

WHO Framework for strengthening and scaling-up services for the management of invasive cervical cancer



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management of invasive
cervical cancer**

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foreword

“Cervical cancer is an NCD we can overcome”

That is World Health Organization (WHO) Director-General Dr Tedros Adhanom Ghebreyesus’s rallying call to eliminate cervical cancer as a public health problem. The burden of cervical cancer cannot be ignored. Each year more than half a million women are diagnosed and more than 310 000 women die. It is preventable or avoidable and disproportionately affects the most vulnerable women globally. Regrettably, the majority of affected women live in low- and middle-income countries, where they are not diagnosed early enough and lack access to life-saving treatment and care. Even in many high-income countries, highly available, effective and cost-effective cervical cancer interventions are under-utilized, and for the most socially and economically vulnerable populations, largely inaccessible. Overcoming cervical cancer is not only feasible, then, but equitable. As a global community, we have been entrusted with one of public health’s most ambitious, yet realistic, goals – to eliminate cervical cancer as a public health problem for the next generation and generations to come. This is achievable, and the resultant benefits for women, families, communities and economies are immense. To succeed, we must act now and must act jointly.

WHO is pleased to bring out the WHO *Framework for strengthening and scaling-up services for the management of invasive cervical cancer*. This Framework is vitally impelled by the WHA 2020 adoption of the Global Strategy to Accelerate the Elimination of Cervical Cancer as a Public Health Problem. The Elimination Strategy sets out a quantified goal – reaching an age-standardized incidence rate of less than 4 per 100 000 women. To achieve this goal everywhere within this century, implementation targets for 2030 that are linked to three pillars of action have been set: to vaccinate more than 90% of girls, to screen more than 70% of eligible women, and to ensure that 90% of women with cervical pre-cancer and invasive disease are able to access treatment and palliative care. We cannot realize accelerated reductions in cervical cancer cases and deaths without the coordinated attainment of all three targets.

Scaling-up capacity in the third pillar – to promote access to care for women diagnosed with invasive cervical cancer – is driven by striking disparities in survival from cervical cancer. Whereas 5-year overall survival in high-income countries is close to 80%, it is only about 20% or less in low-income countries. Attainment of the third target has the potential to save more than 300 000 women lives over the next decade and ensure that no woman with cervical cancer suffers without palliative care.

The Framework presented in this document provides the “how to” for governments seeking to scale-up capacity in cervical cancer management and reap the social and economic benefits of doing so. It provides an important perspective on how quality is an essential principle of cancer programmes. Regardless of the level of resources available to a country, each aspect of invasive cancer management – diagnosis, staging, treatment, palliative care and survivorship care – should be and can be delivered with the utmost attention to quality to increase the likelihood of improving and saving lives. It is not only unethical to ignore quality, it is also a waste of precious resources.

For decades, cervical cancer management has been ignored or deprioritized because of perceptions of high cost and implementation challenges. This is not accurate. Through strategic investments and by following the guidance provided in this technical document, governments can immediately improve access to high-quality cervical cancer management services, including palliative care.

We, at WHO, are ready to fully support governments get on the path to cervical cancer elimination and to save lives through an integrated approach. To succeed, we will need to have everyone involved – governments, private sector, professional societies, educational programmes, service providers, civil society, people of all ages and creed. The elimination of cervical cancer is a global ambition with a global benefit.

Let’s work together to beat the burden of noncommunicable disease, to vanquish cervical cancer and to improve the lives of women and families around the world today. We have no reason to wait.



A handwritten signature in black ink, appearing to read 'B Mikkelsen'.

DR BENTE MIKKELSEN

Director, Department of Noncommunicable Diseases (NCDs)

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abbreviations and acronyms

AIDS acquired immunodeficiency syndrome

BT brachytherapy

cm centimetre

CT computed tomography

EBRT external beam radiotherapy

Elimination Strategy Global Strategy to Accelerate the Elimination of Cervical Cancer as a Public Health Problem

EPPCCC Essential Package of Palliative Care for People Affected by Cervical Cancer

ESMO European Society for Medical Oncology

FIGO International Federation of Gynaecology and Obstetrics

HDI Human Development Index

HIV human immunodeficiency virus

HMIS Health Management Information Systems

HPV human papillomavirus

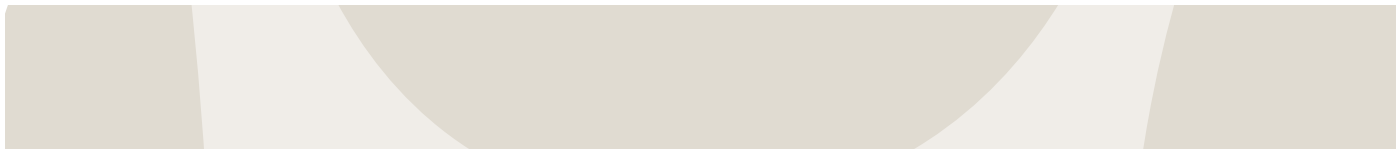
HTA health technology assessment

IAEA International Atomic Energy Agency

IARC International Agency for Research on Cancer

LMIC low- and middle-income country

MCBS Magnitude of Clinical Benefit Scale



MDT	multidisciplinary team
M&E	monitoring and evaluation
MRI	magnetic resonance imaging
NAC	neoadjuvant chemotherapy
NCCP	national cancer control plan
NCD	noncommunicable disease
Ob/Gyn	obstetrics/gynaecology
PBCR	population-based cancer registry
PET-CT	positron emission tomography-computed tomography
PHC	primary health care
QPI	quality performance indicator
SDG	Sustainable Development Goals
SOP	standard operating procedure
TNM	tumour node metastasis
UHC	universal health coverage
US/USA	United States/United States of America
WHA	World Health Assembly
WHO	World Health Organization
WLHIV	women living with HIV

purpose, scope and audience

The main purpose of the World Health Organization (WHO) *Framework for strengthening and scaling-up services for the management of invasive cervical cancer*, hereafter the Framework, is to provide a fundamental reference document to support countries in enhancing comprehensive cervical cancer control. Aligned with the WHO Global Strategy to Accelerate the Elimination of Cervical Cancer as a Public Health Problem, hereafter the Elimination Strategy,^a it underpins its third pillar^b and assists countries to reach the target of treating 90% of women diagnosed with invasive cancer.

SPECIFIC OBJECTIVES OF THE FRAMEWORK INCLUDE:

- providing a rationale for improvement of invasive cervical cancer management services against a wider backdrop of comprehensive cancer control;
- defining the cervical cancer care pathway and highlighting its central role in strengthening continuum of care;
- describing core clinical services in management of invasive cervical cancer; and
- outlining a practical framework for strengthening and scaling up management of invasive cervical cancer within a health system approach.

The scope of this Framework encompasses the core elements in management of invasive cervical cancer: diagnosis, staging, treatment, palliative care and survivorship care. Where relevant, these elements are also described with respect to the general cancer care system, as many elements of care in other cancers are common to those in cervical cancer, and a “silo-ing” of cervical cancer is undesirable. The principles of universal health coverage (UHC) implicitly underlie all discussion.

This Framework is not intended to provide clinical guidance for management of patients with invasive cervical cancer. Nor are components of primary and secondary prevention of cervical cancer included, for which detailed WHO recommendations and guidelines are available on its website.^c

This Framework has been developed for government policy-makers, particularly in low- and middle-income countries (LMICs), who have responsibilities for formulating national cervical cancer control policies, plans and programmes, as well as for hospital managers providing and scaling-up gynaecological cancer management services, including for cervical cancer. Partners supporting the implementation of the Elimination Strategy and other relevant stakeholders are also among key target audiences.

^a Global Strategy to Accelerate the Elimination of Cervical Cancer as a Public Health Problem. Geneva: World Health Organization; 2020 (<https://www.who.int/initiatives/cervical-cancer/strategy>, accessed 18 November 2020).

^b The three pillars of the Elimination Strategy are: (i) vaccination (primary prevention); (ii) screening and precancer treatment (secondary prevention); and (iii) management of invasive cancer (tertiary prevention).

^c Cervical cancer. World Health Organization (https://www.who.int/health-topics/cervical-cancer#tab=tab_1S, accessed 25 September 2020).



structure of the framework

This Framework includes discussion of both clinical and health system considerations for cervical cancer management, supplemented and extended by references for evidence-based best practice. Throughout, case studies illustrate successes that are being achieved with limited resources.

SECTION 1 provides contextual background covering disease burden, summarized WHO recommendations for comprehensive prevention and control, articulation of the Global Strategy to Accelerate the Elimination of Cervical Cancer as a Public Health Problem, including the economic rationale for investing in the Elimination Strategy, and a survey of the global landscape of cervical cancer management services.

SECTION 2 starts with an illustration of cervical cancer care pathways, then details the core clinical elements in the management of cervical cancer. The accuracy of diagnosis and staging, critical to timely and appropriate management, is highlighted by a description of quality pathology services. The treatment modalities of surgery, radiotherapy and systemic therapy are discussed individually, supplemented with resources for additional guidances and information. The importance of palliative and survivorship care to the cancer management continuum is emphasized. In reviewing some of the common barriers to timely access to care, benchmarks for achieving optimal time intervals are also suggested.

In **SECTION 3**, key considerations for strengthening the supportive and enabling health care system structures of effective cancer management are featured, introduced by the WHO definition of quality care. Governance to ensure the effectiveness of services and prevent the waste of resources and effort, health system assessment and planning to promote strategic use and scaling-up of cancer management services, and proposed service delivery models that emphasize primary health care (PHC) are considered in turn. An approach for developing locally appropriate guidelines is outlined. Approaches are also suggested for enhancing the competence and appropriate deployment of the cancer care workforce. Other essential actions presented include improving access to medicines and medical devices to maximize the impact of therapies and establishing sustainable financing that embraces value for money and innovation in finding and deploying funds. The importance of strengthening information systems, particularly population-level cancer registries, is described, and finally the essential role of monitoring and evaluation (M&E) in supporting and bolstering improvements in high quality, comprehensive cancer care systems is underscored.



section



**setting
the scene**

1.1 WHAT IS CERVICAL CANCER?

Cervical cancer is a heterogeneous group of diseases characterized by autonomous and uncontrolled growth of cells originating from the uterine cervix – an anatomical structure connecting the lower uterus to the vagina. Almost all cervical carcinomas are caused by persistent infection by an oncogenic (or high-risk) human papillomavirus (HPV) (1). HPV is a very common infection acquired during sexual intercourse, and most men and women will be infected at some point in their lives.

There are more than 100 types of HPV among which at least 14 are known to be oncogenic (2). HPV16 and HPV18 are the two most oncogenic types and are responsible for 70% of cervical carcinomas reported globally (3). Nearly 80% of high-risk HPV infections clear up spontaneously without any intervention within two years. A small proportion (approximately 10%) of infections can persist for several years, progress to precancerous lesions and, if left untreated, to invasive cancer over a 10–20-year period (1). Invasive cancer may progress further, forming a visible tumour that can invade adjacent organs and tissues (e.g. bladder, rectum, ureters, nerves, blood vessels, pelvic lymph nodes) and spread (metastasize) to distant sites and organs (e.g. supraclavicular and inguinal lymph nodes, liver, lungs, brain and bones) (4).

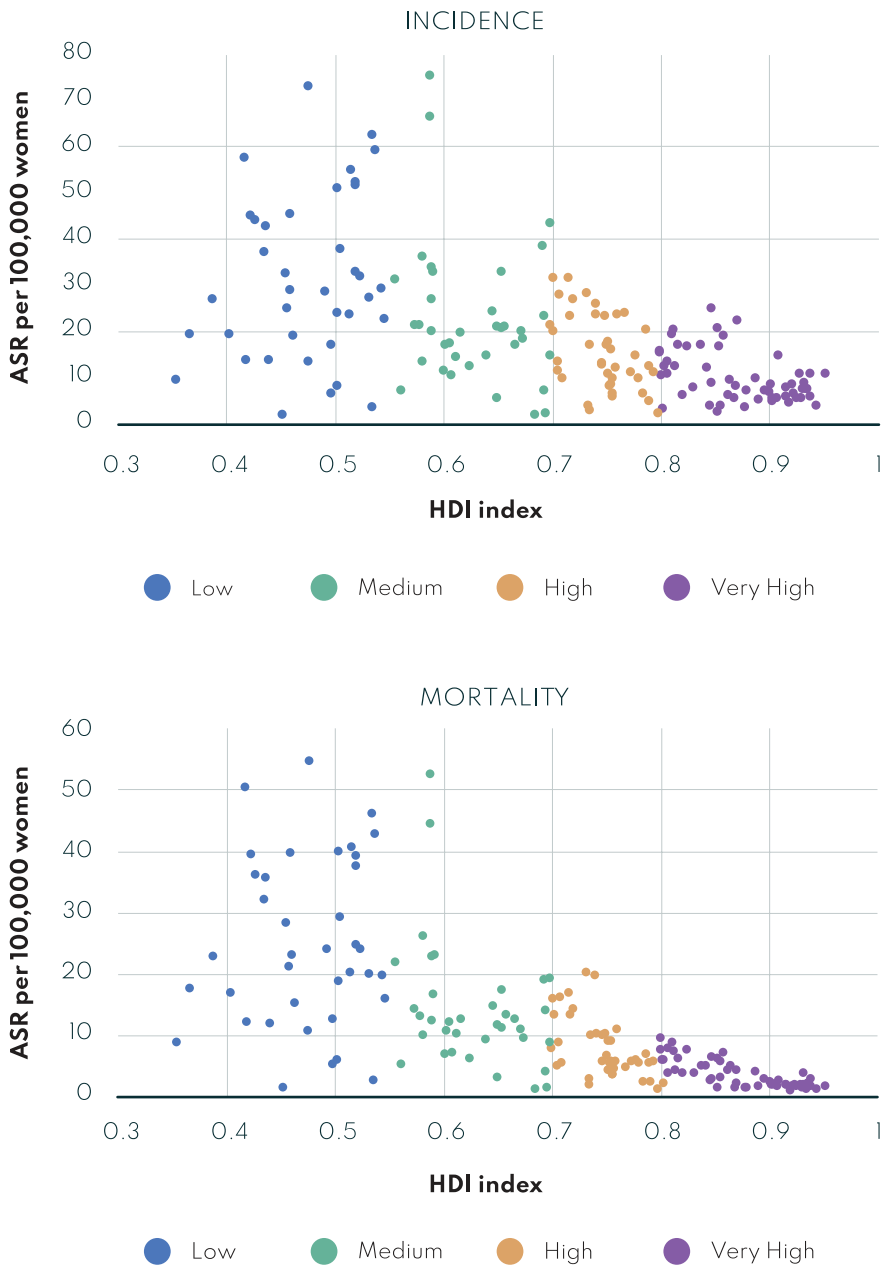
1.2 GLOBAL BURDEN OF CERVICAL CANCER

Worldwide, cervical cancer is the fourth most common cancer in women in terms of incidence and mortality, with an estimated 570 000 new cases and 311 000 deaths in 2018 (5). The estimated age-adjusted incidence rate is 13 per 100,000 women globally and varies widely between countries, ranging from 2 to 75 per 100 000. The age-adjusted mortality rate is 7 per 100 000 women globally, ranging from 1 to 55 per 100 000. Notably, in low- and lower-middle-income countries cervical cancer is the first- and second-most cause of cancer deaths, respectively. Both higher incidence and mortality rates are associated with lower Human Development Index (HDI) classifications (Figure 1.1), leading to a disproportionate burden borne by women in low- and medium-HDI countries (Box 1.1).

Continuing improvements in social and economic development may reduce the cervical cancer burden in the longer term, but incidence and mortality rates will remain elevated in high-risk settings without effective intervention. Using a modified measure of human development, researchers have shown that transitioning middle-income countries may reach the same levels of disease incidence that high-income countries currently have, without benefiting from a reduced mortality, suggesting a lag between deleterious changes in lifestyle and environmental factors and sufficient strengthening of health care systems (6).

FIGURE 1.1

Age-standardized rates of cervical cancer incidence and mortality according to HDI, 2018



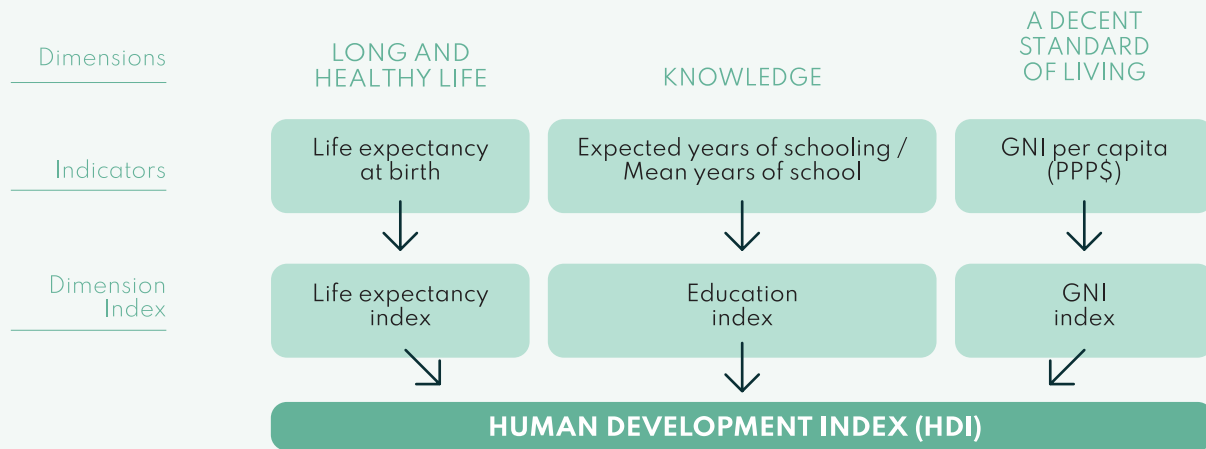
SOURCE: IARC 2018 (5).

BOX 1.1

Human Development Index (HDI)

HDI is a summary measure of average achievement in three dimensions of human development:

- > long and healthy life assessed by life expectancy at birth;
- > access to knowledge based on expected years of schooling for children of school entering age and mean years of schooling for adults aged 25 years and more; and
- > a decent standard of living measured by gross national income per capita.



