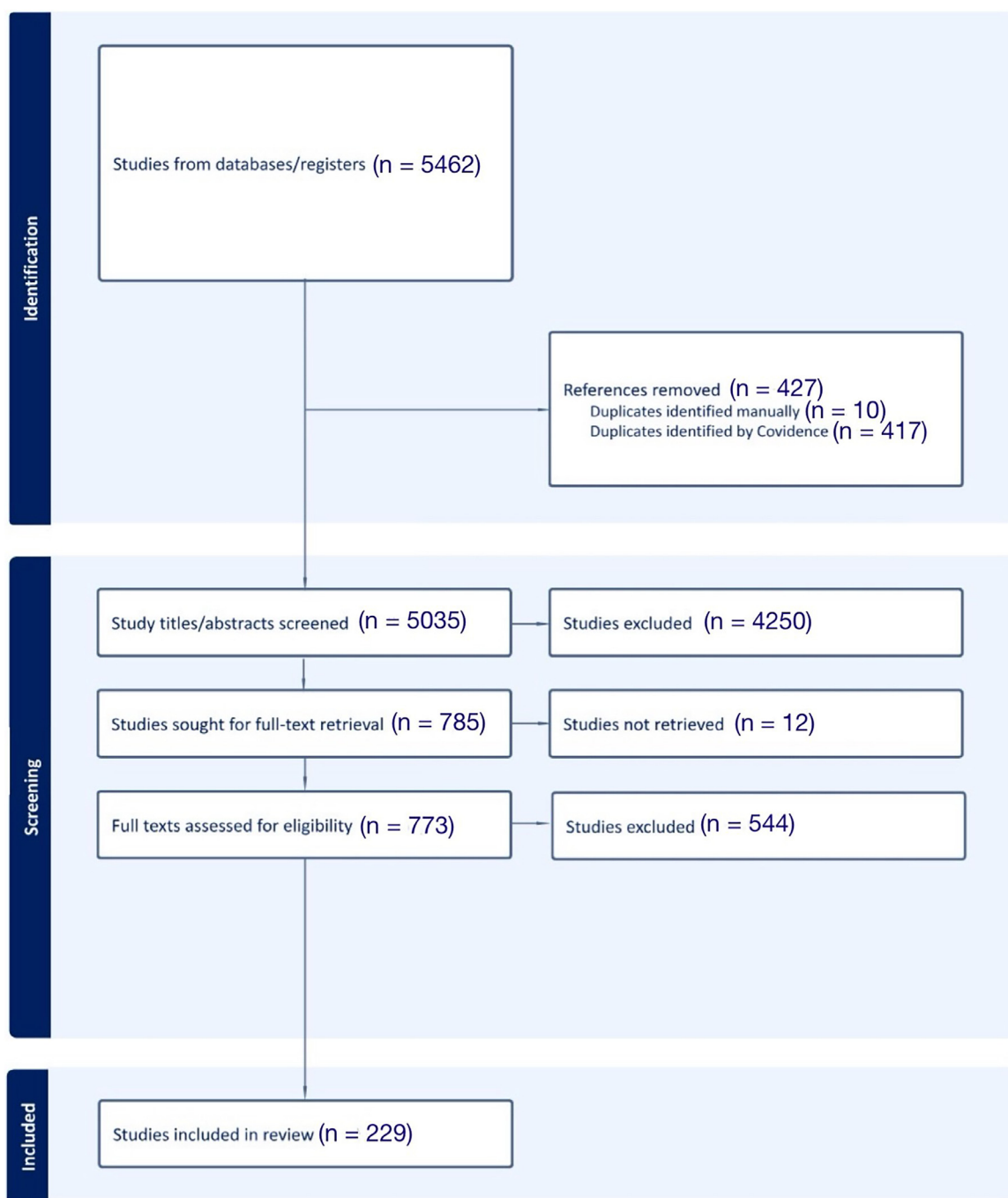


Figure 1 Covidence report.

