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The role and contribution of treatment and imaging modalities in global cervical cancer management – survival estimates from a simulation-based analysis

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Contributors

ZJW, AS, HH, and RA designed the study. ZJW acquired the data and performed the analyses. AS was involved in acquisition of data. All authors interpreted the results and contributed to the writing of the report.

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Declaration of interests

We declare no competing interests. HH receives annual compensation for serving on the Board of Directors of Ion Beam Applications (IBA).

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Abstract

Background: Cervical cancer is the fourth most common cancer among women worldwide, with over 300,000 deaths each year. In addition to screening and prevention, effective cancer treatment is needed to reduce cervical cancer mortality. We discuss the role of imaging in cervical cancer management and estimate the potential survival impact of scaling up imaging in different contexts.

Methods: Using a previously developed microsimulation model of global cancer survival we estimated stage-specific cervical cancer 5-year net survival in 200 countries/territories. We evaluated the potential survival impact of scaling up treatment (chemotherapy, surgery, radiotherapy, targeted therapy) and imaging modalities (ultrasound, X-ray, computerized tomography [CT], magnetic resonance imaging [MRI], positron emission tomography [PET], single photon emission computed tomography [SPECT]) to the mean level of high-income countries, both individually, and as packages.

Findings: Estimated global cervical cancer five-year net survival is 42·1% (95% UI 33·8–48·5). Among individual imaging modalities, expanding MRI would yield the largest survival gains globally, while scaling up ultrasound would yield the largest gains in low-income countries, followed by expanding CT, which would have the most impact in Latin America and Oceania, with PET yielding the largest gains in high-income countries. Scaling up all treatment modalities could improve global 5-year net survival to 52·4% (95% UI 44·6–62·0). In addition to expanding treatment, improving quality of care could raise survival to 57·5% (95% UI 51·2–63·5), and the cumulative impact of scaling up all imaging modalities together with expanded treatment and quality of care improves survival to 62·5% (95% UI 57·7–67·8).

Interpretation: Comprehensive scale-up of treatment, imaging, and quality of care could improve global cervical cancer 5-year net survival by 20 percentage points, with quality of care and imaging improvements each contributing about 25% of these total potential gains. These findings suggest that a narrow focus on the availability of treatment modalities may forgo substantial survival gains. Investments in imaging equipment and personnel, as well as quality of care efforts will also be needed to successfully scale-up cervical cancer treatment worldwide.

INTRODUCTION

Cervical cancer is the fourth most common cancer among women worldwide, with nearly 600,000 women diagnosed and over 300,000 women dying from cervical cancer each year.[1] Nearly 90% of cervical cancer deaths occur in low-income and middle-income countries,[1] with large variations in incidence and survival rates affected by socio-demographic and individual-level factors which influence the risk of developing cervical neoplasia, availability of effective screening and treatment of pre-cancer, and access to early diagnosis and effective treatment for invasive cancer.

In high-income countries, population-based and opportunistic screening programs have contributed to substantial decreases in cervical cancer incidence and a downward shift in stage at diagnosis.[2–4] However, effective coverage rates for cervical cancer screening are very low outside of developed countries, with women with the highest risk of developing cervical cancer the least likely to be screened.[5] Since 2006, vaccines to prevent infection with human papillomavirus (HPV), the causative agent for nearly all cervical cancers, have become available.[6] However, uptake of the HPV vaccine has varied considerably by income group, with less than 3% of girls and women aged 10–20 years having received the full course of the HPV vaccine in low-income and middle-income countries, compared to 33% in high-income countries.[7] Worldwide, across all country income groups, women with lower socioeconomic status, especially those residing in rural areas, are less likely to have access to cervical cancer prevention, screening, and treatment.[8–10]

The World Health Organization (WHO) is developing a strategy to eliminate global cervical cancer which includes triple-intervention coverage targets by 2030: 90% HPV vaccination coverage, 70% coverage of twice-lifetime cervical screening, and 90% treatment availability for pre-invasive lesions and invasive cancer.[11] A recent modelling analysis finds that while vaccination alone would have minimal impact on cervical cancer mortality in the near future, additionally scaling up screening and treatment would reduce mortality by 34·2% (95% UI 23·3–37·8) in low-income and middle-income countries by 2030, with a 99% reduction in cervical cancer mortality possible over the next century by successful implementation of the WHO elimination strategy.[12]

In addition to expanding access to screening and prevention, improving the availability of effective cancer treatment will thus be needed to reduce the burden of cervical cancer mortality. Resource-stratified clinical practice guidelines for women with cervical cancer have been published by the American Society of Clinical Oncology[13] and the National Comprehensive Cancer Network.[14] Both provide guidance for the use of imaging, which plays several roles in the management of invasive cervical cancer. First, imaging complements physical examination in the determination of cancer staging and primary treatment. Second, imaging guides the selection of fields for radiotherapy, one of the critical modalities for cervical cancer treatment. Third, imaging is used to assess treatment response and to evaluate possible recurrence or progression of disease. The presence or absence of good imaging capability is thus a major determinant of the quality of cervical cancer treatment and care. In this analysis we discuss the role of imaging in cervical cancer

management and estimate the potential survival impact of scaling up the availability of different imaging modalities while expanding treatment and quality of care.