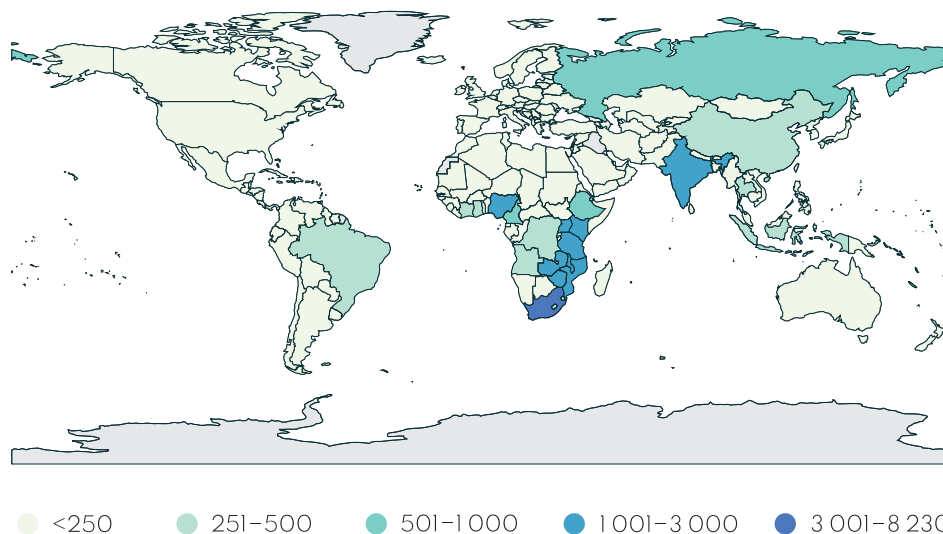
SOURCE: UNDP (7).

Also notable is the disproportionate burden of cervical cancer borne by girls and women living with HIV (WLHIV), who are less likely to clear an HPV infection due to compromised immune systems and are six times more likely

to develop cervical cancer, and at a younger age (8,9). In some countries with high HIV prevalence, more than 40% of cervical cancer cases occur in WLHIV (Figure 1.2).

FIGURE 1.2

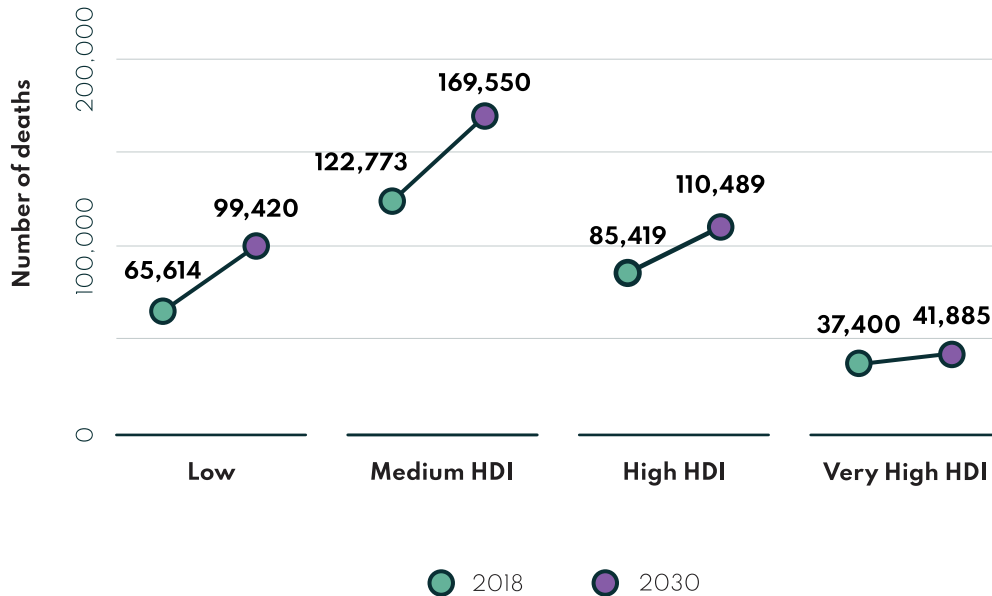
Incident cervical cancer cases among WLHIV



SOURCE: Stelzle 2020 (9).

FIGURE 1.3

Projected number of cervical cancer deaths from 2018 to 2030, by HDI



SOURCE: IARC 2018 (5).

If trends continue, projections indicate that there will be nearly 30% and 50% increases in cervical cancer deaths by 2030 and 2040, respectively. Low- and medium-HDI countries, especially in regions where the burden is already the highest (Africa and Asia), will be most affected (Figure 1.3) (5).

Globally, the average age at diagnosis of cervical cancer is 53 years (with a range of 44–68 years), which is younger than other major cancer types (10). Afflicted women are often in the most productive years of their lives or are the primary caregivers for their families. Thus, beyond the impact on the patient, mortality and morbidity in this population have much broader and larger societal implications. Particularly, maternal mortality devastatingly raises the risk of childhood mortality (11). In countries with high cervical and breast

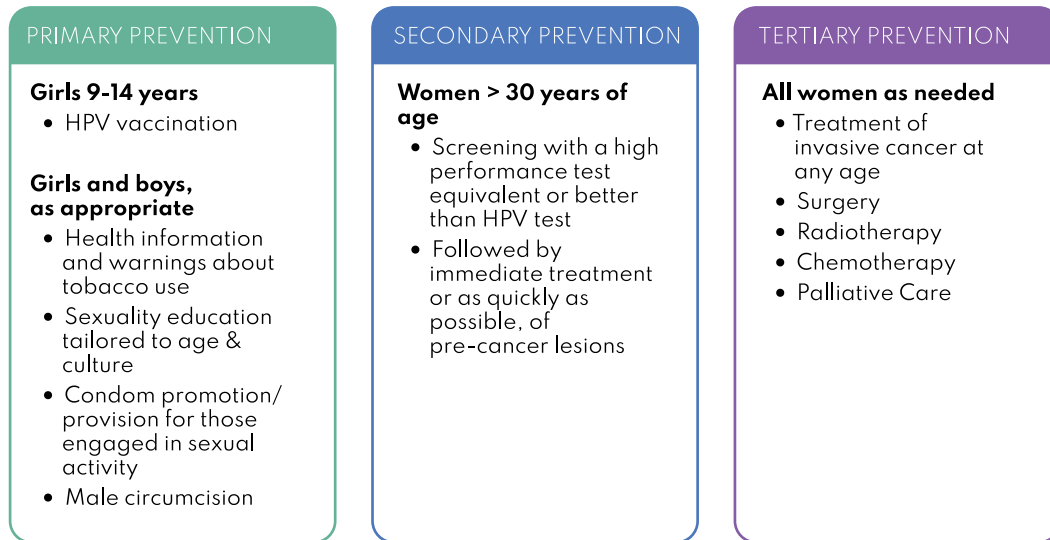
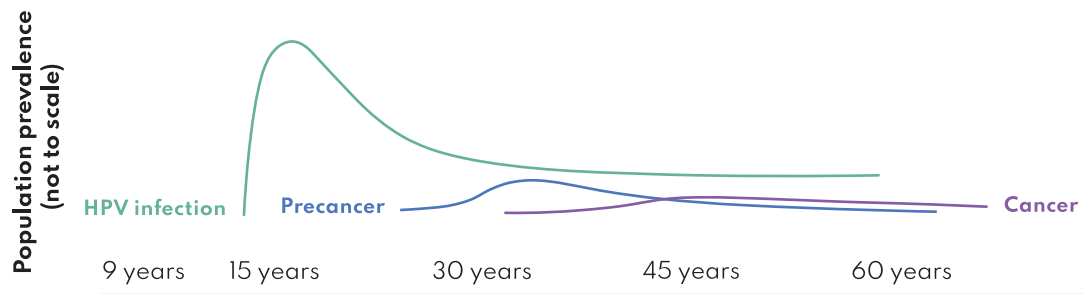
cancer burden, high fertility and high baseline childhood mortality, between 10 and 30 childhood deaths may result from 100 maternal cancer deaths (12).

1.3 COMPREHENSIVE CERVICAL CANCER CONTROL

The global disparity in cervical cancer burden persists even though there are proven interventions to control cervical cancer throughout primary, secondary and tertiary prevention (4,13). Figure 1.4 demonstrates that over the life-course of women three preventative strategies can bring down the prevalence of HPV infection, precancer and invasive disease.

FIGURE 1.4

WHO comprehensive approach to cervical cancer prevention and control



SOURCE: WHO 2020 (13).

Primary prevention mainly refers to HPV vaccination. Currently, WHO recommends prioritizing HPV vaccination for girls aged between 9 and 14 years, prior to becoming sexually active, administered by two vaccine doses (14). In addition to vaccination, age-appropriate information on known risk factors such as tobacco use, age of sexual debut and condom use should be made readily available. WHO publications, tools and other important resources on HPV vaccination, including recommendations on non-primary vaccination targets, can be found at the HPV Vaccine Introduction Clearing House (15).

Secondary prevention involves screening and treatment of precancerous lesions before they advance to invasive cervical cancer. For maximum benefit, screening must cover at least 70% of the target population, be conducted with a high-performance test, and linked to timely and effective treatment of detected cervical disease (13).

Extensive WHO guidelines, publications and tools on cervical cancer screening and treatment of precancerous lesions can be accessed on the WHO website (16). Tertiary prevention comprises stage-appropriate quality management of invasive cervical cancer to prevent cancer deaths, improve survival and enhance health-related quality of life. Core clinical elements required for management of cervical cancer are described more extensively in Section 2.

Preventative cancer strategies, which are embedded in the targets and indicators of the WHO *Global action plan for the prevention and control of noncommunicable diseases 2013–2020*, are good values and good investments for health care systems (17–19). When implemented to scale with adequate coverage in a person-centred and rights-based approach, comprehensive cancer control upholds the principles of UHC.

1.4 GLOBAL STRATEGY TO ACCELERATE THE ELIMINATION OF CERVICAL CANCER AS A PUBLIC HEALTH PROBLEM

Underscoring renewed political will to achieve meaningful reductions in cancer-related mortality, in May 2018 the WHO Director-General announced a global call to action towards the elimination of cervical cancer, and urged all stakeholders to unite behind this common goal

(20). He highlighted the need for cervical cancer services to be embedded in strong health care systems and included in efforts to advance UHC.

In response to strong support from all stakeholder groups and following the WHO Executive Board's direction, made through its decision at the 144th session (21), the WHO Global Strategy to Accelerate the Elimination of Cervical Cancer as a Public Health Problem was developed. In 2020, it was adopted by the 73rd World Health Assembly (22).

WHO has defined, in consultation with global experts and Member States, the threshold for elimination of cervical cancer as a public health problem as an age-standardized incidence rate of less than 4 per 100 000 (13). To achieve this goal within the 21st century globally, the Elimination Strategy recommends that 90–70–90 targets be met by 2030 (Figure 1.5). As applicable to its third pillar, 90% of women diagnosed with invasive cervical cancer must be managed appropriately.

FIGURE 1.5

2030 targets towards the elimination of cervical cancer

90%

of girls fully vaccinated with HPV vaccine by age 15 years.

70%

of women are screened with a high performance test by 35 years of age and again by 45 years of age.

90%

of women identified with cervical disease receive treatment (90% of women with precancer treated, and 90% of women with invasive cancer managed).

SOURCE: WHO 2020 (13).

1.5 AVAILABILITY OF CANCER MANAGEMENT SERVICES: GLOBAL SNAPSHOT

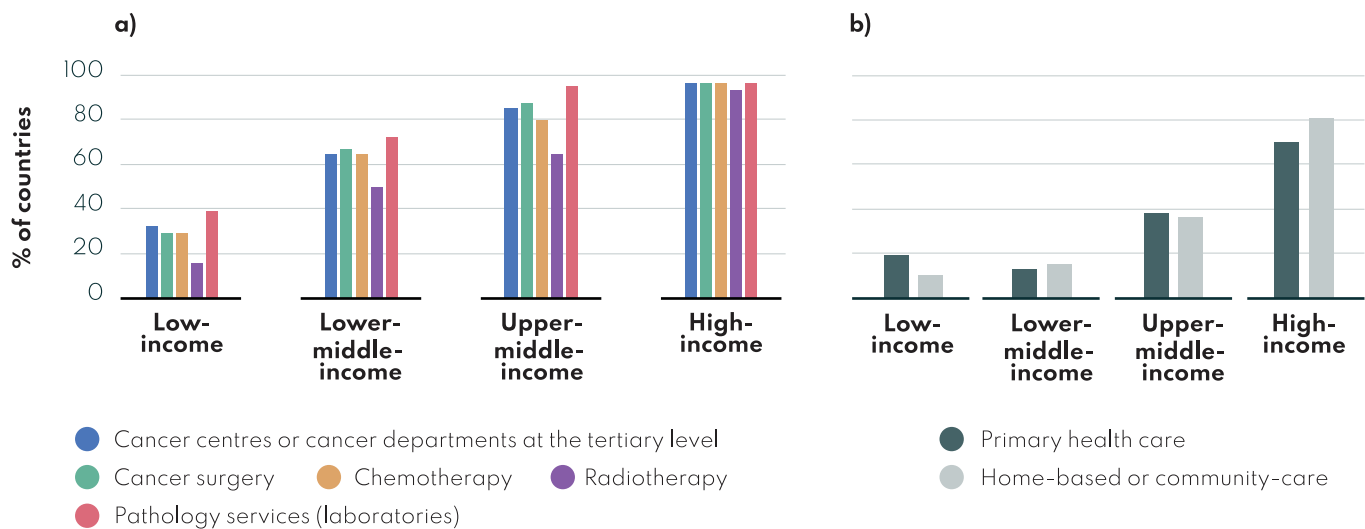
There are striking disparities in availability of cancer management services globally (Figure 1.6) (23). In 2019, while over 90% of high-income countries reported having pathology, cancer surgery, chemotherapy and radiotherapy generally available in the

public sector, less than 40% of low-income countries did so^d. Limited availability of radiotherapy is most acutely felt in low-income countries, where it is generally available in only 16% of countries. This is a particularly pressing issue given the primacy of radiotherapy as a treatment modality for cervical cancer.

Palliative care is rarely accessible in LMICs; in low-income countries it is generally available in only 19% and 10% of primary care and community- or home-based settings, respectively. It is still inadequately integrated into PHC and community- and home-based care, not only in LMICs, but also in high-income countries (23,24).

FIGURE 1.6

General availability of cancer management services by country income level



a) Countries with cancer diagnostic and treatment services general availability* in the public sector

b) Countries with palliative care generally available* in primary health-care setting or community- or home-based care

* General availability is defined as reaching 50% or more of the patients in need.

Country income level is based on World Bank income classification 2019. The numbers of low-income, lower-middle-income, upper-middle-income and high-income countries were 31, 46, 60 and 57, respectively.

SOURCE: WHO 2020 (23).

^d "Generally available" is defined as reaching 50% or more of the patients in need.

1.6 CERVICAL CANCER MANAGEMENT: IMPERATIVE TO INVEST

Prevention of cervical cancer through HPV vaccination and screening is one of the most cost-effective public health strategies, with a high return on investment (18,19). However, management of invasive cervical cancer must be concomitantly strengthened to both realize and leverage the returns on that investment.

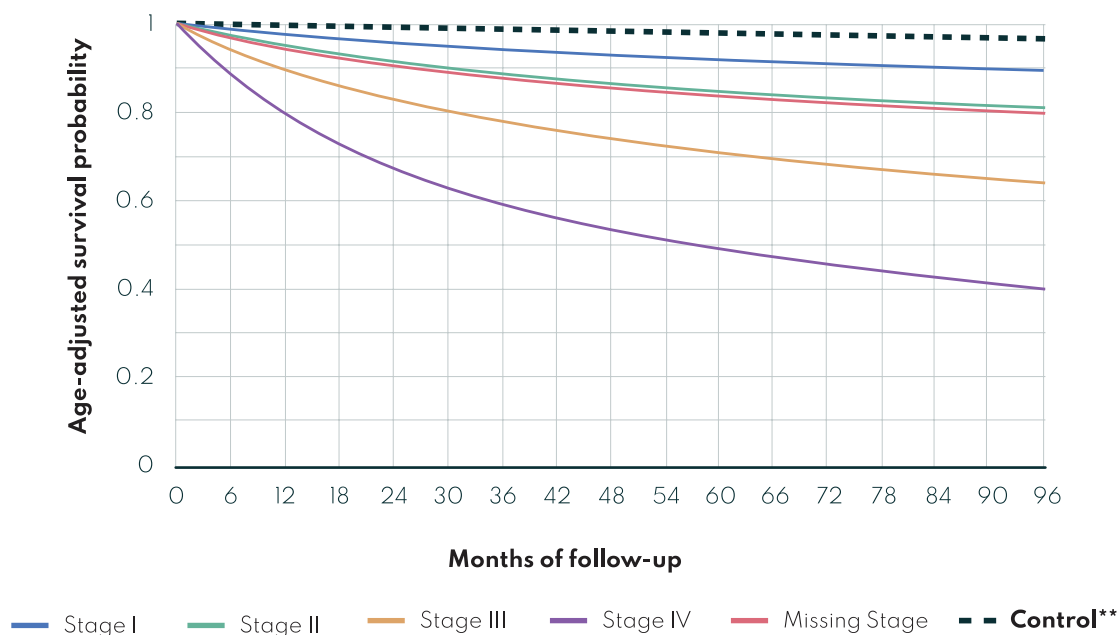
First, even with increased efforts to scale-up HPV vaccination and screening, over half a million women globally will still develop invasive cervical cancer every year in the next one to two decades (25). As of June 2020, HPV vaccination programmes have been introduced in 107 countries around the world, but only 19 have fully vaccinated more than 80%

of the target population (26). Prevention of cervical cancer through universal HPV vaccination will take decades to be realized. Cervical cancer screening will also take years to reach entire target populations in many counties with high disease burdens. Reaching vulnerable and disadvantaged women (e.g. minority groups and those from the poorest income groups or with lower education levels) has often been a challenge, even in high-income countries (27–29). Furthermore, with successful scale-up of cervical cancer screening, screen-detected invasive cancers will inevitably increase, especially in previously unscreened populations, requiring referral and treatment strategies to be fully integrated into planning screening programmes.

Secondly, cervical cancer diagnosed in its early stages has a higher probability of cure than that in advanced stages. The 5-year survival rate (i.e. the percentage of women who are alive five years after their diagnosis) of early-stage cancer can be over 90% in countries where women have access to timely diagnosis and quality treatment (Figure 1.7) (30). Treatment of early-stage cervical cancer is also less complex, less expensive and more effective, with higher long-term survival rates and better quality of life (31–33).

FIGURE 1.7

Cervical cancer survival probability by stage at diagnosis in Ontario, Canada*



* A province with 13.6 million people and with universal coverage for all medically necessary health care in Canada, classified as being “very high” in the Human Development Index (HDI).