Cancer (EORTC) QoL questionnaire (QLQ) Core 30 (EORTC QLQ-C30) and EORTC QLQ cervical cancer module (EORTC QLQ-CX24) were by far the most commonly used, with the QLQ-C30 making up 20.5% of the survey occurrences and the QLQ-CX24 making up 16.0% of occurrences. Study-specific questionnaires were the third most common instrument, adding up to 7.3% of the studies administered (Table 2). This was followed by the Hospital Anxiety and Depression Scale (5.9% of occurrences), the female sexual function index (4.6%), the

Functional Assessment of Cancer Therapy (FACT)-General (FACT-G) (4.3%), the FACT- cervical (FACT-Cx) (3.9%), the 36-item short form survey (SF) (2.3%), and the 12-item SF (1.6%). After that, the EuroQoL-5 dimension, the State-Trait Anxiety Inventory, and the World Health Organization QoL Brief Version each individually made up 1.4% of the questionnaire administrations, followed by the Common Terminology Criteria for Adverse Events, Seattle Angina Questionnaire, and Sexual function-Vaginal changes Changes Questionnaire, which each

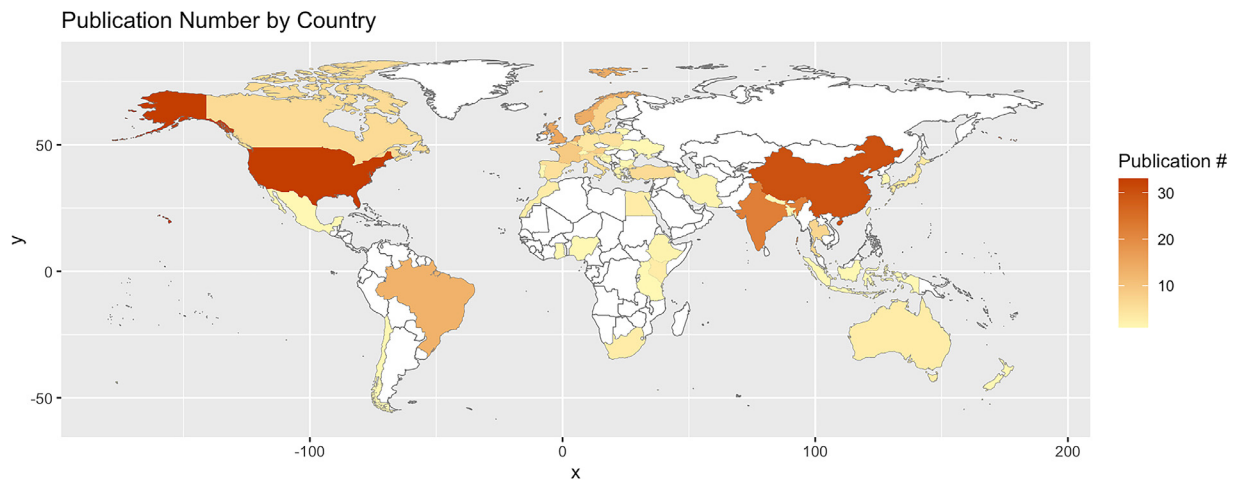


Figure 2 Publication number by country.

Table 1 Frequency of country representation

| Country | Frequency of Occurrence | Country | Frequency of Occurrence |
|--------------|-------------------------|------------------------|-------------------------|
| USA | 33 | Taiwan | 3 |
| China | 30 | Croatia | 2 |
| India | 22 | Ethiopia | 2 |
| UK | 15 | Greece | 2 |
| Netherlands | 14 | Iran | 2 |
| Norway | 14 | Bangladesh | 1 |
| Brazil | 13 | Bosnia and Herzegovina | 1 |
| Denmark | 10 | Bulgaria | 1 |
| France | 9 | Chile | 1 |
| Austria | 8 | Ghana | 1 |
| Korea | 8 | Hungary | 1 |
| Sweden | 7 | Indonesia | 1 |
| Thailand | 7 | Lithuania | 1 |
| Belgium | 6 | Mexico | 1 |
| Canada | 6 | Nepal | 1 |
| Italy | 6 | New Zealand | 1 |
| Turkey | 6 | Nigeria | 1 |
| Poland | 5 | Portugal | 1 |
| Slovenia | 5 | Slovakia | 1 |
| Spain | 5 | Switzerland | 1 |
| Germany | 4 | Tanzania | 1 |
| Japan | 4 | Uganda | 1 |
| Australia | 3 | Ukraine | 1 |
| Egypt | 3 | | |
| Kenya | 3 | | |
| Morocco | 3 | | |
| Singapore | 3 | | |
| South Africa | 3 | | |