METHODS

Overview

To estimate cervical cancer survival we used a previously developed microsimulation (individual-level) model of stage-specific cancer survival in 200 countries/territories which takes into account the availability of specific treatment modalities (chemotherapy, radiotherapy [including brachytherapy], surgery, targeted therapy), and imaging modalities (ultrasound, X-ray, computed tomography [CT], magnetic resonance imaging [MRI], positron-emission tomography [PET], single-photon emission computed tomography [SPECT]).[15] The model also accounts for quality of care, capturing health-system and facility-level factors that account for residual differences in survival not explained by cancer stage or treatment and imaging availability (e.g. interpreting radiologist expertise, technologist acquiring images, nursing standards, infection control, etc).[15] We simulated cervical cancer survival in each country, and evaluated the potential impact of scaling up treatment and imaging modalities, while improving quality of care.

Survival impact of treatment/imaging modalities

To estimate prior probability distributions for the impact of specific treatment and imaging modalities on cervical cancer 5-year net survival, we performed a two-stage survey to elicit expert opinions, described elsewhere.[15] A sample of actively practicing physicians was selected from collaborating institutions based on demonstrable expertise in their field (imaging or treatment of cancer patients), both in high-income and low-resource settings. Respondents were asked to indicate the impact of each treatment/imaging modality on stage-specific five-year net cervical cancer survival using a four-point scale. We received between 17–35 responses for each modality. To provide consensus results, responses with at least 75% agreement were accepted as final responses, while responses with lower levels of agreement were discussed by a panel of experts to forge final consensus. As a simplifying assumption, expert opinion responses for treatment impacts were based on recommended treatment for patients at first presentation. Similarly, survey responses regarding imaging are limited to initial staging. These expert consensus results thus reflect best contemporary care for patients initially diagnosed at different stages of cancer.

Stage at diagnosis

Initial staging and treatment recommendations for women with invasive cervical cancer are primarily based upon physical examination and imaging. The International Federation of Gynecologists and Obstetricians (FIGO) provides guidelines for cervical cancer staging.[16] These were recently updated to include data from imaging or surgical assessment, which in some cases can provide critical information regarding lymph node metastatic disease. Cervical cancer survival varies substantially by stage. For example, estimates of stage-specific survival from 2010–2016 in the US from the Surveillance, Epidemiology, and End Results (SEER) Program reveal a large gradient in 5-year (net) survival by stage: Stage I = 91%; Stage II = 67%; Stage III = 49%; Stage IV = 17%.[17]

While it is commonly assumed that cancers in low-income and middle-income countries are diagnosed at later stages, actual data are scarce on the global stage distribution of cervical cancer. To fill this gap, as part of the model development we performed a literature review of reported stage distribution (I-IV) by country, described elsewhere.[15] Estimates of cervical cancer stage at diagnosis were available from 83 studies in 55 countries. We used a hierarchical modeling approach to regularize the reported estimates and estimate stage distribution for countries for which no data were aviailable.[15]

Survival estimates

Using a previously developed microsimulation model of global cancer survival, we estimated five-year net survival in each country for cervical cancer patients diagnosed in 2018 (based on GLOBOCAN 2018 estimates). Model inputs regarding the availability of treatment modalities were based on previously published estimates, and the availability of imaging modalities was estimated based on data obtained from the International Atomic Energy Agency (IAEA) IMAGINE database.[18] The model was calibrated to empirical data on five-year net cancer survival in 2010–14 from CONCORD-3.[19] Full details on the model development are described elsewhere.[15]

We simulated stage-specific cervical cancer survival in each country, and evaluated the potential impact of individual policy interventions which expand the availability of specific treatment and imaging modalities to the mean level of high-income countries. We also simulated more comprehensive packages of scale-up which simultaneously expand the availability of multiple treatment and imaging modalities. Specifically, we evaluated the incremental survival benefits of sequentially adding imaging modalities to packages of expanded treatment availability and improved quality of care. We estimated the cumulative impact of sequentially expanding access along a continuum: 1) treatment availability (all modalities); 2) quality of care; 3) ultrasound; 4) CT (including x-ray); 5) MRI; 6) SPECT; 7) PET. We ran 1,000 simulations of the model for all policy scenarios, sampling from the 100 best-fitting parameter sets identified by calibration.[15] We report the mean and 95% uncertainty intervals (UI), calculated as the 2·5 and 97·5 percentiles of the simulation results. The simulation model was developed in Java (version 1.8.0).

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all of the data and the final responsibility to submit for publication.

RESULTS

Expert opinion consensus results for the impact of each treatment and imaging modality on five-year net cervical cancer survival are presented in Figure 1. The findings indicate that chemoradiotherapy is critical for managing invasive cervical cancer, while surgery is only beneficial for early-stage cancers. For imaging, expert opinion suggests that MRI is necessary for all stages of cervical cancer, while PET and CT are recommended for more advanced stages.

Assessing the model fit, we found that the model prediction intervals (95% UI) for the training set of cervical cancer calibration targets overlapped with the CONCORD 95% CIs 93·0% of the time, with coverage probabilities of 82·5% and a mean absolute error of 5·35 percentage points.[15] Although the test set of CONCORD estimates (not used for calibration) only comprised three estimates for cervical cancer, the model performed well compared to this small test set: the prediction intervals contained these estimates with 100% coverage and a mean absolute error of 1·96 percentage points.[15] These predictive accuracy checks on data not used to fit the model help to build confidence in the robustness of the model estimates.