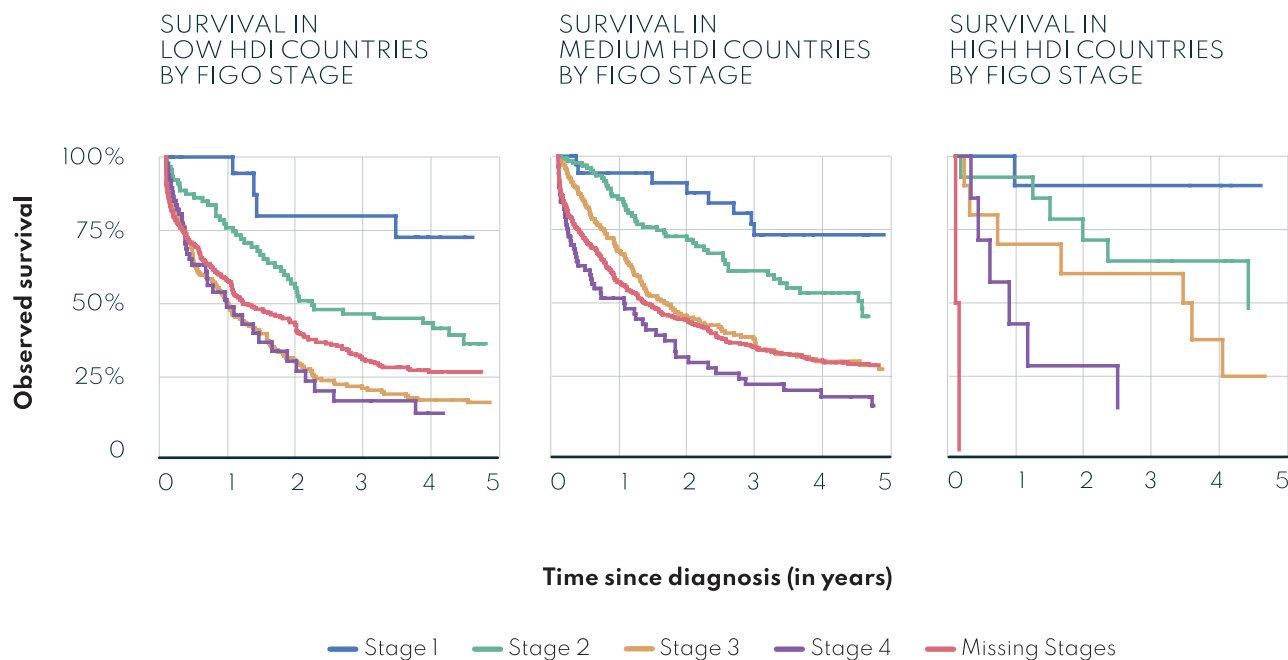
** A comparison group containing all non-cancer females born during the same period of cervical cancer patients.

SOURCE: Reproduced with permission from Liu et al. 2016 (33).

By contrast, in 11 countries of sub-Saharan Africa, where no country is in the “very high” HDI category and, thus, where less favourable cancer care contexts prevail, 66% of diagnoses in 13 population-based cancer registries (PBCRs) were at advanced disease – the International Federation of Gynaecology and Obstetrics (FIGO) stages III and IV (34).

5-year survival of early-stage cervical cancer in low-HDI countries does not exceed 75% and 50% for stages I and II, respectively, and survival of late-stage disease does not exceed 25% (Figure 1.8). Probability of overall 5-year survival from cervical cancer varies across the world, from less than 20% to close to 80%.^e

FIGURE 1.8
Cervical cancer survival by FIGO stage at diagnosis and HDI in 11 Sub-Saharan countries



SOURCE: Reproduced with permission from Sengayi-Muchengeti et al. 2020 (Supplemental information, Appendix Figure 4) (34).

With well-organized cancer management, even women with locally advanced cervical cancers may have improved outcomes if treated in a timely fashion. For patients with incurable or metastatic disease, ensuring access to palliative surgery and systemic treatment, as well as integrating radiotherapy into palliative care for pain management and controlling distressing symptoms (e.g. bleeding), can substantially improve quality of life (35–38).

Finally, substantial scale-up of cancer management services is necessary to make a major impact on sustained cervical cancer mortality reduction.

In projections made by three different groups of researchers to estimate the effects of the recommended Elimination Strategy, various combinations of primary, secondary and tertiary prevention interventions were modelled in five scenarios and compared to the continuation of the status quo low-intensity cervical cancer control in 78 LMICs (39). While vaccination alone or together with screening (Scenarios S1, S4, S5) could reduce mortality from 14 per 100 000 to around 2 per 100 000 within 80–100 years, adding cancer treatment with 90% coverage to vaccination and a single life-time screen could achieve this reduction in about 50 years (Scenario S2).

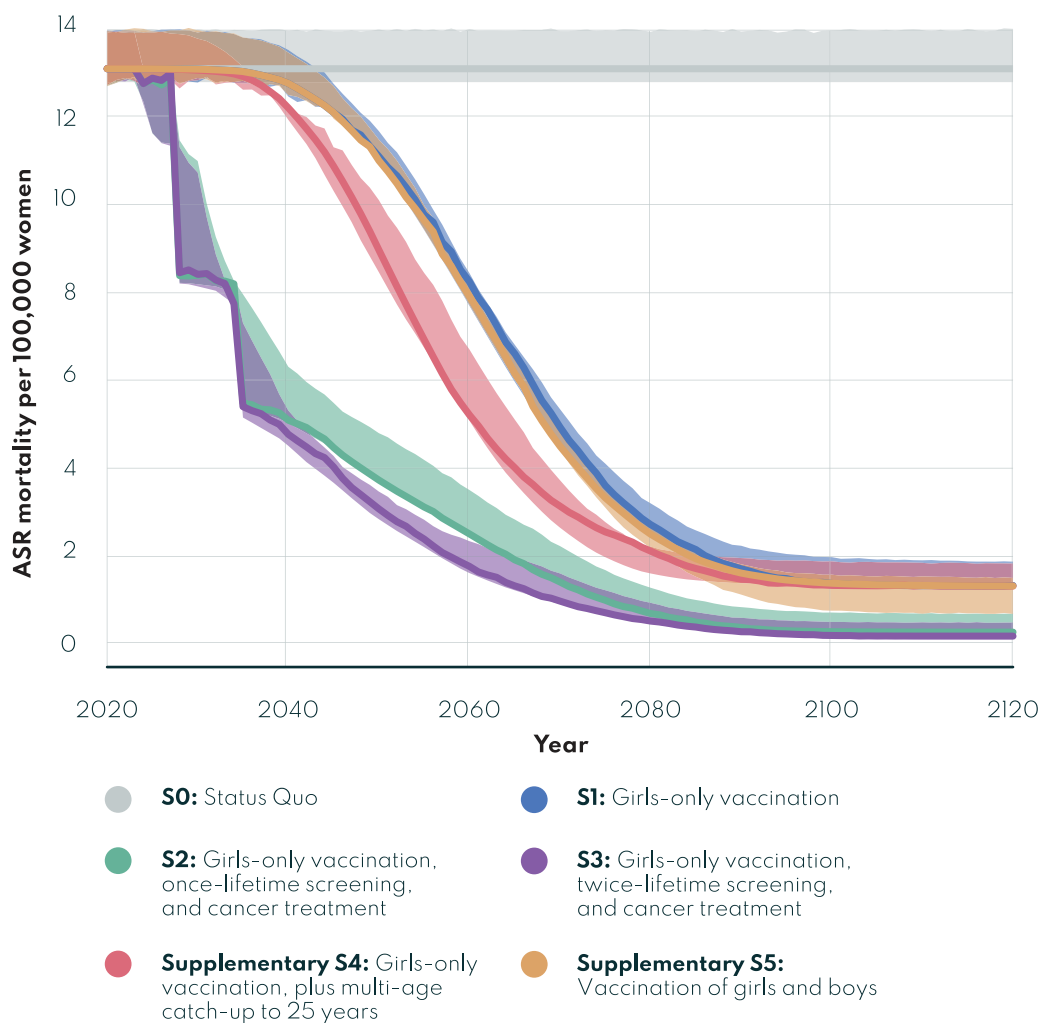
^e Sankaranarayanan R et al. An overview of cancer survival in Africa, Asia, the Caribbean and Central America: the case for investment in cancer health services (http://survcan.iarc.fr/survival/chap32_figures1.pdf, accessed 25 September 2020).

When an additional screening event is added to this high level of treatment coverage and vaccination, representing the recommended Strategy, this achievement could be shortened by another 10 years (Scenario S3) (See Figure 1.9). The simultaneous implementation of all three pillars of cervical cancer control translates into a cumulative 300 000 deaths

averted between 2020 and 2030, or a 34% reduction compared to the status quo. Scaling-up cervical cancer management, therefore, would be a major contributor to the Sustainable Development Goals (SDG) goal of reducing noncommunicable disease (NCD) premature deaths by one third by 2030.

FIGURE 1.9

Age-standardized cervical cancer mortality over time for 78 LMICs, different scenarios for scaling-up cervical cancer control



Solid lines are the median estimates of 3 models; shading around lines represent the range of model estimates.

SOURCE: Reproduced with permission from Canfell et al. 2020 (39).

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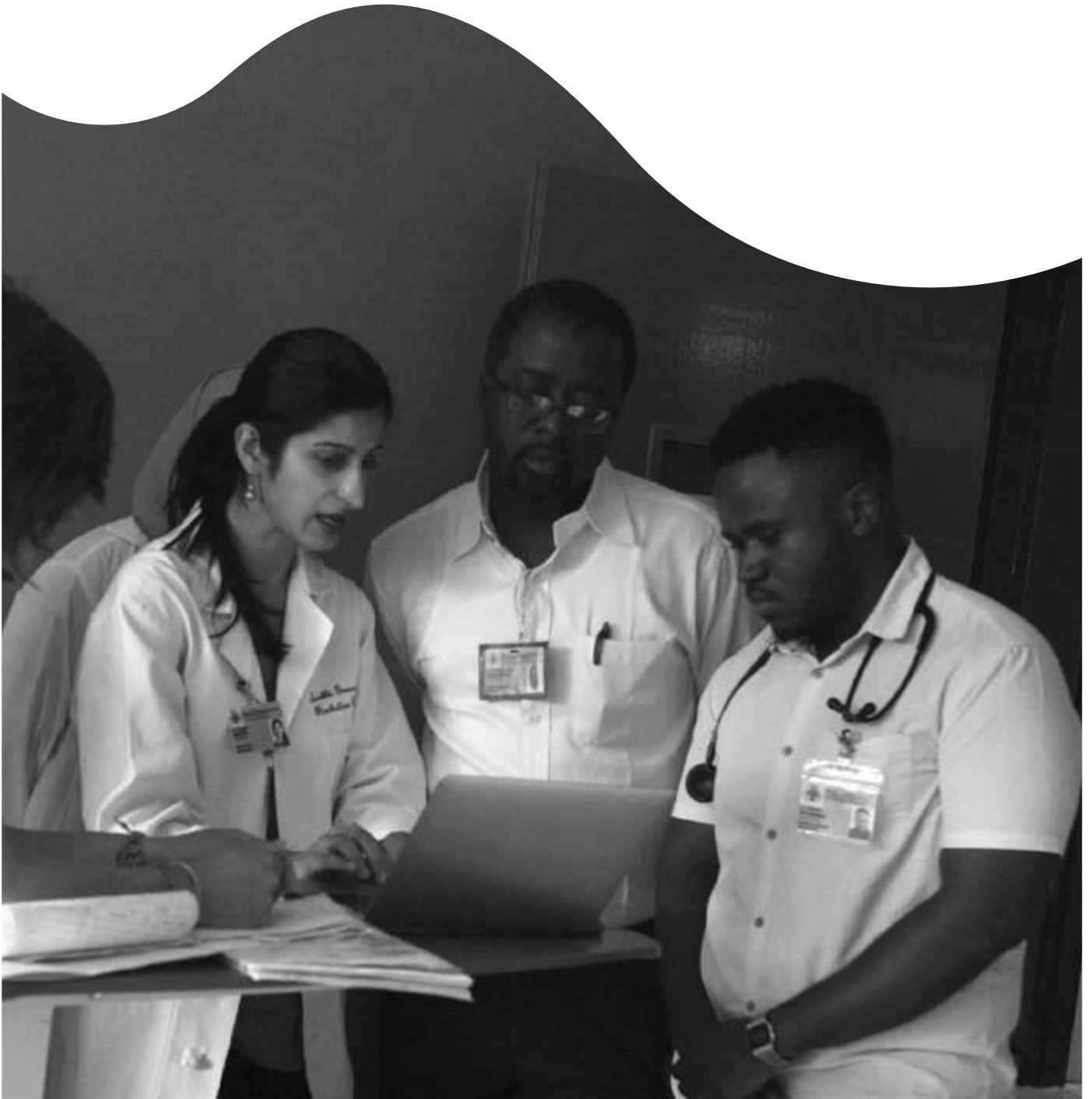


PHOTO: Surbhi Grover

section

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**core elements
of cervical
cancer
management**

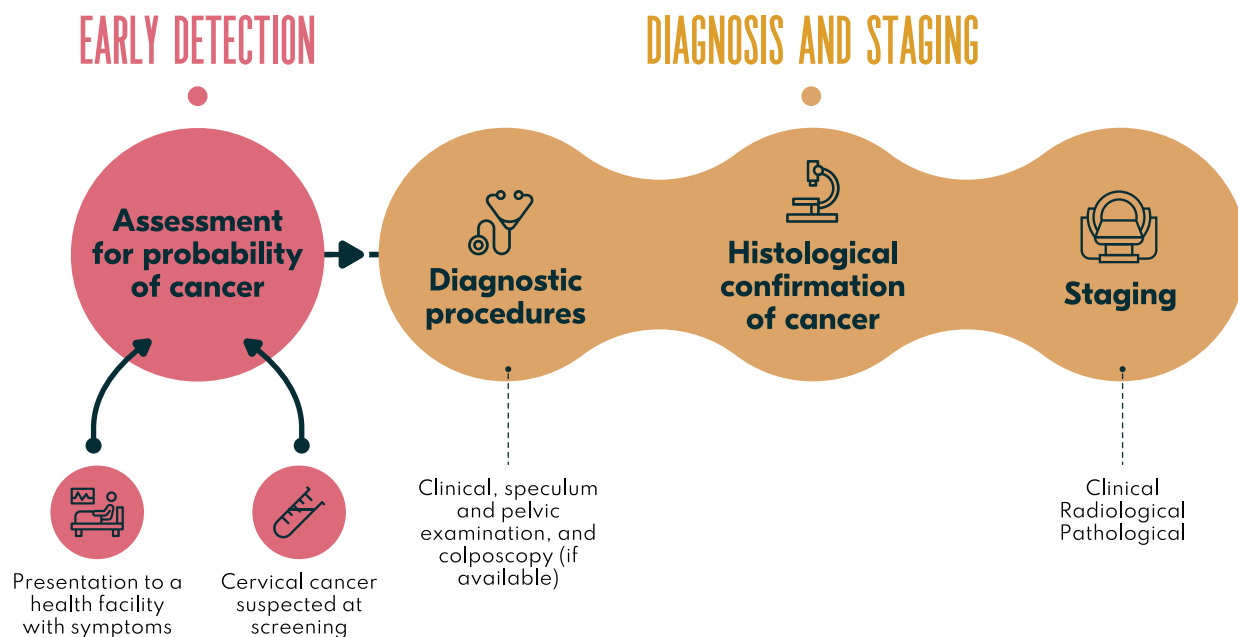
2.1 CERVICAL CANCER CARE PATHWAYS

Cancer care pathways are useful tools that connect all of the steps along the trajectory of a patient’s disease journey. They enable understanding of the sequencing of clinical interventions, as well as the interconnected roles of different health care providers. They also help to highlight and address bottlenecks that might cause delays in diagnosis and treatment, and to plan corrective steps.

There are two possible pathways for women to access cervical cancer management services (Figure 2.1):

- > Screening pathway: invasive cervical cancer is detected through a cervical cancer screening programme.
- > Symptomatic pathway:
 - Non-acute (early diagnosis): invasive cervical cancer is detected when a woman presents for a consultation at a health care facility because of concerning symptoms, e.g. postcoital vaginal spotting. Early-stage cervical cancer can be diagnosed through appraisal of screening history,

FIGURE 2.1
Cervical cancer care pathway



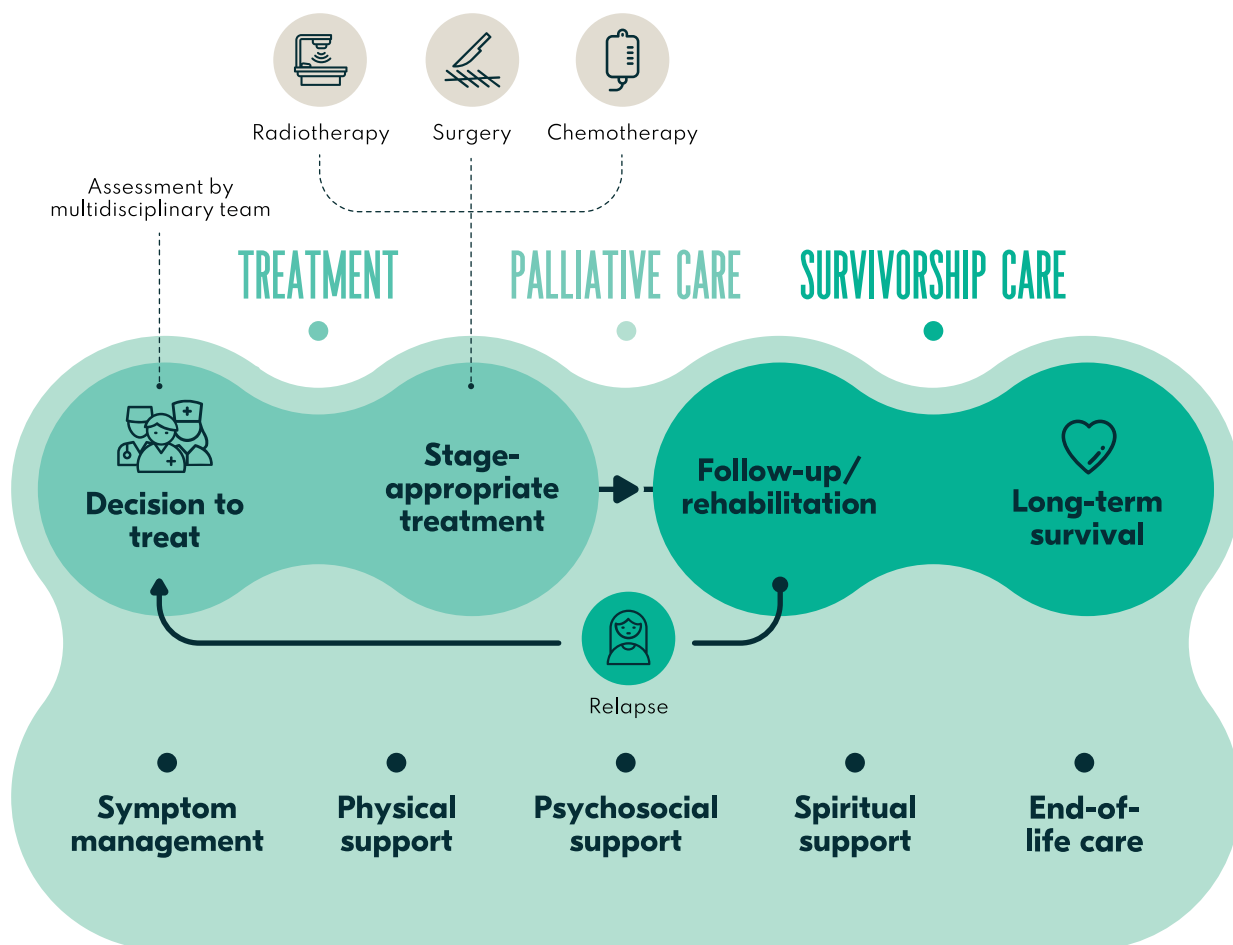
aided or unaided visual inspection of lesions, and timely access to confirmatory services (e.g. pathology).