Table 2 The overall occurrence of instruments by study

| Instrument | Occurrences* | Percentage (%) |
|------------------------------|--------------|----------------|
| EORTC QLQ-C30 | 90 | 20.5 |
| EORTC QLQ-CX24 | 70 | 16.0 |
| Study-specific questionnaire | 32 | 7.3 |
| HADS | 26 | 5.9 |
| FSFI | 20 | 4.6 |
| FACT-G | 19 | 4.3 |
| FACT-Cx | 17 | 3.9 |
| SF-36 | 10 | 2.3 |
| SF-12 | 7 | 1.6 |
| EQ-5D | 6 | 1.4 |
| STAI | 6 | 1.4 |
| WHOQOL-BREF | 6 | 1.4 |
| CTCAE | 5 | 1.1 |
| SAQ | 5 | 1.1 |
| SVQ | 5 | 1.1 |
| Other [†] | 114 | 26.0 |

Abbreviations: CTCAE = Common Terminology Criteria for Adverse Events; EQ-5D = Euroquality-of-life-5 dimension; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality-of-Life Questionnaire Core 30; EORTC QLQ-CX24 = European Organization for Research and Treatment of Cancer Quality-of-Life questionnaire cervical cancer module; FACT-Cx = Functional Assessment of Cancer Therapy-Cervical; FACT-G = Functional Assessment of Cancer Therapy-General; FSFI = female sexual function index; HADS = Hospital Anxiety and Depression Scale; SAQ = Seattle Angina Questionnaire; SF-12 = 12-item short form survey; SF-36 = 36-item short form survey; STAI = State-Trait Anxiety Inventory; SVQ = Sexual function-Vaginal Changes Questionnaire; WHOQOL-BREF = World Health Organization QoL Brief Version.

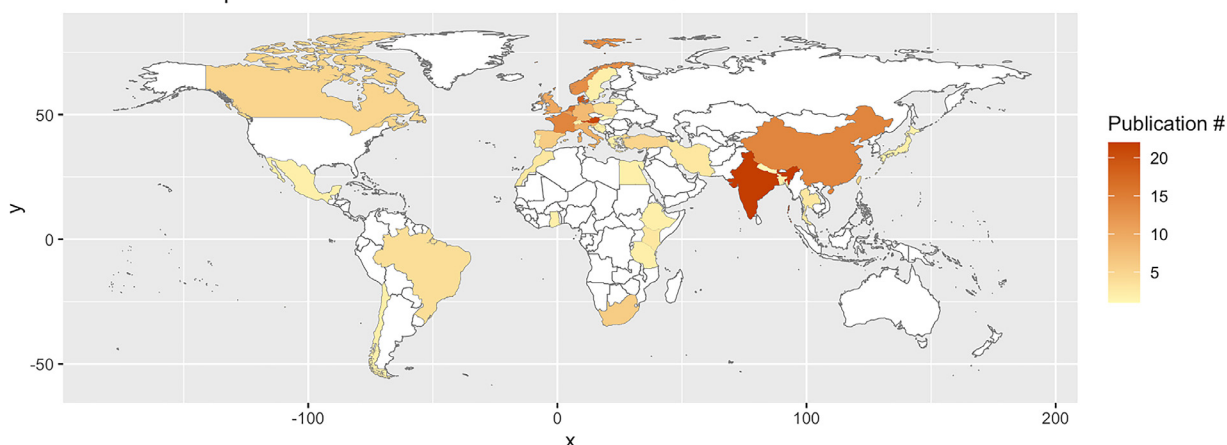
*<5 occurrences.
[†]some studies used multiple survey types

made up 1.1% of occurrences. Under the category of “other,” there were 85 nonstudy-specific instruments that appeared < 5 times, 26.0% of study occurrences.