Posterior means and 95% UIs of cervical cancer stage distribution and stage-specific survival are reported from the calibrated simulation model by country income group and geographic region in Table 1. We estimate that 49·0% (95% UI 15·3–78·5) (35,200/71,800) of cases are diagnosed at advanced stage (III-IV) in low-income countries, compared to 39·8% (95% UI 29·7–51·4) (28,900/72,500) in high-income countries. We also find that stage-specific survival varies widely by country income group and geographic region, and estimate that overall global five-year net survival is 42·1% (95% UI 33·8–48·5), with large variation by country (see Figure 2).

We find that the scale-up of specific treatment modalities that would yield the largest survival gains varies by income group and region (see Table 2). Specifically, we find that scaling up access to radiotherapy would yield the largest survival gains in low-income countries, and in Africa and Oceania in general, while expanding surgery availability would yield the largest gains in lower-middle income countries and upper-middle income countries, and Asia as a whole. In contrast, we find that expanding access to chemotherapy would yield the largest survival gains in Latin America, while improving the quality of care would bring the largest benefits in high-income countries and in Europe and North America, as the availability of treatment/imaging modalities is already high.

For imaging, we also find that the scale-up of individual modalities that would yield the largest survival gains varies by context (see Table 3). Expanding the availability of MRI would yield the largest survival gains globally, and in lower-middle income and upper-middle countries in particular. Expanding ultrasound would yield the largest survival gains in low-income countries, followed by CT, which is estimated to yield the largest survival benefits in Latin America and Oceania. In contrast, expanding PET is estimated to yield the largest benefits in high-income countries. However, the gains from expanding any single treatment or imaging modality individually are small.

We find that scaling up the availability of all treatment modalities to the mean level of high-income countries could improve global 5-year net survival to 52·4% (95% UI 44·6–62·0) (see Table 4). Increasing treatment availability to the mean level of high-income countries while also improving quality of care could raise survival to 57·5% (95% UI 51·2–63·5), and including investments in imaging further improves survival to 62·5% (95% UI 57·7–67·8). We therefore find that comprehensive scale-up of treatment, imaging, and quality of care could potentially improve global 5-year net survival of cervical cancer by 20 percentage points, with quality of care and imaging improvements each contributing 25% of the survival

gains (i.e. half of the total increase). Survival would improve most in low-income and lower-middle income countries (Figure 3a) and Africa and Oceania (Figure 3b).

DISCUSSION

We find that imaging is a critical component of cervical cancer management. Globally we find that comprehensive scale-up of treatment, imaging, and quality of care to mean levels in high-income countries could improve five-year net cervical cancer survival by 20 percentage points, with quality of care and imaging together contributing to half of the increase (about 25% each). We find that the stage distribution of cervical cancer varies by income group and region, with worse stage at diagnosis in low-income countries. Stage-specific and overall 5-year net survival also varies widely due to lack of availability of treatment and imaging modalities, and quality of care. We find that among single treatment modality interventions, expanding radiotherapy availability would yield the largest survival gains in low-income countries, while increasing the availability of surgery would yield the largest gains in lower middle-income and upper middle-income countries, with improvements in quality of care producing the most benefit in high-income countries as treatment is already generally available. We also find that the relative priority of single imaging modality policies differs by context. Specifically, we find that expanding access to MRI would yield the largest survival gains globally, and in lower-middle income and upper-middle income countries in particular. In low-income countries, scaling up ultrasound could yield the largest gains, especially in Africa, followed by CT, which would produce the largest benefits in Latin America and Oceania. In contrast, in high-income countries we find that increasing the availability of PET would yield the largest survival gains, although these gains are small as survival is already relatively high in high-income countries.

However, overall we find that the survival impact of expanding the availability of any single imaging/treatment modality is modest even in lower-income countries; more comprehensive packages of scale-up will be needed to substantially improve cervical cancer survival. We estimate that simultaneously expanding the availability of treatment and imaging modalities and improving the quality of care to high-income levels could improve global 5-year net survival by 20 percentage points. Importantly, we find that improvements in quality of care and imaging availability each contribute 25% of the survival gains (i.e. half of the total increase). This highlights the importance of simultaneous investments in quality of care and medical imaging, which helps to improve the management of cervical cancer in a number of ways, such as determination of cancer staging and primary treatment, selection of fields in radiotherapy planning, and assessment of treatment response.

Clinical staging may be inaccurate in 17–32% of patients with early disease (IB) and up to 65% of patients with advanced disease (IIB-IV), thus adversely affecting patient prognosis.[20] Recent studies have found that imaging impacts initial stage determination for around 40% of cervical cancer patients.[21–23] Improvements in imaging availability and quality may thus improve patient prognosis and also provide more accurate estimates of stage distribution at diagnosis. Our estimates of the impact of improving the availability and quality of imaging are thus likely to be conservative as we assume that the ‘observed’ stage

distribution remains unchanged, whereas with imaging one would expect improved care with more precise staging of cervical cancer.

A recent meta-analysis on the diagnostic performance of imaging modalities for determining local disease extent and nodal metastasis in patients with newly-diagnosed cervical cancer finds that MRI is the method of choice for assessing local extent, but where not available ultrasound can be of value, especially for assessing parametrial invasion.[24] The study also finds that CT, MRI, and PET have high specificity but poor sensitivity for detection of lymph node metastases.[24]

In settings with only basic resources, chest X-ray may be used to rule out gross metastatic disease in the lungs or bones of the thorax. In settings with greater imaging capability, women should undergo CT of the chest, abdomen, and pelvis. Where available, MRI or whole-body PET combined with CT can provide greater accuracy than CT alone. Ideally, CT of the abdomen is used to evaluate the kidneys and presence/potential causes of hydronephrosis, but in resource-constrained settings, ultrasound can also be used.