- Acute: invasive cervical cancer is detected when a woman presents at a health care facility due to an acute or emergency situation, e.g. heavy vaginal bleeding, back pain. Most commonly it is associated with detection of advanced cancer.

Early detection of cervical cancer can occur through both screening and early diagnosis pathways (Box 2.1). They should be easily accessible for women and must

be strengthened to identify invasive cancers at early points of progression, when cancer treatment is more likely to achieve cure, more feasible, better tolerated and less expensive (1). In countries with high HIV prevalence, screening services should be tightly integrated into HIV care and treatment of WLHIV. Integrating HIV and cervical cancer care in areas with both high cervical cancer and HIV burden is particularly important for reducing the future burden of cervical cancer.

Once invasive cancer is detected, further diagnostic and treatment steps are the same regardless of the access pathway.



BOX 2.1

Early diagnosis of cervical cancer

Early diagnosis of cervical cancer involves three key steps described in the WHO *Guide for cancer early diagnosis* (Figure 2.2) (2). The first step, awareness and accessing care, requires the ability of the general public to seek medical attention promptly when symptoms of cervical cancer arise, including:

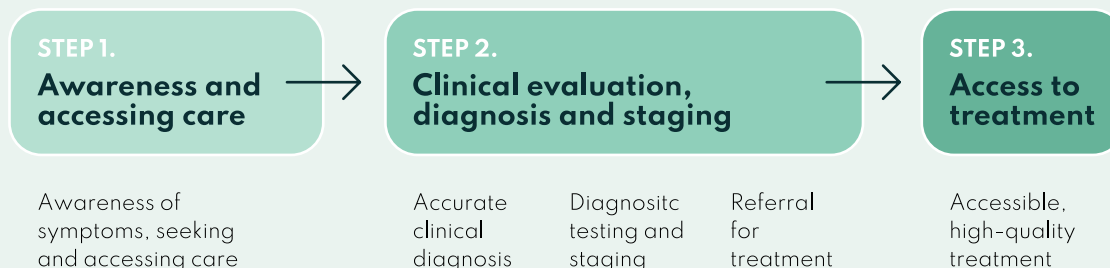
- > intermenstrual or postmenopausal vaginal bleeding
- > postcoital vaginal bleeding
- > foul-smelling vaginal discharge.

Other symptoms such as lower abdominal pain, back pain and swelling of legs may arise in more advanced cervical cancer. It is critical to improve health literacy, reduce stigmatization of cancer, and empower and engage people and communities to access PHC.

The second and third steps are consistent with the core elements of management of invasive cervical cancer (i.e. diagnosis, staging, treatment, palliative and survivorship care) described in Section 2.1.

FIGURE 2.2

Three steps of cervical cancer early diagnosis



SOURCE: Adapted from WHO 2017 (2).

2.1.1 DIAGNOSIS AND STAGING

Quality diagnosis and staging are essential for guiding appropriate treatment for individual patients. They are important also for generating data to understand the epidemiology of the disease and to make assessments and improvements in the cancer management system (see Sections 3.3.5 and 3.4).

When invasive cervical cancer is suspected, the woman should be evaluated at a facility where trained health providers can make a thorough gynaecologic examination and perform a proper cervical biopsy, as definitive diagnosis of cervical cancer must be based on histopathological evaluation (Table 2.1). If the facility does not have pathology services, then specimens can be safely transported in formalin to a centralized laboratory for processing and diagnosis. An organized transport, tracking and communication system (including any remarks on the results by the laboratory) must be in place to ensure that pathology results return quickly and reliably to the provider and patient to prevent loss-to-follow-up and enable start of treatment as soon as possible.

Once the primary diagnosis of cervical cancer is confirmed, the clinical provider in charge must explain the diagnosis and the importance of further evaluation and treatment in a way that is respectful, compassionate and understandable by the patient. Adequate time should be allowed for the patient to process this news, express grief, describe her fears or ask questions (3). Basic training in palliative care can help gynaecologists and oncologists to deliver bad news in the least traumatic and most beneficial way (4).

Further evaluation, or staging, comprises more extensive clinical, pathological and radiological examinations to determine the extent of cancer spread for making treatment decisions and assessing a patient's prognosis by a multidisciplinary team (MDT) (see Section 3.2.3.2). Endoscopy may be required depending on clinical and radiological findings.

The FIGO system and TNM Classification of Malignant Tumours system are the two most commonly used systems for staging (see Box 2.2). The stage is to be assigned after all pathology and imaging results are available, and it is not to be altered later after treatment or recurrence (5,6).

TABLE 2.1

Biopsy procedures

Biopsy method	Abbreviation	Description of the specimen	Intent/advantage	Associated risks/adverse events
Cervical biopsy	CB	Small pieces of tissue removed from areas that are suspicious for cancer on naked-eye or colposcopy examination.	> Diagnosis	> Bleeding
Endocervical curettage	ECC	Small pieces of tissue removed from endocervical canal.	> Diagnosis	> Bleeding > Infection > Uterus perforation (rarely)
Conization	Cone	Cone-shaped excision of the cervix: - by surgical blade (cold knife) - by laser knife - by thin wire loop (loop electrosurgical excision procedure).	> Staging > Treatment of precancers and very early cancers	> Bleeding > Infection > Risk of premature delivery in subsequent pregnancy > Requires anaesthesia > Injury to bladder or rectum (rarely)

SOURCE: Adapted from WHO 2014 (3).

Often, the extent of cervical cancer spread is also described as localized, locally advanced or metastatic. “Localized” suggests the disease is limited to the cervix (FIGO Stage I); “locally advanced” suggests disease is spread to adjacent tissues or organs (FIGO Stage II-IVA); and “metastatic” suggests disease is spread to distant organs (FIGO Stage IVB). Treatment of localized and locally advanced disease can aim for cure, although with differing probabilities of treatment success.

2.1.1.1 PATHOLOGY

Anatomic pathology services are necessary to establish primary diagnoses of cancer, identify histological tumour types (e.g. squamous cell carcinoma, adenocarcinoma) and grade, exclude coexisting or confounding pathologic processes, and accurately determine the stage of disease (7).

BOX 2.2

2018 FIGO staging system

Originally, FIGO staging for cervical cancer had been primarily based on clinical evaluation supported by chest X-ray and endoscopy. In 2018, the approach was updated, allowing the supplemental use of pathology and advanced medical imaging results for staging, depending on the resources available (5,6). The comparison between the FIGO 2009 and 2018 staging systems is provided in Annex 1. The major changes occur in the following:

- > histopathologic measurements based on lesion depth only (Stage IA)
- > substages for Stage IB based on maximum tumour size (Stages IB1, IB2, IB3)
- > substage for cancer of any size with nodal involvement (Stage IIIB or IIIC).

The FIGO 2018 staging system should be applied when updating national clinical practice guidelines and hospital-based protocols.

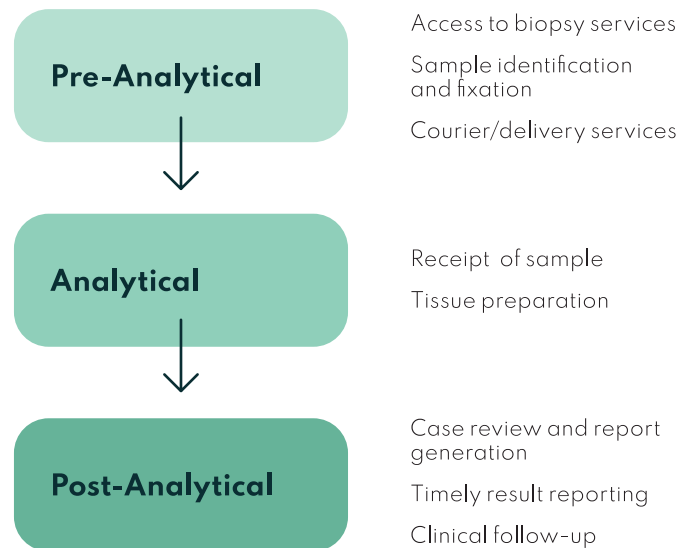
An effective anatomic pathology laboratory requires a well-supported infrastructure, trained staff and a plan for quality management. All stages of the pathology cycle, including pre-analytical, analytical and post-analytical phases, must be considered for optimal delivery of patient care (Figure 2.3) (8).

- > **PRE-ANALYTICAL PHASE:** (i) patient access to a facility where a biopsy can be obtained by a trained clinical provider; (ii) appropriate tissue sample identification and optimal fixation; (iii) timely delivery of the sample to the pathology laboratory.
- > **ANALYTICAL PHASE:** (i) receipt of the sample by the pathology laboratory; (ii) careful tissue accessioning and preparation (routine staining with hematoxylin and eosin will suffice for primary diagnosis and staging of cervical cancer).
- > **POST-ANALYTICAL PHASE:** (i) case review and report generation by a trained pathologist; (ii) timely result reporting to the clinical provider; (iii) effective communication of the results to the patient.

Recall of patients with positive tests for cancer may be required as women may not return on their own for the diagnosis. Annex 2 describes minimum requirements for pathology reporting for cervical cancer (9). Annex 3 presents a sample pathology synoptic reporting form for cervical cancer (8).

Ideally, either a centralized diagnostic review process or a system for re-review of original diagnostic material performed at a health centre or specialized hospital, where treatment will be decided and initiated, should be established. This process ensures high-quality diagnostic services to treating clinicians, acts as a quality control measure for the referring laboratory and availability of specialized ancillary tissue testing (e.g. immunohistochemistry, nucleic acid testing).

FIGURE 2.3
Phases of the pathology testing cycle



SOURCE: Adapted from WHO 2020 (8).

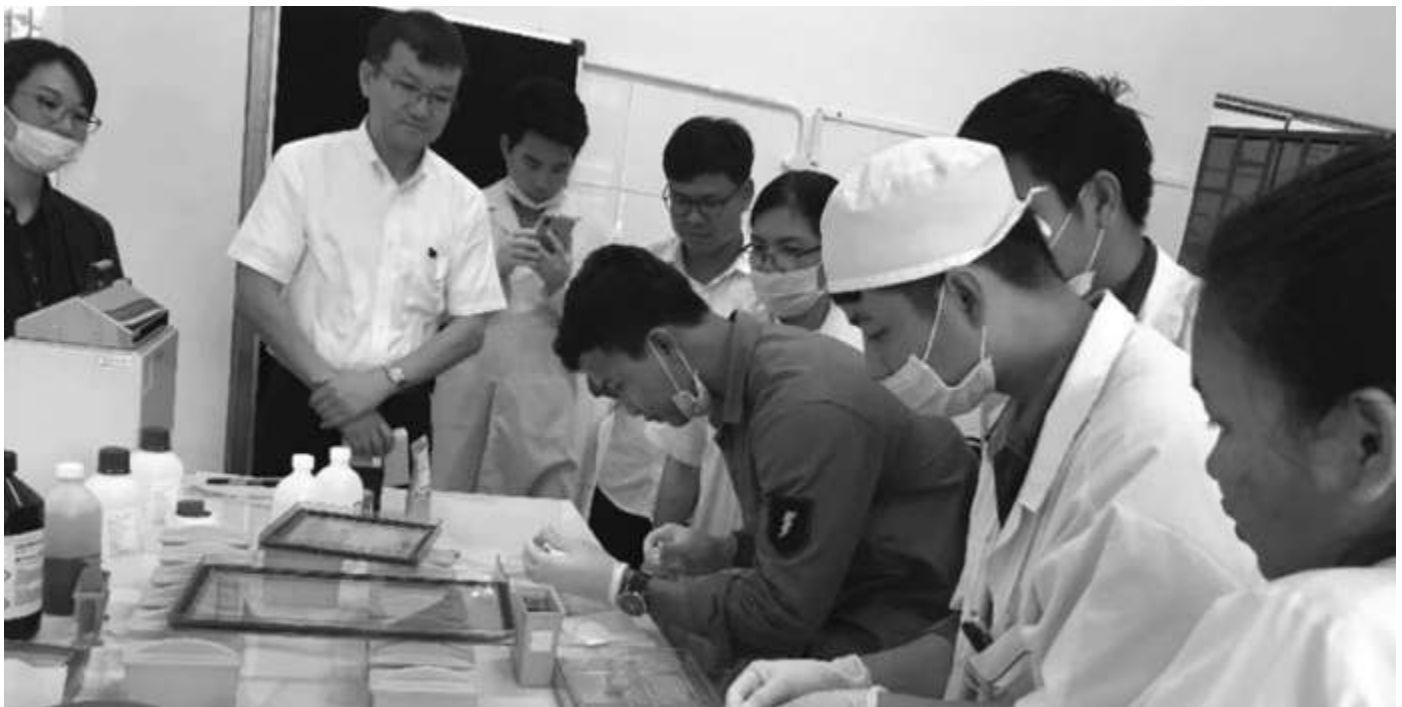


PHOTO: Kaori Ohara



CASE STUDY: CAMBODIA

STRENGTHENING PATHOLOGY WORKFORCE FOR CANCER MANAGEMENT

With successful reduction in maternal mortality over the last decades, cervical cancer has now become the leading cause of morbidity and mortality for women in Cambodia. The National Strategic Plan for NCDs 2013–2020 presents cervical cancer control as a priority. In 2015, the Ministry of Health and Cambodian Society of Gynaecology and Obstetrics initiated a joint project for cervical cancer screening and early diagnosis with support of the Japan Society of Obstetrics and Gynaecology. Through this project, it was revealed that a bottleneck for timely and quality diagnosis of cervical cancer was the limited capacity of pathology services. In 2016, for a population of 16 million, Cambodia had only three public pathology laboratories, four pathologists and 18 pathology technicians. Slides were often difficult to read due to poor preparation. Furthermore, pathologists were working in isolation from other pathologists and with little communication with clinical services.

To improve the delivery of pathology services, on-the-job training for locally employed pathology technicians and

pathologists was initiated as well as clinicopathological conferences. As a result of this 3-year project, the skills of existing pathologists and pathology technicians greatly improved. However, more skilled pathology workforces were needed to further increase the availability of pathology services throughout the country. Because of lack of access to basic education in pathology in Cambodia, efforts are ongoing, with support of the National Center for Global Health and Medicine (Japan), to develop an undergraduate pathology course for medical technology students and a residency course for young physicians at the University of Health Sciences.

A rapidly aging population and the introduction of advanced medical technology have increased the demand for timely and quality diagnosis of cancer in Cambodia. Consolidating and enhancing the existing pathology skill set for the current workforce and strengthening pathology training in undergraduate medical education may also be required in other LMICs to meet their equally growing demand.

ADDITIONAL WHO RESOURCES:

- > WHO *Guide for establishing pathology laboratory in the context of cancer control* (8).
- > WHO *Basic histopathology and anatomical pathology services for developing countries with variable resources* (11).
- > WHO *Guidance on national health laboratory policies, strategies and tools to improve laboratory capacity* (12).

2.1.1.2 MEDICAL IMAGING AND ENDOSCOPY

Medical imaging plays an important role in the evaluation and staging of cervical cancer (Table 2.2). Locally, imaging assesses tumour presence, size of the lesion, presence of stromal invasion and the possible extension to the vagina, parametrium, adjacent organs (bladder and rectum) and pelvic side wall. Imaging techniques also serve to detect lymph node involvement and distant metastases that radically modify the prognosis and treatment recommendations. Additionally, imaging aids treatment monitoring and follow-up of the patient.

Magnetic resonance imaging (MRI) has a high tissue contrast resolution and is considered the gold standard modality in the detection, characterization and local staging of cervical cancer. However, access to MRI remains limited in many LMICs. To fill this gap, trans-vaginal (TV) or trans-rectal (TR) ultrasound represent a useful alternative

when used by trained experts (13,14). The diagnostic performance of TV/TR ultrasound for the evaluation of a tumour size >4 cm, depth of stromal invasion and parametrial invasion is generally quite accurate (13,15–17). When performed at centres with high levels of experience, TV/TR ultrasound yields diagnostic staging performance metrics comparable to that of pelvic MRI (15,17).

Computed tomography (CT) has a low soft tissue contrast resolution and, therefore, has limitations in providing detailed information about tumours of the cervix. However, it serves as a sufficiently accurate tool for recognizing lymph node involvement and distant metastases, in particular, to liver and lungs. Positron emission tomography-computed tomography (PET-CT) is a sophisticated hybrid imaging modality combining anatomical and functional images, particularly effective for assessing metastatic lymph nodes, distant metastases and for evaluating treatment response. If CT or

PET is not available, then a chest X-ray can be used instead to rule out metastatic disease to the lungs prior to any treatment.

Cystoscopy and rectoscopy/proctoscopy are types of endoscopy examinations, aimed at evaluating the interior of the urinary bladder and rectum, respectively. These interventions are recommended only if bladder or rectal invasion of tumour is suspected. Lesions suspected to be

invading either the bladder or rectum should undergo a biopsy and histopathological evaluation. Mere presence of bullous oedema of the bladder mucosa does not indicate extension of cervical cancer to the urinary bladder.

While imaging technologies are key for comprehensive evaluations, countries must develop locally appropriate staging protocols that are based on the availability of resources and existing evidence.