EORTC QLQ-C30 and QLQ-CX24 were used frequently in Asia and Europe but were not used in the US (Fig. 3). The FACT-G and FACT-Cx were used primarily

in the United States and China (Fig. 4). The 36-item SF and the 12-item SF-12 were used in the US, China, and Europe.

Of the 127 studies that reported data on the time points after completion of treatment at which QoL was measured, 72.4% measured QoL within 1 year of

Publication Map for EORTC QLQ-C30 and EORTC QLQ-Cx24**Figure 3** The European Organisation for Research and Treatment of Cancer publication frequency map.

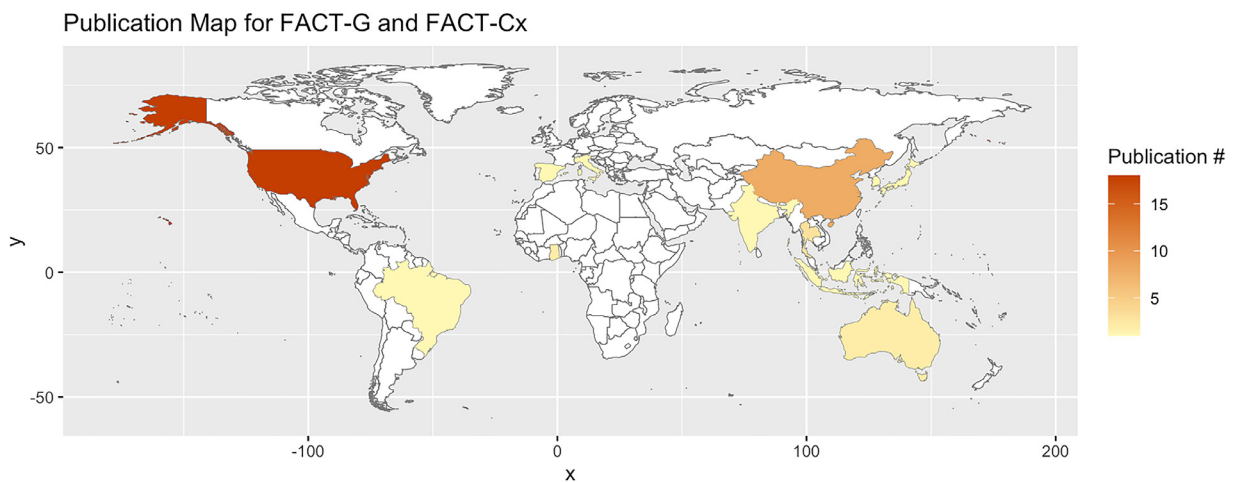


Figure 4 The Functional Assessment of Cancer Therapy publication frequency map.

treatment completion, and 48.8% measured QoL >1 year after treatment completion with some studies using multiple time points for their research. In terms of timeline, 37.0% of studies measured QoL >5 years after treatment completion. The density of data collection was greatest in the 0 to 6 months after the treatment period, with a notable decrease in measurement density over time.

Discussion

Overview

This systematic review focused on how QoL in patients with cervical cancer post-RT is assessed, by examining the global use of different survey instruments. It represents the most exhaustive review in this area, encompassing 229 studies from 51 countries, with notably fewer studies from low-income countries. Lower-middle and low-income countries were represented in only 12.8% of studies. The EORTC QLQ-C30 emerged as the most frequently used survey (20.5% of survey occurrences), followed by the EORTC QLQ-CX24 (16.0% of occurrences). The FACT-G and FACT-Cx, which were mostly used in the US, were used 4.3% and 3.9% of the time. Because the US is using a different tool, this makes it challenging to compare the results of studies with those in Europe. Various other questionnaires were employed as well. Another significant aspect observed was the variable timing of survey distribution, with 72.4% of studies measuring QoL within 1 year of treatment completion, 48.8% with >1 year after completion of treatment, and 37.0% >5 years after treatment. The diversity in survey tools and variable distribution underscores the challenge of understanding QoL in this patient population on a global scale.