Once the extent of disease has been evaluated, appropriate treatment can be planned. Early-invasive disease (stage IA1) may be treated with conization for women who wish to preserve fertility. Slightly more advanced disease (stage IA2) may be treated with radical trachelectomy, or neoadjuvant chemotherapy, followed by conization. Pelvic MRI is commonly used to evaluate depth of invasion of the uterine cervix and thus guide decision making. If MRI is contraindicated, then pelvic transvaginal ultrasound may be used to evaluate the depth of invasion in the uterine cervix. Women with more advanced disease (stage IB1-IIA) may be considered for primary surgery, generally modified radical hysterectomy.

Primary chemoradiation, including both external beam and intracavitary radiation, is also a treatment option for women with stage IB1, IB2 and IIA disease, and is the only curative treatment option for women with IB3, IIB, IIIB, IIIC and IVA disease. Alternatively, if chemotherapy is not feasible, regional hyperthermia is an option to enhance radiotherapy effect.[25] Imaging of the chest, abdomen, and pelvis is therefore of critical importance to identify patients with locally advanced disease but without evidence of para-aortic metastasis, who should be treated with definitive chemoradiation, and those with para-aortic metastasis, who should be treated with extended field radiation with chemotherapy. Similar consideration should be given to radiation of the groin for cervix tumours with distal vaginal involvement.

Accurate imaging of the chest, abdomen, and pelvis can thus be critical for cervical cancer management. In addition to improving survival, determining appropriate primary treatment by evaluating para-aortic (PA) nodes can reduce the number of women referred to surgery, directing them to primary chemoradiotherapy instead, saving on costs of treatment and quality of life decrements due to unnecessary surgery.

CT scans of the abdomen and pelvis are also used for planning fields for radiotherapy. Compared to fluoroscopic simulation, 3D planning allows increased dosing to the tumour and decreased dosing to normal tissues, thus increasing the chance of local cure and

decreasing toxicity to the organs at risk. Imaging is also used for intracavitary brachytherapy planning, and can help to position applicators for optimal dose distribution. While MRI or CT would ideally be used, ultrasound may also be used to rule out perforation of the uterus and X-ray used to verify applicator placement. Interstitial brachytherapy may be done with the use of MRI (or CT at a minimum) to determine needle placement and for treatment planning. Newer brachytherapy approaches, especially those using MRI for guidance, result in reduced toxicity and improved outcomes in patients with locally advanced cervical cancer.[26,27]

PET/CT done at 3 months post-treatment has been found to correlate well with treatment response, risk of recurrence, and disease prognosis, especially after radiation.[28] While PET/CT may not be needed for all cases, it can be helpful to assess treatment response for patients with initial high burden of disease, or for whom assessing response by clinical examination is difficult. Women who develop signs suggestive of recurrent cervical cancer should undergo physical examination and imaging of the chest, abdomen, and pelvis. There is however no conclusive data supporting a role for routine imaging as part of surveillance after definitive therapy.

Although we synthesized data from multiple sources, data limitations mean that we had to make assumptions when developing the model. For example, estimates of cervical cancer stage at diagnosis were only available for selected countries, and then only for general stages I-IV. Due to the scarcity of stage data we were not able to estimate trends in stage at diagnosis over time. More information on the distribution (and survival) of incident cervical cancers by detailed FIGO staging (e.g., IIa vs IIb) would allow us to refine our model assumptions and improve the precision of our estimates. The collection and reporting of accurate stage data in population-based cancer registries (both across and within countries) is critical for global cancer research aimed at informing policy and practice to improve cancer outcomes. Additional funding is needed for population-based cancer registries to systematically incorporate and report stage data. We used the best available data that currently exist and can refine our estimates as more data become available in the future.

Our model results suggest that substantial gains in cervical cancer survival could be achieved by scaling up treatment and imaging modalities and quality of care. However, to achieve such scale-up, investments must be made in equipment, training of engineering and health professionals, and infrastructure such as informatics services. For technologies such as MRI and PET/CT, having adequate human resources is an important consideration in addition to the costs of equipment and installation. For example, technicians are needed to operate the equipment, in addition to the radiologists and nuclear medicine physicians trained to read the results and implement the appropriate protocols for diagnosis. Another barrier to effective treatment of cervical cancer is the global shortage of healthcare professionals with expertise in the development of radiation plans for individual patients.[29]

In addition, efforts aimed at health system strengthening will be needed to improve cancer prevention efforts, early detection of disease, and efficient referral of cancer cases. Indeed, even after scaling up treatment and imaging availability and improving quality of care for invasive cervical cancers, we find that a survival gap still exists between high-income and

lower-income countries due to higher stage at diagnosis (see Figure 3A). This highlights the importance of primary and secondary prevention (ie, HPV vaccination and screening) as critical components of comprehensive cancer control efforts. Once detected, women with suspected invasive cancer should be diagnosed and placed on definitive treatment as quickly as possible, with scans completed within 30 days of referral and imaging reports made available promptly (i.e., within 4–7 days of the scan).[13,14,30] Effective communication between imaging experts and other members of the medical decision-making team will also be needed as a critical component of comprehensive scale-up of treatment and imaging modalities and quality of care that could yield major benefits for cervical cancer survival worldwide.