TABLE 2.2

Summary of medical imaging and endoscopy interventions in the management of cervical cancer

Intervention	Abbreviation	Procedure	Intent/advantage	Associated risks/adverse events
Imaging				
Magnetic resonance imaging	MRI	Imaging modality for detailed visualization of internal structures using non-ionizing electromagnetic radiation.	<ul style="list-style-type: none"> ➤ Assessment of the tumour and local spread (i.e. size, presence of stromal invasion spread to vagina, parametrium, bladder, rectum and pelvic side wall) ➤ Superior soft tissue resolution compared to CT ➤ Addition of diffusion-weighted sequences may aid in tumour characterization, tumour delineation and evaluation of treatment response ➤ Can be used for radiotherapy planning in combination with CT 	<ul style="list-style-type: none"> ➤ Cannot be used in case of: <ul style="list-style-type: none"> • implantable medical devices such as pacemakers, cardiac defibrillators, drugs infusion pump • ferromagnetic metallic implants • foreign metallic material (notably intracerebral and ocular) ➤ Hypersensitivity reaction to contrast agents
Computed tomography	CT	Imaging modality that utilizes ionizing radiation for image production of internal structures with digital reconstruction.	<ul style="list-style-type: none"> ➤ Assessment of lymph nodes (e.g. pelvic, para-aortic) and distant metastases (e.g. liver, lungs) ➤ Is used for radiotherapy planning 	<ul style="list-style-type: none"> ➤ Radiation exposure ➤ Hypersensitivity reaction to iodinated contrast agents ➤ Iodinated contrast agents cannot be used in case of renal failure (notably due to hydronephrosis)

Chest X-ray	CXR	Imaging test that utilizes ionizing radiation to produce an image of the chest.	<ul style="list-style-type: none"> ➤ Assessment of lungs, airways, blood vessels, bones ➤ Widely available 	<ul style="list-style-type: none"> ➤ Radiation exposure
Positron emission tomography-computed tomography	PET-CT	Hybrid imaging, namely the integration of PET (functional information) and CT (anatomical information). Involves injection of a positron-emitting radiopharmaceutical with subsequent detection of the annihilation photon and concomitant CT imaging.	<ul style="list-style-type: none"> ➤ Assessment of distant metastases ➤ Evaluation of treatment response ➤ Can be used for radiotherapy planning 	<ul style="list-style-type: none"> ➤ Radiation exposure ➤ Hypersensitivity reaction to iodinated contrast agents when injected for the CT <p>N.B. Iodinated contrast agents cannot be used in case of renal failure (notably due to hydronephrosis)</p>
Ultrasound	US	Imaging modality that utilizes high-frequency sound waves to provide cross-sectional images of the body.	<ul style="list-style-type: none"> ➤ Assessment of tumour and its local spread ➤ Assessment of hydronephrosis ➤ Can become a possible first-line diagnostic method in resource-limited settings ➤ Can be used safely in pregnancy 	<ul style="list-style-type: none"> ➤ Quality highly dependent on the expertise of the provider
Intravenous pyelography	IVP	X-ray test that uses an injection of iodinated contrast agents to visualize kidneys, ureters and bladder.	<ul style="list-style-type: none"> ➤ Assessment of hydronephrosis 	<ul style="list-style-type: none"> ➤ Radiation exposure ➤ Hypersensitivity reaction to iodinated contrast agents
Endoscopy				
Cystoscopy	—	Medical examination with a cystoscope.	<ul style="list-style-type: none"> ➤ Assessment of bladder invasion (only if symptoms exist) 	<ul style="list-style-type: none"> ➤ Infection ➤ Bleeding ➤ Perforation
Proctoscopy	—	Medical examination with a proctoscope.	<ul style="list-style-type: none"> ➤ Assessment of rectal invasion (only if symptoms exist) 	<ul style="list-style-type: none"> ➤ Bleeding ➤ Perforation

SOURCES: WHO (18); Bhatla et al. 2018 (7).

ADDITIONAL WHO AND IAEA RESOURCES:

- WHO *Manual of diagnostic ultrasound*, vol. 2, 2nd edition (19).
- IAEA *Clinical PET/CT atlas: a casebook of imaging in oncology*, Human Health Series No. 32 (20).
- IAEA *Guided intraoperative scintigraphic tumour targeting (GOSTT)*, Human Health Series No. 29 (21).
- IAEA *Quality Assurance Programme for Computed Tomography: diagnostic and therapy applications*, Human Health Series No. 19 (22).
- IAEA *Quality assurance for PET and PET/CT systems*, Human Health Series No. 1 (23).

2.1.2 TREATMENT

Treatment for cervical cancer depends on the stage of disease and may involve either one modality or combinations of surgery, radiotherapy, systemic therapy (including chemotherapy) and palliative care. Surgery and radiotherapy are treatments targeting specific anatomical sites of cancer, whereas systemic therapy is focused on spread of cancer cells beyond the visible areas of the primary site of cancer. Chemotherapy can also be used to enhance radiotherapy when administered as a radiosensitizer.

Stage-appropriate treatment options should be based on national evidence-based clinical practice guidelines. Each case should be discussed by an MDT to arrive at a treatment plan (see Section 3.2.3.2). The MDT should discuss the plan with the patient, and individualized treatment should incorporate her overall health status, age, preference and locally available health care resources. Consent must be obtained from patients, and prior to initiating treatment they should be appropriately counselled about expected and possible adverse effects, including toxicities. All treatments must be delivered with ensured quality, safety and minimal toxicities. All treatments should also be integrated with palliative care to maximize the patient's well-being regardless of prognosis (24). Even when physical symptoms are mild or absent, many patients will benefit from psychological, social or spiritual support.

2.1.2.1 SURGERY

Surgery is one of the primary modalities for treatment of early-stage cervical cancer. Also, it can be indicated

in case of recurrent disease or for palliative intent (e.g. urinary and bowel diversion). Determination of the type of surgery required is based on the stage of disease, desire for preserved fertility and condition of the patient's health (Table 2.3). Important information includes tumour size, parametrial and vaginal involvement, haematologic function and regional and distant lymph node status. The primary goal is to select patients for surgery who will not need adjuvant radiotherapy, as dual therapy greatly affects patient morbidity.

A subset of patients undergoing surgery may, nevertheless, require adjuvant radiotherapy and/or chemotherapy due to high- or intermediate-risk features found upon pathological examination of the surgical specimen (25).

- High-risk features: any one of three factors (positive surgical margins, lymph node involvement, parametrial spread).
- Intermediate features: any two of three factors (tumour size over 4 cm, lymphovascular space invasion, greater than one third stromal invasion).

Delivery of timely and quality surgery relies on the availability of a well-equipped operating room, a well-trained surgical and anaesthesia team, proper surgical instruments, disposables and medicines, blood transfusion services and post-operative care. Less complex surgery, such as simple hysterectomies, can be performed by a general gynaecologist. More complex surgery (e.g. radical hysterectomy and pelvic lymphadenectomy) should ideally be performed by a gynaecologic oncologist or a surgeon specially trained in cervical cancer surgery (26).

TABLE 2.3

Summary of surgical interventions for the management of cervical cancer

Intervention	Abbreviation	Procedure	Intent/advantage	Associated risks/ adverse events
Simple hysterectomy (Type A)	SH	Surgical removal of the uterus and cervix (conization of cervix should be performed to exclude invasive foci before proceeding to SH).	<ul style="list-style-type: none"> Curative for micro-invasive lesions (FIGO Stage IA1). 	<ul style="list-style-type: none"> Infertility Bleeding Infection
Modified radical hysterectomy (Type B)	mRH	Surgical removal of the uterus, cervix with 1–2 cm of the vagina, medial part of cardinal and uterosacral ligaments, and pelvic lymph nodes.	<ul style="list-style-type: none"> Curative for small invasive lesions (FIGO Stage IA1 with LVSI, IA2). 	<ul style="list-style-type: none"> Infertility Bleeding Infection Risk of urinary tract injury and/or dysfunction
Radical hysterectomy (Type C)	RH	Surgical removal of the uterus, cervix with upper 1/4 to 1/3 of the vagina, cardinal and uterosacral ligaments, and pelvic lymph nodes.	<ul style="list-style-type: none"> Curative for larger invasive lesions (FIGO Stage IB1, IB2, selected IIA). 	<ul style="list-style-type: none"> Infertility Bleeding Infection Risk of urinary tract injury and/or dysfunction
Radical trachelectomy	RT	Surgical removal of the cervix with upper 1/4 to 1/3 of the vagina, medial parts of cardinal and uterosacral ligaments, and pelvic lymph nodes. May be performed vaginally or abdominally.	<ul style="list-style-type: none"> Curative for selected invasive lesions (FIGO Stage IA2, IB1) when fertility is desired. 	<ul style="list-style-type: none"> Bleeding Infection Risk of miscarriage and premature delivery Risk of urinary tract injury and/or dysfunction
Pelvic lymphadenectomy	PLD	Surgical removal of the pelvic lymph nodes.	<ul style="list-style-type: none"> Identification of lymph node spread. 	<ul style="list-style-type: none"> Bleeding Infection Lymphoedema of lower extremities Risk of urinary tract injury and/or dysfunction

SOURCE: Adapted from Bhatla et al. 2018 (7).



CASE STUDY: ZAMBIA

TOWARDS GYNAECOLOGIC ONCOLOGY SUBSPECIALIST TRAINING AND INFRASTRUCTURE

LMICs are facing an unprecedented rise in annual cancer incidence rates of nearly 70% by 2030, relative to 2010. Gynaecologic malignancies, including those originating in the cervix, uterine corpus, ovary, fallopian tube and vulva, will represent a substantial fraction of these new cases. Most will require surgery at some point during the course of the disease. Efforts are thus under way in Zambia to develop gynaecologic oncology services, as it is well established that outcomes of gynaecologic cancer patients are better when treated by appropriately trained surgical subspecialists.

GENERAL GYNAECOLOGISTS WITH A SPECIAL INTEREST IN GYNAECOLOGIC ONCOLOGY

Historically, gynaecologic oncology services in Zambia were provided by general gynaecologists with a special interest in the field, but who were without formal, certified subspecialty training. Surgical procedures were primarily performed by the senior surgeon with only secondary emphasis on transferring oncologic surgical skills to junior staff and obstetrics/gynaecology (Ob/Gyn) registrars, who primarily served as observers and first assistants.

THE TRANSITION TO GYNAECOLOGIC ONCOLOGY SUBSPECIALIST TRAINING

In 2006, the prospect for implementing gynaecologic oncology subspecialist training in Zambia was enhanced after a United States board-certified gynaecologic oncologist joined the full-time staff of the Department of Obstetrics and Gynaecology at the University Teaching Hospital of Zambia (UTH). The surgical education curriculum was subsequently modified, with greater emphasis placed on training junior staff and Ob/Gyn registrars to surgically manage gynaecologic malignancies. A novel approach to surgical skills transfer was initiated, consisting of high volume repetition of radical surgical procedures performed over short-time intervals (e.g. two of the same type of radical surgical procedure/day x 5 days). When combined with intense intra-operative mentoring and post-operative case review, junior Ob/Gyn staff learned how to perform some of the more complex gynaecologic oncology procedures (e.g. Type II or modified radical abdominal hysterectomy, radical hemivulvectomy, ovarian tumour debulking). Driven by increased interest among junior staff and Ob/Gyn regis-

trars in learning surgical anatomy and radical operative procedures, alongside a rising volume of gynaecologic cancer cases, in 2015 the UTH leadership established a gynaecologic oncology subspecialty clinical unit at its Women and Newborn Hospital in Lusaka. Zambia's medical licensing body Health Professions Council of Zambia simultaneously recognized gynaecologic oncology as a surgical subspecialty.

FORMAL GYNAECOLOGIC ONCOLOGY TRAINING – OUTSIDE OF ZAMBIA

In 2017, a Zambian Ob/Gyn specialist was selected to attend a 1-year gynaecologic oncology fellowship at Tata Memorial Hospital in India. Upon returning to Zambia he established a new gynaecologic oncology unit at the national cancer centre (Cancer Diseases Hospital) in Lusaka. Two additional Ob/Gyn specialists presently matriculating in the Tata Memorial fellowship are scheduled to complete their training in 2020 and 2021. Upon returning to Zambia they too will establish new gynaecologic oncology service infrastructures in regions of the country in which radiation and chemotherapy services are now being scaled up.

FORMAL GYNAECOLOGIC ONCOLOGY TRAINING – IN-COUNTRY

The country's National Cancer Control Strategic Plan and National Surgical, Obstetric & Anaesthesia Strategic Plan emphasize "in-country" surgical oncology subspecialty training. In accordance with this policy, a 2-year gynaecologic oncology fellowship was established in 2018 in the Department of Obstetrics and Gynaecology at the UTH-Women and Newborn Hospital. Co-sponsored by the International Gynaecologic Cancer Society (IGCS), local leadership is provided by the first graduate of the Tata Memorial gynaecologic oncology fellowship along with obstetrics and gynaecology staff with experience in managing gynaecologic malignancies. Educational support is provided by gynaecologic oncology mentors from the University of North Carolina, Chapel Hill, West Virginia University, Morgantown, and the University of Washington, Seattle. Graduates of the programme will be disseminated to large provincial hospitals across the country.

ADDITIONAL WHO RESOURCES:

- WHO *Surgical care systems strengthening: developing national surgical and anaesthesia plans* (26).
- WHO *Surgical care at the district hospital* (27).

2.1.2.2 RADIOTHERAPY

Radiotherapy uses guided ionizing radiation to destroy cancer cells. Utilized most often in combination with chemotherapy, it is the primary curative treatment for women with cervical cancer who are not candidates for primary surgery. The type of radiotherapy required depends on the stage of the disease and performance status of the patient. For curative treatment, two types of radiotherapy delivery are necessary: external beam radiotherapy (EBRT); and brachytherapy (BT). In some cases, radiotherapy is used as adjuvant treatment after surgery (Table 2.4).

For cervical cancer particularly, radiotherapy may be especially beneficial and prioritization of radiotherapy services may be considered. A modelling study estimated a 17% population benefit for 5-year overall survival was attributed to radiotherapy alone (compared to no radiotherapy) for all stages combined (28). In comparison, the overall contribution of curative and adjuvant cytotoxic chemotherapy to 5-year survival in adults is estimated to be less than 3% (29), which is similar to that of radiotherapy for all cancers together (30).

Radiotherapy is distinguished from other cancer treatment modalities by several characteristics:

- Medical use of ionizing radiation is regulated by a national governmental regulatory body for radiation safety and protection in addition to other forms of medical regulation.

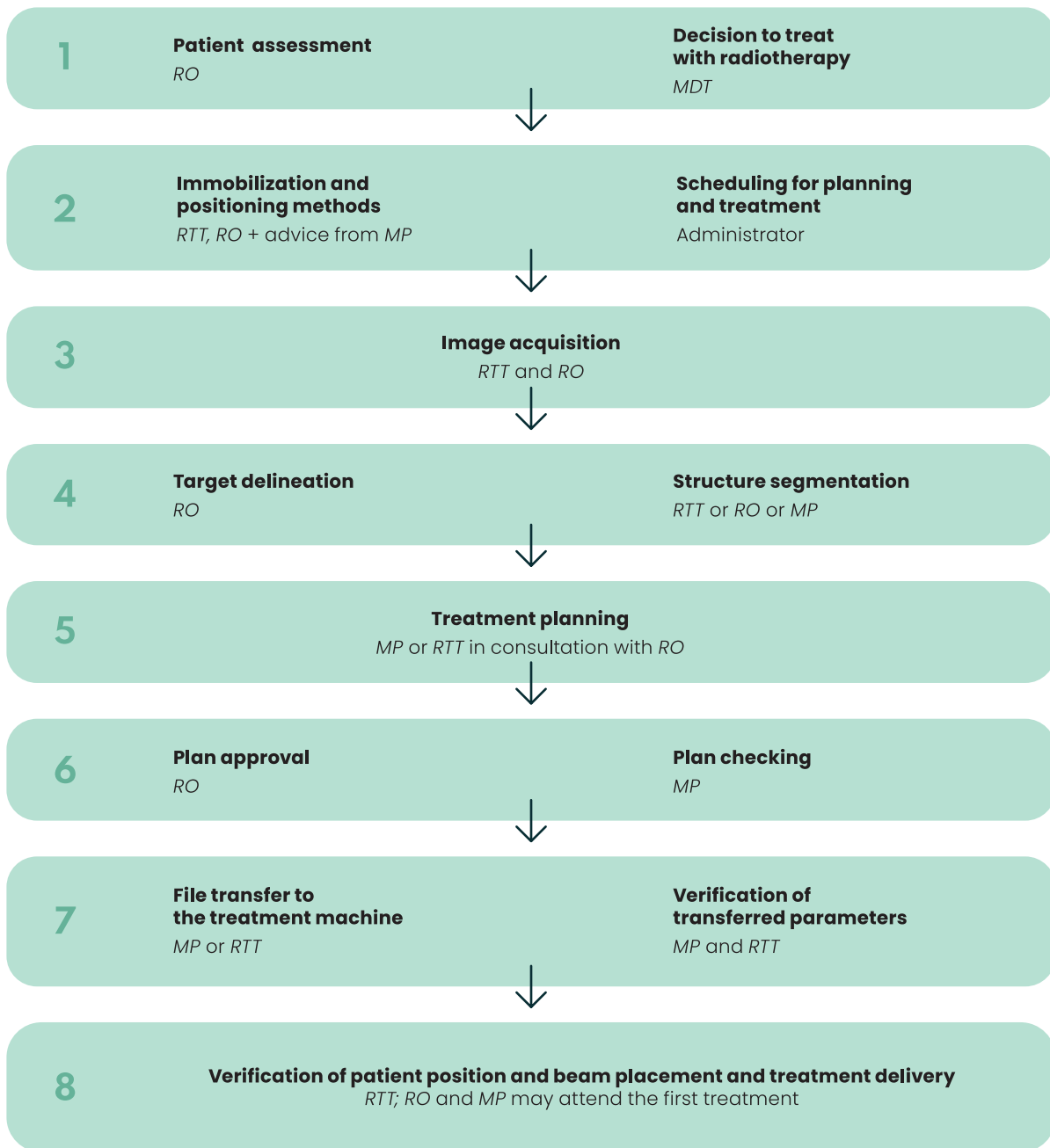
- Radiotherapy requires custom-built physical infrastructure and highly specialized equipment.
- For safe and high-quality delivery of radiotherapy, a core team of medical professionals, including radiation oncologists, medical physicists and radiation therapy technicians (RTTs) is needed.
- A course of radiotherapy usually lasts for five weeks or longer, is administered daily (five working days with a break over the weekend) and often as an outpatient service. It cannot be delivered remotely or moved close to patients' homes.

Figure 2.4 illustrates the typical process for EBRT, involving several steps and interaction between different members of the radiotherapy team. Each step requires quality control aiming to guarantee that the therapeutic dose of radiation is delivered strictly in accordance with its prescription. Quality assurance and control in radiotherapy have clinical and equipment-specific components and ideally require a quality management system in every radiotherapy department. A description of a typical BT process can be found elsewhere (31).

Patients should be evaluated weekly while on treatment to control any adverse effects (e.g. anaemia, drop in leucocyte count, diarrhoea, nausea and dermatitis) and to minimize treatment breaks. Once radiotherapy is started, it is critical that the full course (EBRT and BT) is completed within eight weeks for best outcomes (33,34).

FIGURE 2.4

Typical EBRT process and key personnel for delivery of 3-D conformal radiotherapy



MDT: multidisciplinary team; **MP:** medical physicist; **RO:** radiation oncologist; **RTT:** radiation therapist (radiotherapy technologist).

NOTES: There are eight distinct steps with major subtasks in each of them. Members of the radiotherapy team responsible for each of the subtasks are listed in italics.

SOURCE: Adapted from IAEA 2008 (32).