Global variation

Our survey results demonstrate a pronounced regional variation in the adoption of QoL surveys with the EORTC QLQ-C30 and QLQ-CX24 surveys predominantly used in Europe, China, and India, with some extension to South America and Canada (Fig. 3). These surveys were notably absent from studies conducted within the US. In contrast, the FACT-G and FACT-Cx find their most frequent application in the US, with considerable usage also in India, China, Australia, Brazil, and some European countries like the United Kingdom and Sweden (Fig. 4). This widespread implementation across various countries and in multiple languages, however, does not suggest a superiority of one questionnaire over the other based on psychometric data.¹⁴ The distribution patterns of the FACT-G and EORTC instruments reveal distinct regional preferences that likely stem from their origins and initial validation processes. Specifically, the EORTC QLQ-C30 was initially validated through research involving European patients with lung cancer,¹⁵ whereas the FACT-G was validated using studies on patients with various types of cancer in the US.¹⁶ This difference in regional usage reflects the surveys' popularity, which lends itself to the comparison of surveys in their respective areas of origin, highlighting the impact of cultural and systemic factors on the choice and implementation of patient-reported outcome measures in global health care research.

The 2 surveys have a different approach to achieving a similar goal. The EORTC QLQ-C30 (which is available in 79 languages) uses 30 items to measure QoL through questions about general symptoms that negatively affect QoL, focusing on appetite, pain, mood, and similar manifestations. The FACT-G, on the other hand, is translated into 53 languages and uses 27 items in the form of statements that are grouped into "well-being scales."¹⁴ It is quite possible that because the EORTC is validated in 26

more languages, that may be the reason for it being used in many more studies than FACT (Table 2). Interestingly, each survey uses a unique lens to determine QoL even though they contain similar content. The EORTC QLQ-C30 emphasizes the importance of specific symptoms with added questions related to cognition, while the FACT-G categorizes their items with the lens of “well-being,” going as far as having a section of the scales dedicated to functional well-being.¹⁴ It is difficult to compare the results of these surveys because they each have their own unique scoring systems with different scales. Furthermore, both surveys have specific additional questions that are related to cervical cancer (EORTC QLQ-CX24 and FACT-Cx). The FACT-Cx is all of the statements in the FACT-G plus 15 more that address specific concerns related to cervical cancer survivors, while the EORTC QLQ-CX24 is made up of 23 questions that you would administer in addition to the EORTC QLQ-C30.¹⁷ It is important to note that the FACT-Cx already includes all of the questions asked on the FACT-G. This means that the FACT-G is never administered together with the FACT-Cx because those questions have already been covered. This is relevant because when the percentage of FACT-G question uses is added to the percentage of FACT-Cx uses (Table 2), it comes out to 36 occurrences, or 8.2%, making it the most used type of study tool after the EORTCs.

Use of alternative surveys

The results from this review highlight the use of alternative studies to assess QoL during a patient’s treatment. There were 99 different QoL surveys used to evaluate data. Providers’ use of such a wide variety of surveys to gain insights into patients’ general functioning and QoL underscores certain limitations in assessing QoL. One noteworthy aspect is the absence of a standardized approach because health care professionals can select surveys based on their perception of the most relevant side effects when evaluating QoL in patients. While this flexibility offers a nuanced understanding of patient experiences, it undermines the ability to make comprehensive and comparative assessments across different studies and populations. For instance, surveys like the female sexual function index¹⁸ and Hospital Anxiety and Depression Scale,¹⁹ while extensively used, focus on specific aspects of QoL and are not always exclusively designed for patients with cancer, which calls into question the utility of these studies for this specific purpose. Moreover, these most commonly used instruments can be extensive and time-consuming, so the development of a simplified survey that could be adjusted to a local context would be ideal for moving the QoL study forward globally.

Additionally, our review revealed that researchers often resort to creating study-specific questionnaires when existing surveys do not align with their specific goals, which made up 7.3% of survey occurrences. This approach, though innovative, further fragments the landscape of QoL assessment, making it challenging to draw broader, generalizable conclusions. Furthermore, this fragmented approach could result in some patients and their symptoms being overlooked.