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Research in context

Evidence before this study

Recent data on cervical cancer five-year net survival is provided by the CONCORD-3 study. GLOBOCAN 2018, produced by the International Agency for Research on Cancer, also provides modeled mortality estimates for cervical cancer. The World Health Organization is developing a strategy for eliminating cervical cancer globally, which includes targets for vaccination coverage, screening, and treatment. A recent modelling analysis finds that while vaccination alone would have minimal impact on cervical cancer mortality in the near future, additionally scaling up screening and treatment could reduce mortality by 34% in low-income and middle-income countries by 2030. We searched PubMed using the search terms “cervical cancer”, “survival”, “global” and “imaging” on May 11, 2020, without language or publication date restrictions, and find no estimates of the impact of imaging modalities on global cervical cancer survival.

Added value of this study

Using a microsimulation model of global cancer survival this study provides estimates of cervical cancer stage distribution and five-year net survival (stage-specific and overall) for 200 countries and territories. We provide expert opinion consensus on the impact of treatment (chemotherapy, surgery, radiotherapy and targeted therapy) and imaging modalities (ultrasound, X-ray, computerized tomography [CT], magnetic resonance imaging [MRI], positron emission tomography [PET], and single photon emission computed tomography [SPECT]) and discuss the role of imaging in cervical cancer management. We also estimate the potential survival impact of scaling up specific treatment and imaging modalities in different contexts. Among single imaging modalities, we find that expanding MRI would yield the largest survival gains globally, while scaling up ultrasound could yield the largest gains in low-income countries, followed by expanding CT, which would have the most impact in Latin America and Oceania. In contrast, increasing the availability of PET would yield the largest gains in high-income countries.

Implications of all the available evidence

Cervical cancer survival varies substantially by country, largely due to differences in the availability of treatment and imaging modalities, and quality of care. Comprehensive scale-up of treatment and imaging modalities and quality of care could potentially improve global cervical cancer 5-year net survival by 20 percentage points. Quality of care and imaging improvements each contribute about 25% of these gains in 5-year net survival (i.e. half of the total increase). In addition to expanding treatment availability, investments will therefore also be needed in imaging equipment, human resources, and quality of care efforts to successfully scale up treatment of invasive cervical cancer worldwide.

Modality	Stage I	Stage II	Stage III	Stage IV
Treatment				
Chemotherapy	Necessary*	Necessary*	Necessary	Necessary
Radiotherapy	Necessary*	Necessary*	Necessary	No impact
Surgery	Necessary	Small impact	No impact	No impact
Targeted therapy	No impact	No impact	No impact	No impact
Imaging				
Ultrasound	No impact	Small impact	Small impact	Moderate impact
X-ray	No impact	No impact	No impact	No impact
CT	Small impact	Moderate impact	Necessary	Necessary
MRI	Necessary	Necessary	Necessary	Necessary
PET	No impact	Necessary	Necessary	Necessary
SPECT	No impact	No impact	No impact	Small impact

*For patients with bulky Stage I/II disease or parametrial extension

Figure 1:

Expert opinion consensus of impact of treatment and imaging modalities on 5-year cervical cancer net survival given initial stage at diagnosis

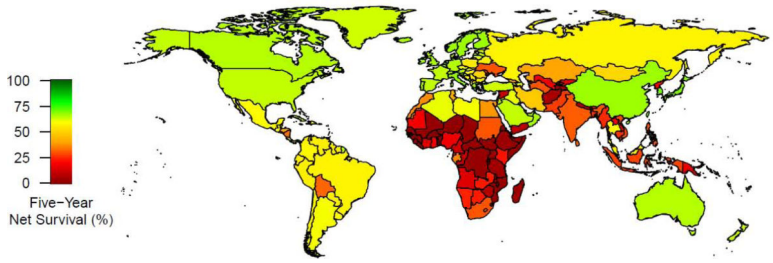

Figure 2.
Estimated 5-year cervical cancer net survival by country

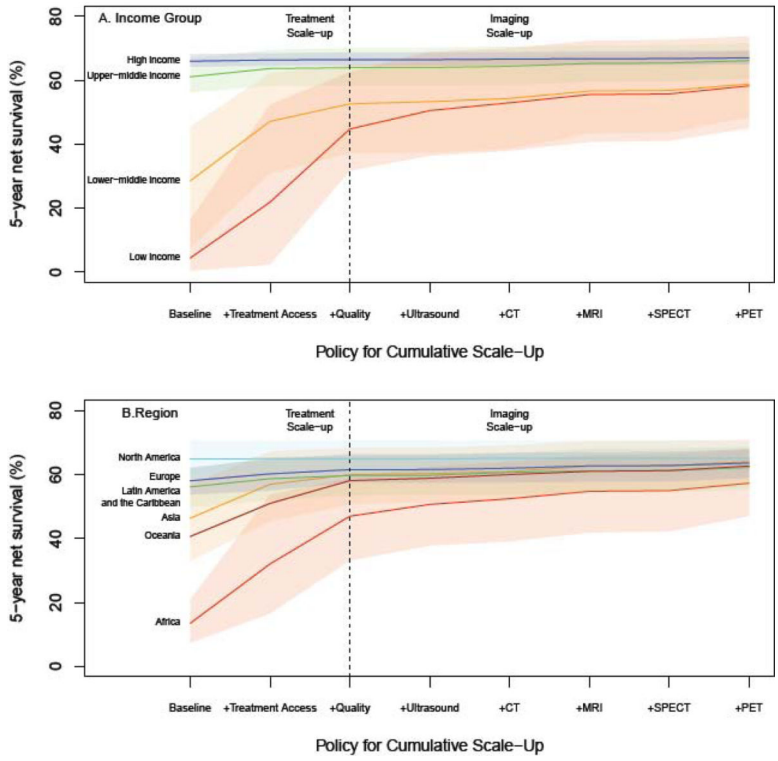

Figure 3.