TABLE 2.4

Summary of radiotherapy interventions in the management of cervical cancer

Intervention	Abbreviation	Procedure	Intent/advantage	Associated risks/ adverse events
External beam radiotherapy	EBRT	Radiotherapy delivered from a distance.	<ul style="list-style-type: none"> > Curative for small to large lesions in combination with BT and chemotherapy. > Palliative to control bleeding and/or pain. 	<ul style="list-style-type: none"> > Infertility > Menopause > Vaginal dryness > Bowel, urinary, haematological and skin toxicity
Brachytherapy	BT	Radiotherapy delivered from a sealed radioactive source placed inside the vagina and uterus, close to the tumour.	<ul style="list-style-type: none"> > Curative for small to large lesions in combination with EBRT. 	<ul style="list-style-type: none"> > Vaginal stenosis; vaginal dryness > Radiation proctitis > Bowel and bladder toxicity > May require anaesthesia
Adjuvant radiotherapy	aRT	EBRT and/or BT administered after surgery.	<ul style="list-style-type: none"> > Eradication of any microscopic disease in the irradiated area. 	<ul style="list-style-type: none"> > Bowel, urinary, haematological and skin toxicity

SOURCE: Adapted from WHO 2017 (35).

ADDITIONAL IAEA RESOURCES:

- > IAEA *Management of cervical cancer: strategies for limited-resource centres – a guide for radiation oncologists*, Human Health Reports No. 6 (36).
- > IAEA *Implementation of high-dose rate brachytherapy in limited-resource settings*, Human Health Series No. 30 (37).
- > IAEA *Planning national radiotherapy services: a practical tool*, Human Health Series No. 14 (38).
- > IAEA *Setting up a radiotherapy programme: clinical, medical physics, radiation protection and safety aspects* (39).
- > IAEA *Radiotherapy facilities: master planning and concept design considerations*, Human Health Reports No. 10 (40).
- > IAEA *Radiotherapy in cancer care: facing the global challenge* (41).



CASE STUDY: ZAMBIA

BOOSTING THE QUALITY OF CERVICAL CANCER CONTROL PROGRAMME THROUGH RADIOTHERAPY IMPROVEMENT

The phased planning and implementation of high-quality radiotherapy services in Zambia created an entry point for the step-wise expansion of comprehensive, sustainable cancer control services throughout the country, with priority given to control of cervical cancer. Starting in 2005 with collaboration between the Ministry of Health, International Atomic Energy Agency (IAEA), WHO and OFID (OPEC Fund for International Development), Zambia initiated the construction of the first radiotherapy centre in Lusaka, training of specialized clinicians (radiation oncologists), training of radiation therapists, medical physicists and radiotherapy equipment maintenance technicians, and the purchasing of essential equipment.

Expansion of the programme included purchase of the country's second cobalt unit, second BT unit, a CT simulator, MRI, and planning software that facilitated 3-dimensional treatments in both BT and EBRT. The creation of a 252-bed inpatient capacity, an 80-bed chemotherapy suite, a dedicated training and research and development centre, and enhanced diagnostic, treatment and palliative care services at Cancer Diseases Hospital (CDH) transformed it into a comprehensive centre with paediatric, gynaecologic and surgical oncology services. Currently in the third phase, the programme is decentralizing to all provinces, adding two more regionally based linear accelerators, a BT centre and a CT simulator. Crucially, creating a treatment centre in each province will address disparities in access to cancer management. In 2018, while 25% of nationally diagnosed cases were seen in the CDH, some provinces were sending only 6% of their cases to the centre. The fourth phase should see PET/CT and cyclotron facilities at CDH and deepened research capacity, including a research reactor at the National Centre for Nuclear Science.

Right from the onset, strengthening sustainability and local capacity were key concerns. Community mobilization issues were identified in the first phase. Although substantial technical and funding support has been provided by an array of both public and private international partners, the Government of the Republic of Zambia has largely been financing the development and operation of the radiotherapy services. Sustainability was further enhanced with the establishment of the CDH Training College, offering a radiation therapy training programme since 2012. In January 2016, local

training of radiation oncologists commenced. This has been achieved through collaboration with the Zambian Society of Clinical & Radiation Oncologists (ZASCRO), Zambia Colleges of Medicine and Surgery (ZACOMS) and the Levy Mwanawasa Medical University. The curriculum for training of clinically qualified medical physicists is nearly complete.

Through the quality improvement of radiotherapy services, benchmarks for attaining best practice and the highest standards of cancer control have been established. The CDH has also participated in the creation of technical guidance documents for invasive cervical cancer control. A dedicated oncology service unit (National Cancer Control Unit) now exists at the Ministry of Health to implement strategically planned programmes and offer national guidance in cancer control.

Impetus for improvement of cervical cancer control was gained from additional initiatives. Besides developing a specialized treatment unit for gynaecologic cancers at the CDH, evidence-based interventions have been implemented in primary and secondary prevention. A national HPV vaccination programme has commenced, and the formerly ineffective Pap smear screening programme has been transformed into a successful nurse-led see-and-treat programme, with quality assurance of visual-inspection-with-acetic acid assisted by cervicography and backed up by online expert consultation. HPV DNA testing has been introduced at cervical cancer screening and ART clinics, so as not to leave behind WLHIV in the control and prevention of cervical cancer.

From its foundational stages, the cancer control programme in Zambia has used quality radiotherapy and capacity-building as the launch pad into and growth of cancer control services. Through to its future projects, the programme will likely continue to create synergies for accelerating the elevation of invasive cervical cancer management in the country; these efforts will in total contribute to the national goal of reducing premature cancer mortality by 30% by 2030.

2.1.2.3 SYSTEMIC TREATMENT

Systemic treatment, including chemotherapy, refers to the administration of antineoplastic medicines that target rapidly dividing cells, which is a hallmark of cancer cells (3). It is rarely used alone as the primary treatment of cervical cancer, but rather administered along with radiotherapy as a radiosensitizer for definitive courses of cervical cancer treatment (i.e. concurrent chemoradiation). The most common option for concurrent chemoradiation is cisplatin, or carboplatin if cisplatin is contraindicated, given weekly during EBRT. It is also given for high-risk cases after surgery (i.e. adjuvant chemotherapy) with or without adjuvant radiotherapy (Table 2.5).

Use of chemotherapy prior to surgery (neoadjuvant chemotherapy or NAC) remains controversial. It has been demonstrated that outcomes of patients with locally advanced cancers treated with NAC followed by surgery are inferior to those of patients treated with chemoradiation (42–44). Also, current data suggest there is no improvement in overall survival when NAC and surgery is compared with surgery alone (45–48). However, NAC and surgery may be an option in settings where radiotherapy is not available or surgeons are not comfortable with the resection of large early stage cervical lesions.

Safe and timely delivery of systemic treatment requires appropriate systems for forecasting, stocking, preparing and disposing of cancer medicines (see Section 3.3.3.1) (49). The core team includes medical/clinical oncologists or physicians with training in oncology, nurses trained in administration of cytotoxic medicines and supporting patients during cancer treatment, and pharmacists trained in preparing and monitoring chemotherapy. Appropriate infrastructure, such as availability of designated clean rooms with ventilation to prepare cytotoxic medicines, biosafety cabinets and necessary personal protective equipment (PPE) are required for safe chemotherapy administration. Patients must be monitored closely while on treatment and managed in a timely fashion for any adverse effects. The treatment facility should be adequately prepared for treatment of life-threatening adverse events, e.g. neutropenic sepsis.

Targeted agents for cervical cancer have emerged for the treatment of patients with advanced disease recently, mainly in resource-rich settings (50). However, so far none of the targeted agents has been included in the WHO *Model lists of essential medicines* for the management of cervical cancer. Their role in the improvement of the life expectancy and quality of life of patients is still marginal, and evidence of effective implementation in LMICs is still lacking (51). The magnitude of clinical benefit for bevacizumab in advanced cervical cancer has been estimated as 3/5 according to the European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS) (52,53).



PHOTO: Shyam Shrivastava

TABLE 2.5

Summary of chemotherapy interventions in the management of cervical cancer

Intervention	Abbreviation	Procedure	Intent/advantage	Common adverse events
Neoadjuvant chemotherapy	NAC	Chemotherapy administered before surgery.	<ul style="list-style-type: none"> ➤ Reduction of tumour volume to achieve operability and decrease intra-operative blood loss in settings where radiotherapy is not available 	<ul style="list-style-type: none"> ➤ Haematological toxicity ➤ Gastrointestinal (nausea, vomiting, appetite loss, diarrhoea) ➤ Hair loss
Concurrent chemotherapy	CC	Chemotherapy administered in concurrence with radiotherapy.	<ul style="list-style-type: none"> ➤ Radiosensitizing effect ➤ Cytotoxic and anti-proliferative effects 	<ul style="list-style-type: none"> ➤ Neuropathy ➤ Nephropathy
Adjuvant chemotherapy	AC	Chemotherapy administered after surgery or radiotherapy.	<ul style="list-style-type: none"> ➤ Prevention of cancer recurrence ➤ Treatment of micrometastases 	

SOURCE: Adapted from Kumar and Gupta 2016 (54).



PHOTO: Department of Radiation Oncology, Dr Cipto Mangunkusumo, Jakarta, Indonesia



CASE STUDY: RWANDA

CAPACITY-BUILDING FOR MEDICAL ONCOLOGY SERVICES IN TREATING INVASIVE CERVICAL CANCER

Cervical cancer is the leading cause of cancer mortality in women in Rwanda. In 2012, the Rwandan Ministry of Health made a plan to address this issue through development of a national HPV vaccination programme, a systematic approach to screening and precancer treatment, and capacity-building in management of invasive cancers. Like many low-income countries, Rwanda faced multiple challenges in cervical cancer treatment. There were few medical professionals relative to the population size and no specialists with expertise in the treatment of gynaecologic cancers. There were no facilities equipped to mix and administer chemotherapy. Medical record-keeping was inadequate for close tracking of patients throughout and after their care. Pathology capacity and expertise were limited. There was no radiotherapy facility in the country. All of these issues most affected the poor and middle class.

Faced with these multiple and significant challenges, the Rwandan Ministry of Health took a planned and coordinated approach to develop a competent oncologic workforce. Capacity-building programmes targeted increasing expertise in women's cancers through recruitment of full-time medical teaching faculty from outside the country. The Ministry of Health partnered with Partners in Health, Inshuti Mu Buzima (the autonomous Rwandan affiliate of Partners in Health) and the Dana Farber Cancer Institute in the United States, to engage expertise and resources for chemotherapy services, including other supporting services. Through these partnerships, common, treatable cancers were identified, and standard protocols for chemotherapy administration were developed that emphasized known efficacy, medicines and technologies availability, and patient and staff safety.

The Butaro district hospital was the first site to develop cancer programmes in the country. Without oncologists available onsite, task-shifting of cancer care, including chemotherapy, was undertaken. Key staff were sent to the Dana Farber Cancer Institute for short-term training, while committed volunteer specialists travelled to Butaro to teach staff onsite. Conferences were held at least weekly in which the onsite cancer care team reviewed cases with specialists from Dana Farber. Similarly, pathologists at Dana Farber worked with technicians and pathologists at Butaro to build capacity in tissue diagnosis. Medical records were kept using the OpenMRS open-source electronic medical record platform. The use of standard protocols facilitated the development of standard operating procedures (SOPs) and the identification and procurement of essential medicines.

An additional challenge was to optimize treatment within Rwanda's resources. The majority of women presented with advanced stage disease and required both chemotherapy and radiotherapy. As establishing a radiotherapy treatment facility in Rwanda would take time, partnerships were created to facilitate treatment outside the country for women likely to benefit. MDTs and collaborations with the national teaching hospital in Kigali were developed to offer surgery or NAC plus surgery to women with earlier stage cancer. A recent review showed that 38% of women completing chemoradiotherapy for cervical cancer through this programme were alive at 15 months after treatment, showing that many women were saved through thoughtful mobilization of limited resources. Rwanda has now leveraged this success to open a radiotherapy treatment facility in the country.

2.1.3 PALLIATIVE CARE

Palliative care is prevention and relief of physical, psychological, social and spiritual suffering of patients facing serious illness and prevention and relief of psychological, social and spiritual suffering of family members. Palliative care should be integrated with and complement prevention, early diagnosis and treatment of cervical cancer. It also is applicable to those living with long-term physical, psychological, social or spiritual sequelae of cervical cancer or its treatment (55). Initial assessment for palliative care needs should be done at the time of cervical cancer diagnosis, and palliative care always should be integrated into the treatment plan for invasive cervical cancer.

The Essential Package of Palliative Care for People Affected by Cervical Cancer (EPPCCC) is outlined in Annex 4. The EPPCCC can and should be applied by health care workers with at least basic training in palliative care at all levels of health care systems (Table 2.6) (56). Primary care clinicians should receive basic palliative care training, and intermediate-level palliative care training should be required for oncologists and gynaecologists. The EPPCCC should not be considered sufficient to meet all palliative care or symptom relief needs. Whenever possible, the EPPCCC should be augmented to enable improved prevention and relief of the often severe, refractory and multifaceted suffering from cervical cancer. The augmented package includes

TABLE 2.6

Palliative care interventions, delivery platforms and providers

Intervention	Delivery platform			
	Mobile outreach/ home care	Primary care level (community health centres)	Secondary care level (district hospitals)	Tertiary care level (cancer centres)
Initial control of moderate to severe symptoms/control of refractory suffering			<ul style="list-style-type: none"> Small palliative care team consisting of one or two part-time doctors with basic or intermediate training in palliative care provides outpatient care and inpatient palliative care 	<ul style="list-style-type: none"> Palliative care team consisting of full- or part-time doctors with intermediate training in palliative care provides outpatient care and inpatient palliative care Ideally, a palliative care specialist physician should lead the team
Ongoing care for patients with well-controlled symptoms	<ul style="list-style-type: none"> Community health workers provide surveillance and emotional support as often as daily A nurse, doctor, social worker or trained lay counsellor from the community health centre visit as needed 	<ul style="list-style-type: none"> Nurse and possibly also a doctor, social worker or lay counsellor with basic training in palliative care provide outpatient care and inpatient hospice care (if the family is unable to provide adequate care at home) 	<ul style="list-style-type: none"> Small palliative care team consisting of one or two doctors with basic or intermediate training in palliative care provides outpatient care and inpatient hospice care (if the family is unable to provide adequate care at home and if no inpatient care is available at community health centres) 	

SOURCE: Adapted from WHO 2018 (55).

palliative radiotherapy, palliative surgery, advanced medical therapies, nerve blocks for pain control and psycho-oncology.

For patients with cervical cancer, palliative care includes:

- assessment and relief of the most common and severe symptoms such as pain, vaginal bleeding, malodorous vaginal discharge, anxiety, depression and sexual dysfunction;
- mitigation of social suffering due to poverty, stigmatization, social isolation and abandonment;
- clear, compassionate and culturally appropriate

communication about diagnosis, prognosis and treatment options; and

- care planning and coordination to help assure treatment adherence and continuity of care.

Palliative care can be provided from delivery platforms at household, primary, secondary and tertiary care levels (Table 2.6). Some women with metastatic disease at the time of diagnosis may benefit from palliative radiotherapy to control distressing symptoms such as vaginal bleeding and bone pain or from palliative surgery such as diverting colostomy to relieve

faecal incontinence due to rectovaginal fistula (57). Palliative chemotherapy may also be administered to relieve symptoms, although the benefit must be weighed against potential harm (7). Uncomplicated symptoms, or more complex symptoms that have

been well-controlled in the hospital, often can be managed at home or in community health centres close to patients' homes.

ADDITIONAL WHO AND IAEA RESOURCES:

- WHO *Integrating palliative care and symptom relief into primary health care: a WHO guide for planners, implementers and managers* (55).
- WHO *Planning and implementing palliative care services: a guide for programme managers* (56).
- WHO *Guidelines for the pharmacological and radiotherapeutic management of cancer pain in adults and adolescents* (57).
- IAEA *Radiotherapy in palliative cancer care: development and implementation*, Human Health Reports No. 2 (58).

2.1.4 SURVIVORSHIP CARE

Survivorship care after effective cancer treatment should continue for at least five years unless there is a recurrence (1). It entails preventing and monitoring for recurrent cervical cancer or new cancers; palliative care to relieve any persistent or late-onset physical or psychological symptoms such as pelvic pain, sexual dysfunction or post-traumatic stress disorder (see Section 2.1.3); and primary care to promote health and manage any chronic health problems (Figure 2.5). Depending on the local health care system, it can be provided at household, primary, secondary or tertiary care levels by adequately trained gynaecologists, oncologists and primary care providers, or by the gynaecologic oncologist in collaboration with the primary care team.

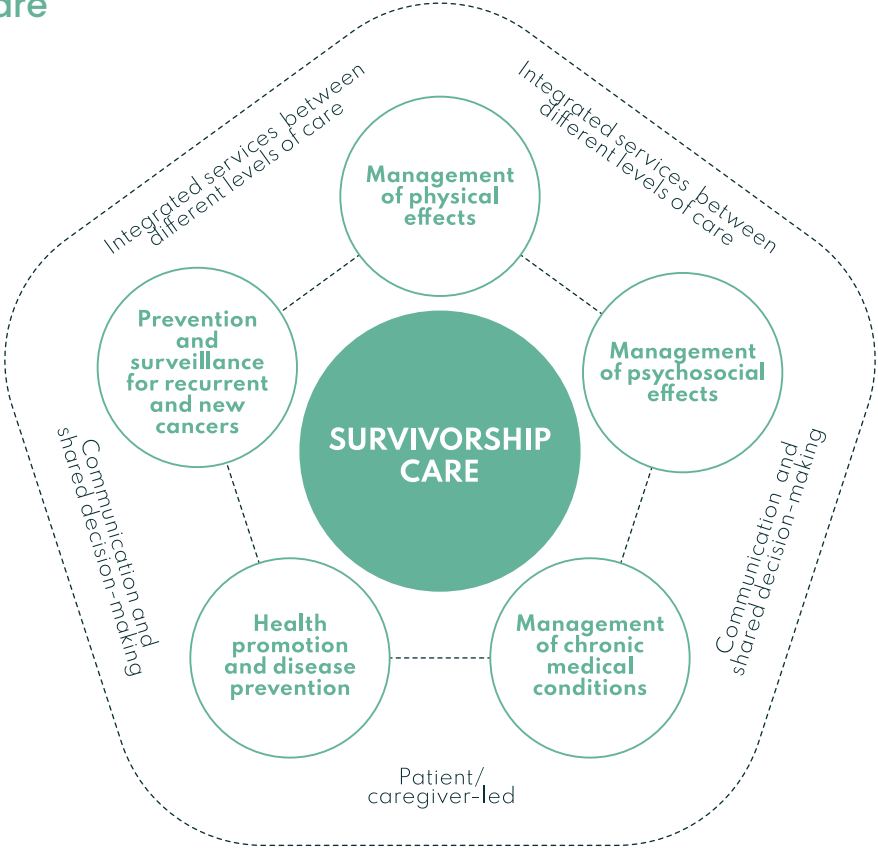
Routine follow-up imaging and cervical cytology have not been shown effective in detecting recurrence in cervical cancer survivors (50). Rather, a system should be in place that enables patients to easily report new or changing symptoms and for these symptoms to be evaluated rapidly with physical examination and appropriate imaging. Clear guidance should be provided to primary care staff for follow-up of treated women, and an efficient referral system should be in place to enable rapid evaluation of patients with possible recurrence at secondary or tertiary care levels. Women with confirmed recurrence should be presented at multidisciplinary tumour boards for appropriate management.