Variations in survey distributions

This review highlighted notable variability in many studies regarding the distribution of surveys, with many not specifying this information in their methodology. A significant proportion of the reviewed papers surveyed patients after receiving treatment without specifying how much time had elapsed since treatment completion. Most of the reviewed papers (42.9%) did not detail when the survey was being distributed in relation to the treatment timeline. However, among those who provided this information, the most frequently mentioned time frame was within 1 year of treatment (72.4%). This was followed by periods ranging from 1 to 5 years and then periods extending beyond 5 years posttreatment. While some studies were explicitly longitudinal or assessed QoL at a distinct time point, numerous papers either provided an average time because of treatment or omitted this detail entirely. While it is necessary to recognize that the choice for when to distribute surveys depends on the individual study goal, this variation could also likely lend itself to a skewed understanding of symptoms. Evidence suggests that early side effects (within weeks of treatment completion) and late side effects (within months or years after RT) differ greatly in the type and severity of symptoms patients experience.²⁰ For instance, early in treatment, patients are more likely to present urinary symptoms such as dysuria and hematuria. In contrast, symptoms of sexual dysfunction (ie, vaginal stenosis and impaired lubrication) tend to appear later.²¹ These differences underscore the importance of a standardized approach to survey distribution because it facilitates a deeper understanding of the progression and evolution of symptoms. This knowledge could also create a timeline for when to expect certain symptoms, which could assist with proactive treatment of these side effects in the future.

Strengths and limitations

This systematic review has several notable strengths, including the comprehensive inclusion of a large number of studies. Notably, the requirements specifically excluded studies involving patients who had undergone surgery, reducing 1 potential confounding factor that could

significantly impact patients' QoL. However, the study also faced certain limitations. One key limitation was the exclusion of non-English papers, potentially leading to the omission of relevant studies. Using only English papers could also have contributed to the results determining which countries were doing most of this QoL research. Additionally, challenges in accessing some studies further constrained the review's scope. Of the accessible papers, many included data that covered multiple types of cancers, meaning that much of the data was unusable because of the inability to separate factors such as the specific ages, stages, and confounding cancers of our target population. This heterogeneity limited our ability to generalize these findings across studies.

Future directions

Future research should focus on developing standardized, globally applicable QoL survey tools sensitive to diverse patient experiences across regions and cultures—enabling meaningful comparisons across studies. Throughout this process, it is important to recognize that more questions do not equate to a better survey. Tools in the future should continue to aim to be succinct and ask only necessary questions to prevent any survey fatigue that may skew results and decrease patient participation. Future studies should evaluate the feasibility of simplifying studies to the least number of questions in order to ensure that patients would be able and willing to participate in this research. Overall, tools would ideally be patient-specific while maintaining direct comparability of the results across all studies. This is something that the EORTC Computerized Adaptive Tests Core is attempting to do. This is a computer-adaptive version of the EORTC survey that uses item banks to adapt the questionnaire to fit a specific patient. As it is being completed, the form simultaneously decreases the number of irrelevant questions and creates a tailored and pertinent form for that study participant.²² By using this singular system that can serve the goals of many studies and assess different types of patients, the data can still be directly compared on the same scales across a broader landscape.

Additionally, the underrepresentation of low- and middle-income countries in current research highlights the necessity for inclusive studies that are aware of the economic discrepancies and lack of resources contributing to these countries being represented less often. Conducting such studies longitudinally is crucial for understanding the evolution of QoL across various treatment stages and into long-term survivorship. Guidelines outlining the distribution and timing of these surveys may also be a necessary next step for consistent, reliable assessment of patients.

Conclusion

In conclusion, this study comprehensively reviews the existing literature to understand the methodologies and geographic scope of QoL assessment in patients with cervical cancer post-RT. The findings reveal a fragmented landscape, marked by using various QoL surveys distributed at variable times during patient treatment. While offering detailed insights, this variability leads to considerable confusion and inconsistency in data interpretation. This study ultimately highlighted a pressing need for standardization in QoL measurements. Such standardization is necessary to enable patients and health care providers to make well-informed decisions regarding cancer treatment and ensure patient experience is not overlooked.

Disclosures

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Supplementary materials

Supplementary material associated with this article can be found in the online version at [doi:10.1016/j.adro.2024.101700](https://doi.org/10.1016/j.adro.2024.101700).

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