Estimated 5-year cervical cancer net survival with cumulative scale-up of treatment and imaging (A) By income group. (B) By geographical region. Shaded regions indicate 95% UI. Dashed vertical line indicates the point at which imaging scale-up begins to be added to the cumulative scale-up policices. UI=uncertainty interval. SPECT=single photon emission CT.

Table 1:

Cervical cancer stage at diagnosis and survival by income group and region, means (95% UI)

	Stage I		Stage II		Stage III		Stage IV	
	% of cases	5-year net survival (%)	% of cases	5-year net survival (%)	% of cases	5-year net survival (%)	% of cases	5-year net survival (%)
GLOBAL	23·1 (11·9-33·9)	74·3 (53·5-87·3)	32·4 (19·0-45·0)	42·1 (27·2-54·2)	34·2 (20·4-48·2)	30·5 (21·3-42·7)	10·4 (4·2-21·7)	10·1 (2·9-17·1)
Low Income	15·5 (0·1-58·8)	10·3 (0·3-29·9)	35·5 (9·7-69·0)	4·1 (0·4-16·0)	36·8 (6·7-64·5)	2·6 (0·2-9·9)	12·3 (1·6-35·7)	1·6 (0·0-6·2)
Lower-Middle Income	15·6 (3·8-35·5)	49·5 (9·6-81·1)	34·6 (20·1-54·0)	31·8 (6·5-52·0)	38·7 (19·3-62·2)	23·1 (5·9-41·2)	11·2 (2·2-34·3)	7·7 (0·3-16·4)
Upper-Middle Income	27·7 (11·9-43·5)	89·9 (83·0-94·3)	33·4 (18·5-54·5)	62·3 (51·9-70·8)	31·5 (15·3-47·7)	44·9 (32·0-53·6)	7·4 (2·1-19·0)	13·4 (4·9-20·9)
High Income	40·6 (29·8-51·0)	92·6 (89·0-95·7)	19·5 (9·7-31·9)	67·7 (59·4-75·2)	25·4 (10·4-44·1)	50·1 (42·0-58·8)	14·5 (6·0-24·7)	16·8 (10·6-22·1)
Africa	14·7 (1·1-39·3)	32·7 (4·5-66·4)	34·0 (16·5-59·3)	14·9 (5·7-28·4)	37·5 (13·0-57·5)	10·7 (3·2-27·0)	13·8 (2·1-32·5)	4·3 (0·2-10·7)
Asia	24·7 (11·0-40·6)	76·9 (56·3-90·3)	33·4 (19·3-53·9)	46·1 (26·5-60·9)	33·6 (16·8-51·3)	33·1 (20·6-46·6)	8·3 (1·8-23·4)	11·2 (2·1-20·0)
Europe	30·1 (13·6-47·8)	89·4 (82·4-95·0)	26·6 (11·6-48·9)	60·2 (48·0-70·8)	30·5 (12·7-50·8)	43·6 (32·4-53·1)	12·7 (3·2-24·4)	14·4 (5·8-21·3)
Latin America and the Caribbean	20·3 (8·5-35·6)	89·6 (82·7-94·7)	34·2 (20·8-52·0)	60·4 (47·8-70·9)	35·9 (20·5-53·6)	44·1 (30·1-54·8)	9·6 (3·0-22·1)	13·3 (3·8-21·6)
North America	39·9 (27·9-53·2)	93·3 (89·9-96·4)	14·6 (5·8-26·2)	69·6 (61·1-77·3)	27·6 (8·5-45·0)	51·9 (45·3-60·0)	17·9 (5·9-30·2)	18·2 (11·9-23·9)
Oceania	27·8 (10·9-49·9)	76·0 (42·1-93·5)	27·0 (9·3-50·1)	35·3 (11·0-66·9)	32·5 (10·4-50·4)	27·3 (9·7-48·6)	12·7 (3·4-28·2)	11·6 (2·1-22·2)

Table 2:

Five-year net survival by income group and region under various policies that expand availability of single treatment modalities to the mean level of high-income countries, means (95% UI)