PHOTO: Groesbeck Parham

FIGURE 2.5

Survivorship care



SOURCE: Adapted from WHO 2020 (1).



PHOTO: Surbhi Grover

2.2 COMMON BARRIERS AND DELAYS

Delays in timely access to services may occur at multiple steps of cervical cancer care pathways (Table 2.7). They are generally associated with health care system failures and inadequacies, such as unorganized referral systems, lack of trained health workforce and unavailability of essential diagnostic and treatment services (1).

TABLE 2.7

Common barriers in access to cervical cancer management

Common barriers at patient and health care system levels	
<p>Early detection</p>	<p>PATIENT</p> <ul style="list-style-type: none"> > lack of awareness and knowledge about cervical cancer > fear and concerns about gynaecologic examination > cancer stigma > sociocultural barriers > charges for health care services and self-borne costs (e.g. transportation, childcare, loss of wages) <p>HEALTH CARE SYSTEM</p> <ul style="list-style-type: none"> > inadequate clinical assessment at the primary care level > lack of a well-defined referral pathway to diagnosis and staging
<p>Diagnosis and staging</p>	<p>PATIENT</p> <ul style="list-style-type: none"> > charges for diagnostic services (pathology, medical imaging, endoscopy) and self-borne costs (e.g. transportation, childcare, loss of wages) > long waits for diagnostic results > fear and concerns about diagnostic evaluation (e.g. pain, infertility) > misconception that cervical cancer is a fatal diagnosis <p>HEALTH CARE SYSTEM</p> <ul style="list-style-type: none"> > fragmented services > inadequate patient counselling (pre- and post-diagnosis) > lack of a well-defined referral pathway to treatment > omission of diagnostic work-up in health care benefit package > lack of organized transportation and reporting systems for pathology specimens > inadequate supply of diagnostic equipment and supplies > lack of quality assurance mechanisms for pathology and medical imaging > inadequately trained and insufficient laboratory human resources > lack of workflow planning to match demand and supply of services > lack of effective systems for patient follow-up

Treatment	<p>PATIENT</p> <ul style="list-style-type: none"> > poor treatment compliance > charges for health care services and self-borne costs (e.g. transportation, accommodation during treatment, childcare, loss of wages) > fear and concerns about cancer treatment <p>HEALTH CARE SYSTEM</p> <ul style="list-style-type: none"> > omission of cancer treatment in the health care benefit package > lack of a well-defined referral for stage-appropriate management > lack of patient navigation services to help prevent low patient compliance rates > fragmented services > lack of workflow planning to match demand and supply of services > lack of facilities and trained personnel > inadequate systems to ensure reliable supply chain of medicines, equipment and supplies
Palliative care	<p>PATIENT</p> <ul style="list-style-type: none"> > misconception that palliative care is only for patients in terminal stages of disease > fear of opioids > sociocultural barriers <p>HEALTH CARE SYSTEM</p> <ul style="list-style-type: none"> > legislative restrictions > regulatory restrictions (e.g. lack of authority for doctors with palliative care training to prescribe opioids and/or other essential palliative medicines) > limited access and affordability of essential palliative medicines (especially opioids) > lack of personnel with basic palliative care training > lack of home-based care and accessible community services for palliative care > lack of support for caregivers
Survivorship care	<p>PATIENT</p> <ul style="list-style-type: none"> > charges for health care services and self-borne costs (e.g. transportation, childcare, loss of wages) > lack of awareness and knowledge about the importance of follow-up <p>HEALTH CARE SYSTEM</p> <ul style="list-style-type: none"> > lack of patient navigation services > inadequate patient counselling (post-treatment) > lack of effective patient-tracking systems > lack of appropriately trained staff

SOURCES: WHO 2017 (2); Brand et al. 2019 (59).

The timeframe from symptom onset to treatment initiation should generally be less than 90 days (13 weeks) to avoid loss-to-follow-up and to optimize the effectiveness of treatment (2). Table 2.8 describes optimal duration

between different steps along the cervical cancer care pathway based on best practices. It is critical for each country to set their target durations according to the national context.

TABLE 2.8

Benchmarks from highly developed cancer care systems

From	To	Benchmark
First visit to a health facility	Diagnosis of cancer	Within 4 weeks (2)
Receipt of biopsy specimen at a pathology laboratory	Return of pathology report	Within 2 weeks (60–62)
Diagnosis of cancer	Initiation of treatment	Within 4 weeks (2)
Diagnosis of cancer	Initiation of palliative care	Within 8 weeks (63)
Initiation of definitive radiotherapy	Completion of definitive radiotherapy (EBRT and BT)	Within 8 weeks (34)



CASE STUDY: RWANDA REDUCING TURNAROUND TIME OF PATHOLOGY SERVICE

New histopathology services were implemented in Butaro, Rwanda, to combat, among other challenges, an exceptionally long turnaround time for cancer diagnostics nationally. A partnership of the Ministry of Health, Partners in Health and Brigham and Women's Hospital instituted a step-wise phased plan to build out infrastructure and health workforce in pathology services starting in 2012. In January 2012, then-current laboratory infrastructure, personnel and activities at the Butaro District Hospital and supporting laboratories were investigated and documented to create an assessment report that: (i) detailed the resource needs at Butaro with respect to infrastructure renovations, equipment, consumables, personnel, training and SOPs; (ii) identified where resources would be made available within Rwanda and through international partners; and (iii) outlined a timeline for phased capacity building.

In March 2012, laboratory equipment was provided to the facility using both established manufacturer and supplier networks and donations. In April 2012 (prior to laboratory set up), two laboratory technicians were selected to undergo training in histotechnology between May and June 2012. From July to October 2012, the trained laboratory technicians began processing tissue specimens with support from onsite histotechnologists from the United States. Specimen grossing and generation of paraffin blocks was implemented. Slide staining and cutting was initiated at the facility, and blocks and slides were transported to the Brigham and Women's Hospital (BWH) in Boston, Massachusetts, where they were further processed. Within the first six months after implementation, a high performance rate was achieved, with 437

specimens submitted and processed, including many specimens from other facilities in Rwanda that were sent to Butaro. These represented patients who otherwise would have been unlikely to receive pathology-based diagnoses. The median time from specimen receipt to the result was 32 days at this point.

Since 2014, challenging pathology cases received at Butaro have been photographed and presented to a group of specialist pathologists from around the world using a static image telepathology system. This transitioned to whole slide imaging in 2016. Prior to the appointment of a full-time pathologist at Butaro, 32% of cases, 1407 of a total of 4355, were uploaded to iPath® (an online platform for pathology consultation and teaching) for diagnosis, with turnaround averaging 14 days. Following the appointment of a full-time pathologist at Butaro, the number of challenging cases uploaded as whole slide images (WSI) in the last year (2016) averaged 16% of 1411 cases reviewed using WSI. Diagnoses were successfully generated for 90.5% of these cases and a small number of truly challenging cases were sent to BWH for additional diagnostic work up. Turnaround time has dropped to ~69 hours. The telepathology service has been particularly helpful with analysing difficult hematopathology, bone and soft tissue tumours, which require considerable specialist expertise. The most impactful aspect of this implementation was the acquisition of a permanent pathologist onsite with access to high-quality histology and immunohistochemistry. An ongoing challenge is the need for clinical laboratory techniques and equipment to support liquid tumour diagnostics (e.g. flow cytometry).



CASE STUDY: BOTSWANA

PILOTING A GYNAECOLOGIC ONCOLOGY CLINIC MDT AT PRINCESS MARINA HOSPITAL TO OVERCOME TREATMENT DELAY AND LOSS-TO-FOLLOW-UP

Cervical cancer is both the most commonly diagnosed cancer and the leading cause of cancer death among women in Botswana. More than 75% of patients in Botswana present with locally advanced disease, and treatment delays and loss-to-follow-up are barriers to their receiving urgently required care. In accordance with current guidelines, locally advanced cervical cancer in Botswana is treated with cisplatin-based chemotherapy and radiation. It is provided free of charge to citizens. Although chemotherapy is provided through the public sector, radiation requires coordination with and referral to the country's private health care sector. Effective treatment of cancer necessitates input from and coordination between various subspecialty providers over the course of a patient's care, and disruptions in communication between providers can ultimately lead to treatment delays that adversely affect patient outcomes. The benefit of a multidisciplinary approach to cancer care in which various expert providers meet to discuss patient cases has already been demonstrated in high-income countries. This approach was, therefore, piloted in 2015 in a weekly MDT clinic for gynaecologic oncology patients at Princess Marina Hospital (PMH), the largest referral hospital in Botswana.

The goal of the MDT clinic is to facilitate communication between the various providers involved in the care of cervical cancer patients and to further streamline treatment to prevent treatment delays and loss-to-follow-up. Patients with a new diagnosis of cervical cancer are referred along with background information, including stage, date of biopsy, results of biopsy specimen assessment and HIV status. Records are collected by a nurse coordinator to ensure completeness. A team consisting of a radiation oncologist, medical oncologist, gynaecologist, pathologist, nurse coordinator and palliative care specialist then meets prior to clinic to discuss all patients. Patients are examined by an oncologist or gynaecologist, and further investigations are planned if required for staging prior to treatment initiation. A treatment plan is determined, and referral paperwork for radiotherapy in the private sector is prepared if needed. The patient is counselled on the treatment plan and given a follow-up appointment in two weeks to ensure there are no delays in further investigations or processing. HIV-positive or patients with unknown status are referred to the HIV clinic for treatment or testing. While receiving treatment, patients are seen weekly either in the oncology ward at

PMH or the private hospital where radiation is delivered. Once treatment is completed, they return to the MDT clinic for follow-up appointments to evaluate treatment response, manage side effects and determine the need for further treatment.

The effectiveness of the MDT clinic in preventing loss-to-follow-up has been enhanced by the addition of Out Patient (OP) Care®, a mobile application used to track patient records and send text message reminders to patients about their follow-up appointments. The application has also improved clinic flow. Prior to the implementation of this application, patients carried physical copies of their records, and misplacement of these records would make it difficult for providers to make informed treatment decisions, which could result in either over-treatment or inadequate therapy. The application functions both as a portable electronic medical record (EMR) and as a patient-tracking tool, allowing for appointment scheduling. Smartphones purchased specifically for this purpose are supplied to staff to use the application during clinic hours. When patients first present to the MDT clinic, they are enrolled in the application with their consent. Identifying information, including name, date of birth, national identification number, picture and mobile number are input, along with clinical information, including cancer diagnosis, stage, treatment plan or previously completed treatment, HIV status, and previous and future appointment dates. Any important documents, including visit notes, pathology reports and imaging studies can be photographed and uploaded securely to the application. Follow-up appointments are scheduled in the application, and patients receive text message reminders about their appointments one week and two days prior. During subsequent appointments, the patient's existing profile can be updated with new records, allowing for continuity of care and better follow-up.

The MDT clinic has established a combination of close coordination between various expert providers and streamlined recordkeeping to greatly improve delivery of care to cervical cancer patients in Botswana. Given its success, this model can be scaled to improve cancer care in LMICs worldwide.

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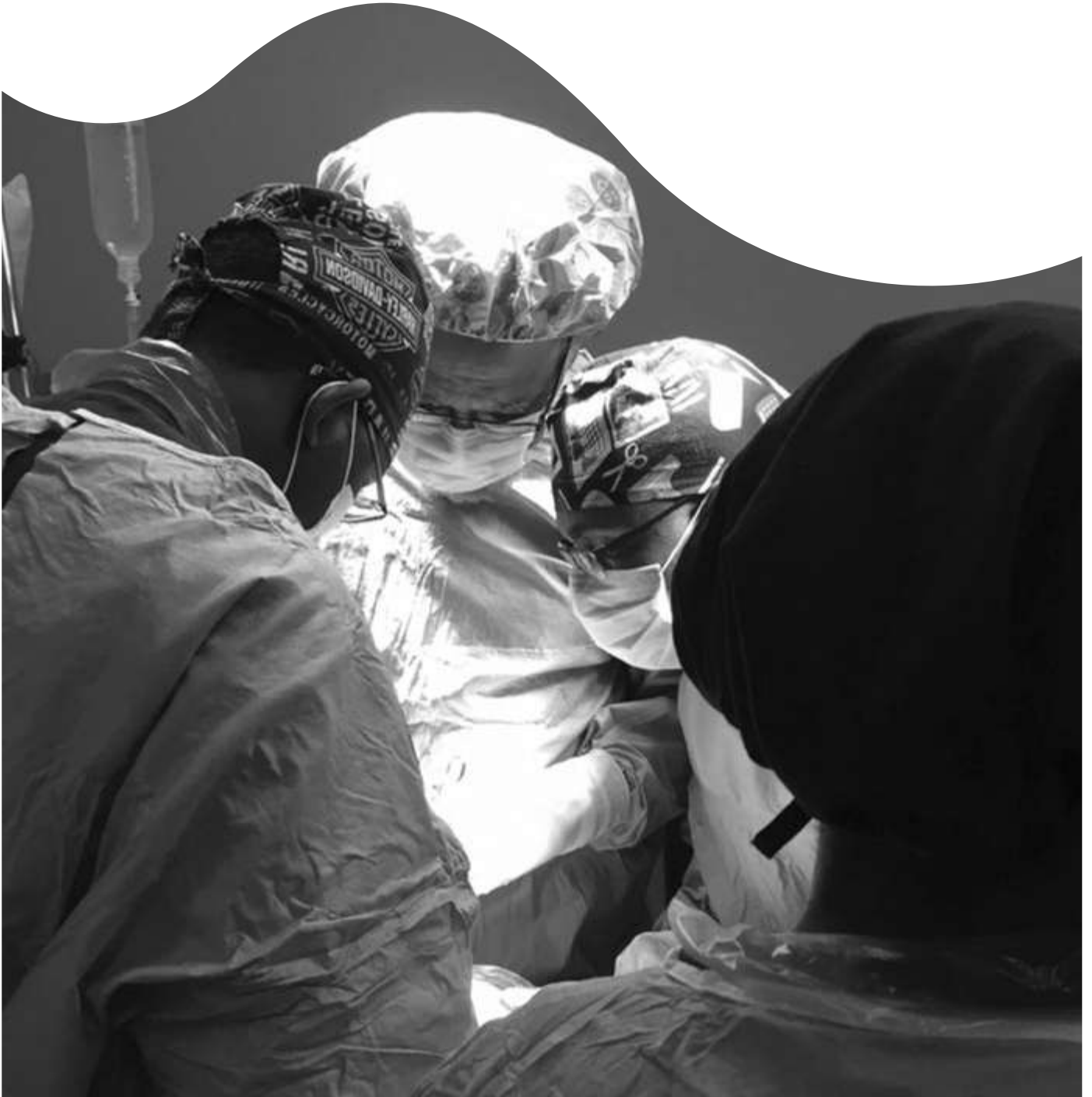


PHOTO: Friends of Africa, Inc

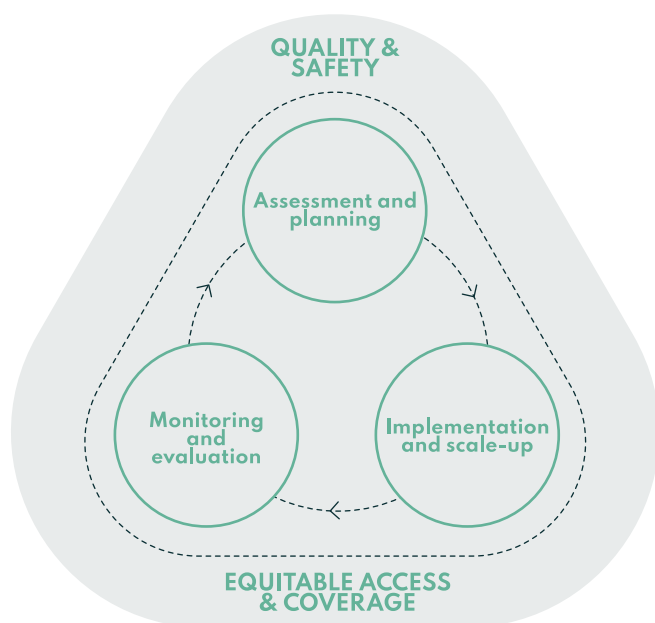
section

**effective
implementation
of quality
cervical cancer
management
services**

Effective implementation of a cancer management system is a cycle of: (i) assessment and planning; (ii) implementation and scale-up; and (iii) M&E (1). Concurrent with strengthening these components, it is critical to promote and ensure the overall quality of the system and to provide equitable access and coverage to all who need cervical cancer management (Figure 3.1).

FIGURE 3.1

Stages of implementation



SOURCE: Adapted from WHO 2020 (1).

3.1 ELEMENTS OF QUALITY CARE

To address the needs and to improve the health outcomes of women with cervical cancer, quality must be systematically and deliberately embedded in all services, ideally through the execution of a national policy and strategy of quality, and with the collaboration of all stakeholders (2). Otherwise, even when guided by a comprehensive cancer management plan and regardless of the type or scale of interventions provided, the organization and implementation of services cannot realize their potential health gains. This is a challenge for countries of all income levels.

While the specific quality interventions used to improve services are particular to each country's health system context, its stage of development of cervical cancer care, and the perspectives of its stakeholders, accepted definitions and principles may be applied. WHO and other leading global institutions have identified the key elements of health care quality as being effective, safe, people-centred, timely, equitable, integrated and efficient (Figure 3.2). To guide implementation of quality these elements can be defined as follows (3,4):

- > **Effective:** providing evidence-based health care services to those who need them.
- > **Safe:** avoiding harm to people for whom the care is intended.
- > **People-centred:** providing care that responds to individual preferences, needs and values.
- > **Timely:** reducing waiting times and sometimes harmful delays for both those who receive them and those who give care.
- > **Equitable:** providing care that does not vary in quality on account of age, sex, gender, race, ethnicity, geographical location, religion, socioeconomic status, linguistic or political affiliation.

- > Integrated: providing care that is coordinated across levels and providers and makes available the full range of health services throughout the life-course.
- > Efficient: maximizing the benefit of available resources and avoiding waste.