		Baseline	Chemo-therapy	Radio-therapy	Surgery	Targeted therapy	Quality
Global	Survival (%)	42·1 (33·8-48·5)	43·4 (34·3-50·6)	45·4 (37·5-53·6)	45·7 (35·9-52·8)	42·2 (33·9-48·6)	44·1 (34·8-53·0)
	Gain (%)	---	*1·3 (0·0-3·8)*	*3·2 (0·7-9·4)*	*3·6 (0·3-10·0)*	*0·1 (0·0-0·5)*	*2·0 (0·1-7·3)*
Low income	Survival (%)	4·4 (0·4-16·4)	5·5 (0·7-18·5)	9·5 (0·8-29·7)	8·1 (0·6-27·9)	4·4 (0·4-16·4)	9·3 (2·2-28·4)
	Gain (%)	---	*1·1 (0·0-4·3)*	*5·2 (0·3-13·5)*	*3·7 (0·1-17·5)*	*0·0 (0·0-0·0)*	*5·0 (0·0-19·1)*
Lower middle income	Survival (%)	28·5 (7·5-45·5)	30·8 (7·7-47·8)	34·6 (16·7-49·6)	35·9 (11·8-50·3)	28·6 (7·5-45·5)	31·8 (8·2-50·0)
	Gain (%)	---	*2·2 (0·1-8·2)*	*6·0 (0·3-21·3)*	*7·4 (0·3-21·1)*	*0·1 (0·0-0·2)*	*3·2 (0·0-16·1)*
Upper middle income	Survival (%)	61·1 (56·2-66·8)	61·9 (56·8-67·2)	61·8 (56·5-67·2)	61·9 (57·1-67·6)	61·3 (56·3-66·9)	61·3 (56·5-67·2)
	Gain (%)	---	*0·8 (0·0-2·5)*	*0·7 (0·0-2·6)*	*0·8 (0·0-2·9)*	*0·2 (0·0-0·8)*	*0·2 (0·0-1·4)*
High income	Survival (%)	66·0 (64·2-68·2)	66·1 (64·4-68·3)	66·1 (64·3-68·2)	66·1 (64·3-68·3)	66·1 (64·3-68·2)	66·1 (64·3-68·4)
	Gain (%)	---	*0·1 (0·0-0·6)*	*0·1 (0·0-0·3)*	*0·1 (0·0-0·5)*	*0·1 (0·0-0·3)*	*0·1 (0·0-0·5)*
Africa	Survival (%)	13·5 (7·4-20·9)	15·6 (8·4-25·6)	19·8 (10·0-33·4)	17·8 (9·3-30·5)	13·5 (7·4-21·0)	17·3 (8·8-33·9)
	Gain (%)	---	*2·1 (0·1-5·6)*	*6·3 (0·6-14·9)*	*4·3 (0·3-15·3)*	*0·0 (0·0-0·1)*	*3·8 (0·0-13·4)*
Asia	Survival (%)	46·4 (33·1-56·9)	47·7 (33·5-58·2)	49·5 (38·0-60·6)	51·0 (35·9-60·6)	46·5 (33·2-56·9)	48·2 (33·8-61·4)
	Gain (%)	---	*1·3 (0·0-5·4)*	*3·1 (0·1-13·1)*	*4·6 (0·0-14·5)*	*0·1 (0·0-0·8)*	*1·8 (0·0-10·8)*
Europe	Survival (%)	58·1 (53·8-62·2)	58·6 (54·3-63·1)	59·1 (54·1-63·5)	58·5 (54·0-63·2)	58·3 (54·0-62·4)	59·2 (54·8-63·4)
	Gain (%)	---	*0·5 (0·0-2·5)*	*1·0 (0·0-4·7)*	*0·4 (0·0-1·7)*	*0·2 (0·0-0·5)*	*1·1 (0·0-6·8)*
Latin America and the Caribbean	Survival (%)	56·2 (49·9-61·8)	57·1 (50·9-63·7)	56·9 (50·7-62·3)	56·8 (50·0-62·3)	56·3 (50·0-61·9)	56·7 (50·6-62·3)
	Gain (%)	---	*0·9 (0·0-4·7)*	*0·7 (0·0-2·3)*	*0·6 (0·0-3·2)*	*0·1 (0·0-0·7)*	*0·5 (0·0-2·6)*
Northern America	Survival (%)	64·9 (60·1-70·6)	64·9 (60·1-70·6)	64·9 (60·1-70·6)	65·0 (60·4-70·6)	64·9 (60·1-70·6)	65·0 (60·2-70·6)
	Gain (%)	---	*0·0 (0·0-0·1)*	*0·0 (0·0-0·1)*	*0·1 (0·0-0·9)*	*0·0 (0·0-0·1)*	*0·1 (0·0-0·9)*
Oceania	Survival (%)	40·7 (27·3-61·9)	41·3 (27·3-61·9)	45·2 (27·9-65·0)	43·8 (27·9-64·9)	40·7 (27·3-62·0)	44·7 (29·9-65·7)
	Gain (%)	---	*0·7 (0·0-6·0)*	*4·6 (0·0-18·8)*	*3·1 (0·0-17·5)*	*0·1 (0·0-0·5)*	*4·1 (0·0-28·3)*

Table 3:

Five-year net survival by income group and region under various policies that expand availability of single imaging modalities to the mean level of high-income countries, means (95% UI)

		Baseline	Ultrasound	CT (+X-ray)	MRI	PET	SPECT
Global	Survival (%)	42·1 (33·8–48·5)	42·3 (34·0–48·7)	42·5 (34·0–48·8)	42·7 (34·0–49·9)	42·4 (34·0–48·8)	42·2 (33·8–48·6)
	Gain (%)	---	*0·2 (0·0–1·1)*	*0·4 (0·0–1·2)*	*0·6 (0·1–2·1)*	*0·3 (0·0–0·8)*	*0·1 (0·0–0·2)*
Low income	Survival (%)	4·4 (0·4–16·4)	4·9 (0·4–19·7)	4·5 (0·4–17·0)	4·5 (0·4–17·0)	4·4 (0·4–16·4)	4·4 (0·4–16·4)
	Gain (%)	---	*0·5 (0·0–3·7)*	*0·2 (0·0–0·9)*	*0·1 (0·0–0·6)*	*0·0 (0·0–0·1)*	*0·0 (0·0–0·0)*
Lower middle income	Survival (%)	28·5 (7·5–45·5)	28·9 (7·6–45·5)	29·0 (7·5–45·7)	29·3 (7·7–47·3)	28·8 (7·5–45·6)	28·6 (7·5–45·5)
	Gain (%)	---	*0·3 (0·0–2·4)*	*0·5 (0·0–2·1)*	*0·8 (0·0–3·1)*	*0·3 (0·0–1·2)*	*0·0 (0·0–0·1)*
Upper middle income	Survival (%)	61·1 (56·2–66·8)	61·1 (56·2–66·8)	61·5 (56·2–67·0)	61·9 (56·7–67·3)	61·6 (56·6–67·5)	61·2 (56·5–66·8)
	Gain (%)	---	*0·0 (0·0–0·1)*	*0·4 (0·0–1·5)*	*0·8 (0·0–3·3)*	*0·5 (0·0–1·9)*	*0·1 (0·0–0·4)*
High income	Survival (%)	66·0 (64·2–68·2)	66·0 (64·2–68·2)	66·1 (64·3–68·2)	66·1 (64·3–68·4)	66·2 (64·4–68·3)	66·0 (64·3–68·2)
	Gain (%)	---	*0·0 (0·0–0·0)*	*0·1 (0·0–0·6)*	*0·1 (0·0–0·6)*	*0·2 (0·0–0·8)*	*0·0 (0·0–0·3)*
Africa	Survival (%)	13·5 (7·4–20·9)	13·9 (7·5–21·8)	13·7 (7·4–21·6)	13·8 (7·4–21·5)	13·6 (7·5–21·1)	13·5 (7·4–21·0)
	Gain (%)	---	*0·5 (0·0–2·2)*	*0·3 (0·0–0·8)*	*0·4 (0·0–1·6)*	*0·1 (0·0–0·6)*	*0·0 (0·0–0·1)*
Asia	Survival (%)	46·4 (33·1–56·9)	46·6 (33·1–56·9)	46·7 (33·1–57·2)	47·2 (33·2–58·9)	46·7 (33·1–57·2)	46·5 (33·1–56·9)
	Gain (%)	---	*0·2 (0·0–1·5)*	*0·3 (0·0–1·4)*	*0·8 (0·0–2·8)*	*0·3 (0·0–1·0)*	*0·1 (0·0–0·3)*
Europe	Survival (%)	58·1 (53·8–62·2)	58·1 (53·8–62·2)	58·4 (54·0–62·5)	58·7 (54·1–63·9)	58·6 (54·0–62·7)	58·1 (53·9–62·4)
	Gain (%)	---	*0·0 (0·0–0·2)*	*0·3 (0·0–2·2)*	*0·6 (0·0–3·1)*	*0·5 (0·0–1·8)*	*0·0 (0·0–0·3)*
Latin America and the Caribbean	Survival (%)	56·2 (49·9–61·8)	56·2 (49·9–61·8)	57·0 (50·2–62·8)	56·5 (50·0–64·0)	56·8 (50·6–62·5)	56·3 (49·9–61·9)
	Gain (%)	---	*0·0 (0·0–0·3)*	*0·8 (0·0–3·4)*	*0·3 (0·0–3·2)*	*0·6 (0·0–2·5)*	*0·1 (0·0–0·5)*
Northern America	Survival (%)	64·9 (60·1–70·6)	64·9 (60·1–70·6)	64·9 (60·1–70·6)	64·9 (60·1–70·6)	64·9 (60·1–70·6)	65·0 (60·3–70·7)
	Gain (%)	---	*0·0 (0·0–0·0)*	*0·0 (0·0–0·1)*	*0·0 (0·0–0·0)*	*0·0 (0·0–0·0)*	*0·1 (0·0–0·7)*
Oceania	Survival (%)	40·7 (27·3–61·9)	40·9 (27·3–61·9)	41·1 (27·3–62·4)	40·8 (27·3–62·6)	40·9 (27·3–62·1)	40·7 (27·4–61·9)
	Gain (%)	---	*0·3 (0·0–2·9)*	*0·4 (0·0–3·2)*	*0·2 (0·0–1·0)*	*0·2 (0·0–1·6)*	*0·1 (0·0–0·5)*

Table 4:

Policy scenarios to scale-up availability of treatment/imaging modalities to the mean level of high-income countries

Cumulative Scale-up Scenarios	Scale-up to mean of high-income countries											Estimated global 5-year net survival (%), mean (95% UI)
	Treatment					Imaging						
	Chemo-therapy	Radio-therapy	Surgery	Targeted therapy	Quality of care	Ultra-sound	X-ray	CT	MRI	SPECT	PET	
Baseline												42·1 (33·8-48·5)
+ Treatment Access	X	X	X	X								52·4 (44·6-62·0)
+ Quality	X	X	X	X	X							57·5 (51·2-63·5)
+ Ultrasound	X	X	X	X	X	X						58·5 (51·7-64·4)
+ CT (includes X-ray)	X	X	X	X	X	X	X	X				59·4 (52·3-65·7)
+ MRI	X	X	X	X	X	X	X	X	X			60·9 (55·1-67·2)
+ SPECT	X	X	X	X	X	X	X	X	X	X		61·1 (55·3-67·2)
+ PET	X	X	X	X	X	X	X	X	X	X	X	62·5 (57·7-67·8)