The complexity of the cancer care system and the costs of quality interventions, from developing consensus guidelines (Section 3.3.1) to ensuring competence in cancer

workforce (Section 3.3.2) to establishing a surveillance and information system (Section 3.3.5), make quality implementation especially difficult. National governments must decide on what areas to prioritize given the constraints of the resources available to them and and in consideration of the particular challenges in achieving any of the elements of quality defined above. One conceptual framework that guides prioritization puts patients at the highest level, followed by patient-

FIGURE 3.2

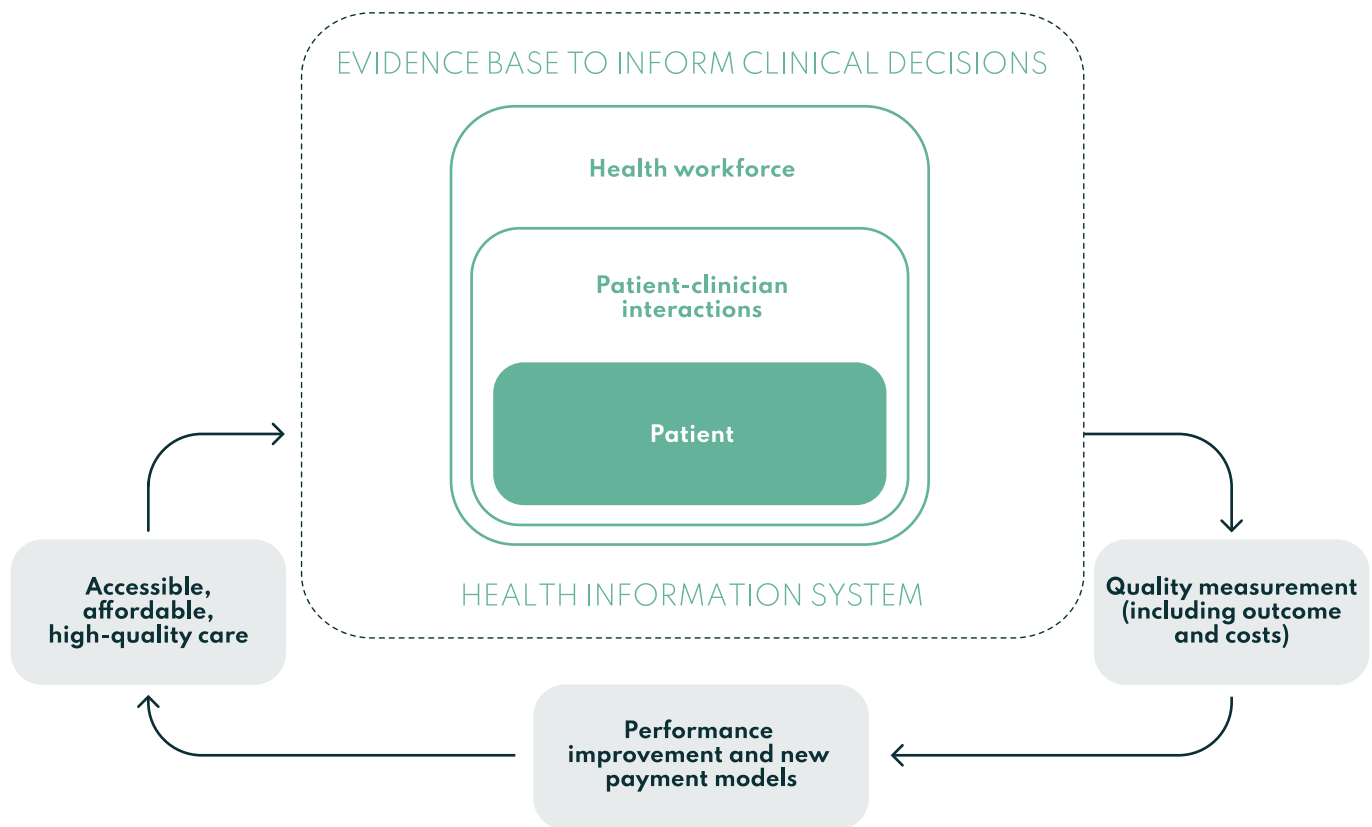
Elements of health care quality



SOURCE: Adapted from WHO/OECD/World Bank 2018 (2).

FIGURE 3.3

Conceptual framework of a high quality, interconnected cancer care delivery system



SOURCE: Adapted from Institute of Medicine 2013 (5).

clinician interactions, and then other key components of quality cancer care (Figure 3.3). Cyclical processes of quality measurement, performance improvement and expanded access and affordability feed back into these components in the rectangle to make necessary adjustments to quality interventions.

The use of structural (e.g. facilities, human and physical resources), process (e.g. management interventions) and outcome (e.g. survival) indicators is a concrete approach to measuring and assessing progress against established standards of high-quality treatment and for creating a system of continuous improvement. However, given the global concern for high-quality cancer care, the development of indicators has proliferated and their validation, and adaptation if necessary, requires considerable effort. For countries implementing a quality strategy, WHO suggests criteria for assessing indicators (3).

3.2 ASSESSMENT AND PLANNING

3.2.1 STRENGTHENING GOVERNANCE FOR CERVICAL CANCER CONTROL

Cancer care governance is the coordination by a body or bodies of authority of the collective activities of cancer care system actors, including government (all levels), policy-makers, health care providers, professional organizations, nongovernmental organizations and private companies involved in the supply of medicines and medical devices.

Governance at the most basic level is centred in a well-formulated national cancer control plan (NCCP). Planning and prioritization of cervical cancer management interventions follow principles outlined in Chapter 6 of the WHO *Report on cancer: setting priorities, investing wisely and providing care for all*, and should ensure that the three C's of national cervical cancer policies extend to cancer management services (1):

- > comprehensiveness: critical components of cancer care along the care continuum included;
- > consistency: evidence-based policies aligned with global norms and standards; and
- > coherency: links to other national or regional health-related plans or strategies.

Recent analysis of data from the WHO NCD cancer capacity survey has demonstrated that more than 60% of low-income countries are offering cervical cancer screening without having access to treatment of invasive cancer, and more than 75% without access to palliative care (6). This contradicts the WHO comprehensive approach to cervical cancer control, when proper treatment of detected invasive cancers and the compassionate measures to deal with pain and suffering of cancer patients are not met (7).

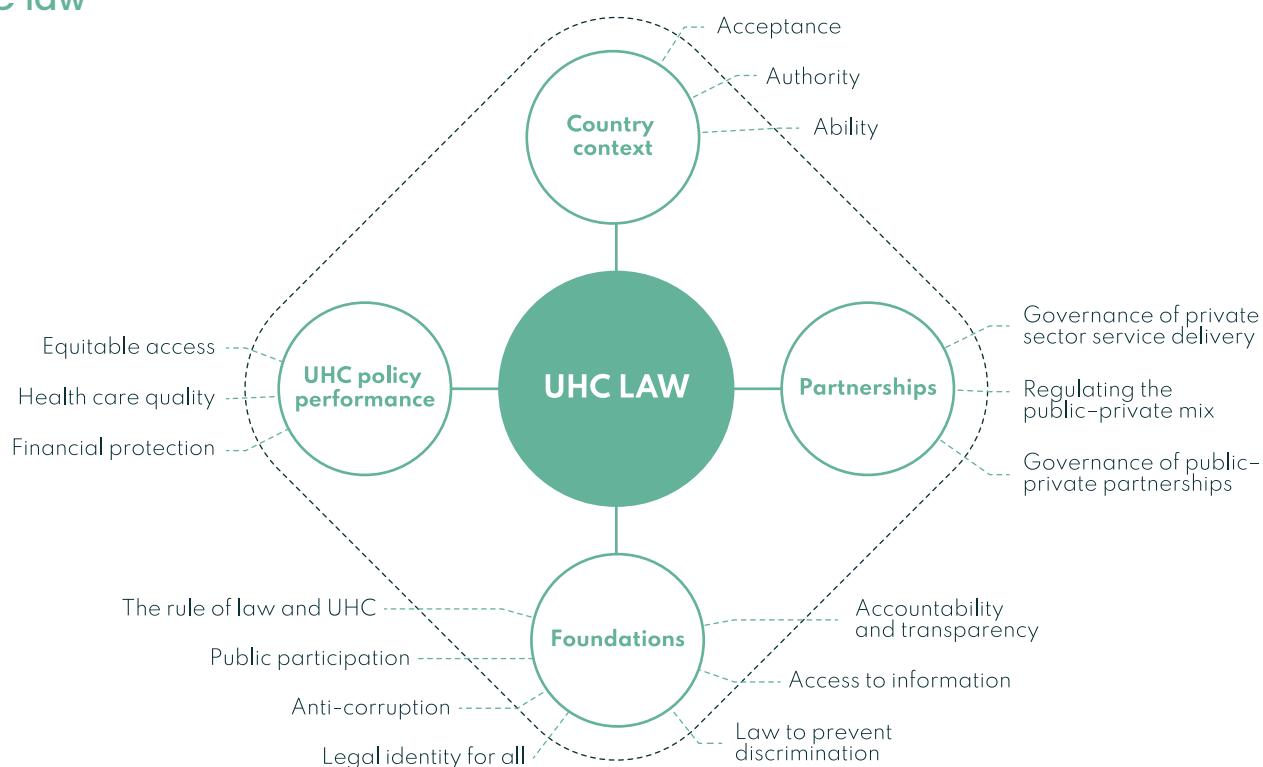
Governance structures and processes should thus be explicitly included in any NCCP to maximize benefits for patients and the cancer care system. Strong governance can promote effective, sustainable, high-quality care in line with evidence-based cervical cancer management and UHC. Conversely, weak governance can lead to unimproved cancer outcomes and unmitigated inequality of care. Also importantly, the considerable

economic returns, in terms of both productivity and broader social benefits, of cervical cancer investment cannot be attained because resources are wasted and expenditures have no impact.

Cancer care governance is strongest when operationalized with statutory, legal or regulatory force. For example, UHC Law, as defined by WHO, provides a potential institutional framework for cervical cancer diagnosis, treatment, palliative care and supportive care that also accommodates the principles of UHC: identify priority interventions, and achieve broad coverage while ensuring quality and financial protection (Figure 3.4) (8).

While models of governance need to be highly context specific, guiding principles include transparency, consistency, coherence, stability, participation, accountability, integrity and capacity (1,9,10). These principles guide the formation of institutional structures, the coverage of treatment interventions, the lines of responsibility and accountability, and the processes in providing cancer care, including those ensuring quality and safety.

FIGURE 3.4
UHC law



SOURCE: Adapted from WHO 2019 (8).

In the introduction or scaling-up of cervical cancer control, particular attention must be paid to the integration with and linkages to relevant existing programmes in women's health, such as reproductive health or gynaecological/obstetric services, so that resources and efforts can be leveraged and not duplicated. This requires governance structures to have meaningful representation from these services and a common understanding of the established principles. For instance, a governing board for cervical cancer should have a representative from HIV programmes and from WLHIV to ensure that standards guiding respective referral pathways for management are coherent and that any stigma-reducing measures (such as privacy legislation) are upheld.

However, strengthening governance is a costly investment and it is challenging to implement well, especially when coordinated across multiple ministries, donors and nongovernmental organizations. Too onerous a process, for example, can compromise effectiveness and the flexibility to make changes (10). While the specific mechanisms that lead to improved health outcomes in LMICs are still being studied (11), WHO does provide technical assistance to countries to strengthen health system governance within the framework of achieving the SDGs, and ultimately UHC (12). Furthermore, there is yet little evidence to form cancer system-specific guidance; however, some governance principles have received recent focus. For example, a study of accountability measures found that cancer care leaders considered financial incentives, regulations, information, professionalism and stewardship to be key elements (13).

3.2.2 SITUATION ANALYSIS

To address needs and improve cervical cancer management, countries first need to have an accurate understanding of the current health system capacity as well as existing delays and barriers in access to cervical cancer management services. As overall health care systems from one country differ significantly from another, a local assessment is paramount. At a minimum, these include (14):

- > demographics and epidemiology of cervical cancer
- > governance structure, policies and plans

- > service availability and utilization
- > availability of trained health workforce
- > availability of essential medicines and medical devices
- > financing and budget
- > existing health information system.

WHO provides a sample assessment tool to conduct a rapid health system review, or situation analysis, for cervical cancer control (14). Results from the situation analysis can then assist with the development of realistic and clear action plans across the WHO health system building blocks (i.e. governance, service delivery, health workforce, access to medicines and medical devices, financing, and health information systems) according to the national context.

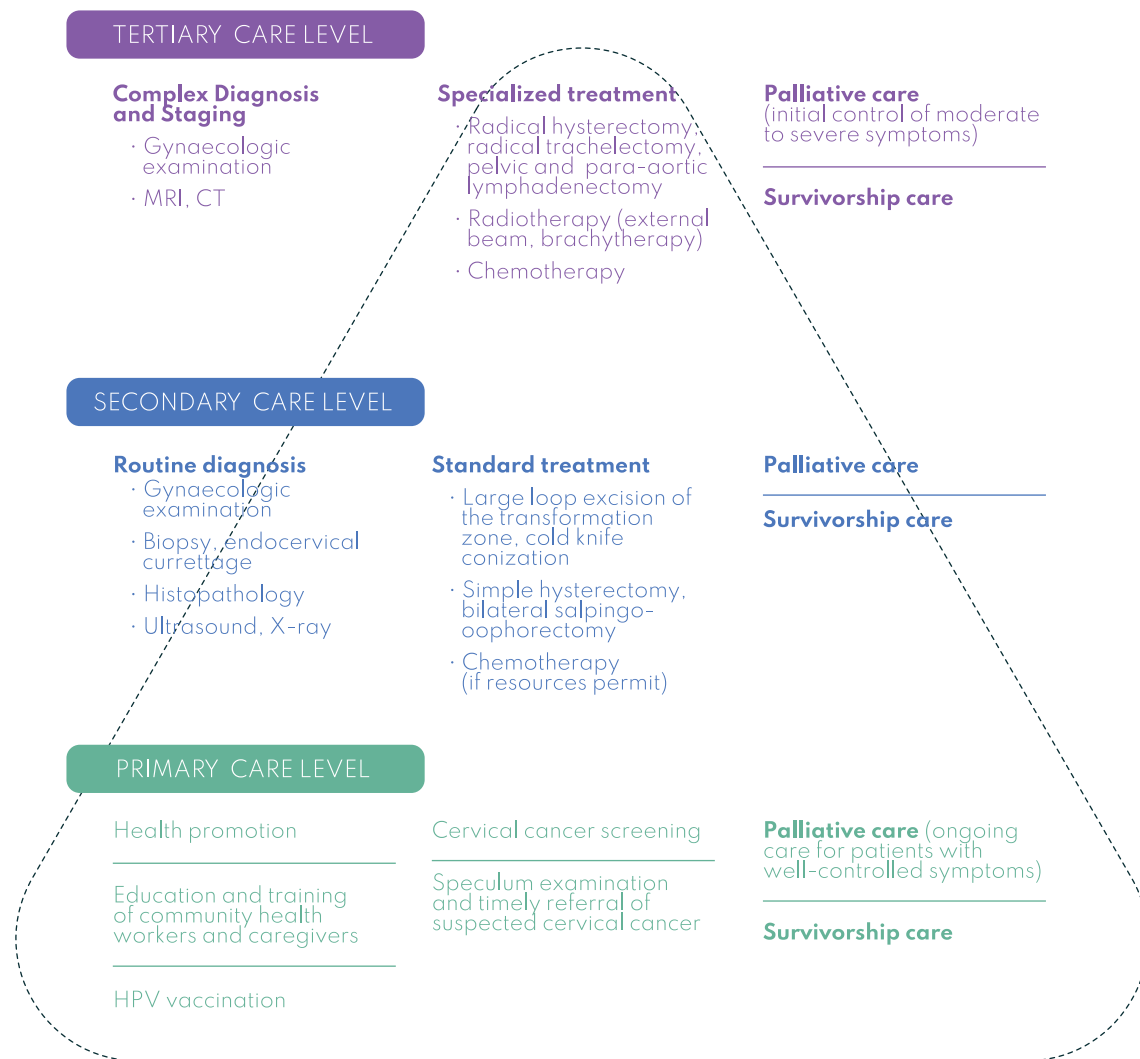
3.2.3 OPTIMIZING SERVICE DELIVERY MODEL

An effective health care system ensures a close relationship between all levels of care and helps to ensure people receive the best possible care closest to home (15). Services and referral systems can be established in different ways and there is no single best approach for all settings. However, in general, WHO recommends that less-complex services be located in communities that are most easily accessible to the target groups (16). More complex and specialized services should be centralized at the secondary and tertiary care levels, where expertise and more sophisticated technologies are concentrated and can be provided in a sustainable manner. This assists in making cost-effective use of facilities across various levels of care.

Figure 3.5 shows an example of how cervical cancer management services can be distributed across different levels of care. The most important point is to have a defined referral mechanism in place to ensure seamless transition between different levels of care. Assignment of responsibilities should be agreed upon, communicated and coordinated between providers and facilities at various levels. A sample referral form for referrals that are made from and into a facility is provided in Annex 5 (15).

FIGURE 3.5

Sample distribution of cervical cancer management services by hospital capacity



SOURCES: Adapted from WHO 2008 (15) and Parham 2015 (17).

3.2.3.1 IMPORTANCE OF PHC

As with any disease, the response to cervical cancer burden must be based on strong PHC to ensure that the disease is diagnosed early, and women are referred to treatment without delay. Indeed, in line with the 2018 Astana Declaration (18), PHC is at the centre of comprehensive cervical cancer control. The important role of PHC providers in management of invasive cervical cancer include:

- recognize symptoms associated with cervical cancer (see Section 2.1) and evaluate for probable cervical cancer;
- understand implications of delays (see Section 2.2) and make further decisions, including referral;

- understand adverse events associated with cancer treatment and evaluate patients presenting for follow-up;
- recognize symptoms suspicious for recurrence of cervical cancer and refer patients in a timely fashion; and
- provide ongoing palliative care, including control of uncomplicated symptoms (e.g. pain, nausea) and emotional, social and spiritual support for patients and their families with cancer.

For efficient and effective provision of PHC, protocols or guidelines for early diagnosis should be available so that PHC providers can readily make appropriate decisions.

Annex 6 provides WHO guidance on the approach to assessment and referral of women with suspected cervical cancer at PHC (19). In some countries, cervical cancer screening protocols or guidelines may also need to be amended to delineate referral pathways for suspected cervical cancer.

3.2.3.2 MDT-BASED CANCER CARE

Particularly at the tertiary-care level, a multidisciplinary approach to cancer care is pivotal for providing quality cancer management services and improving patient outcomes (20). It relies on joint decision-making by health care providers specialized in different areas of cancer care to determine the optimal treatment and care plan for individual patients. It has also been shown to minimize delays in diagnosis and treatment, reduce duplication of tests, and improve accuracy of diagnosis (21). Refer to the case study in Section 2.2 for an example of the MDT model in reducing common barriers of treatment delays and loss-to-follow-up.

The composition and structure of the MDT can vary. However, for gynaecologic oncology, including cervical cancer, it is usually composed of gynaecologic oncologists (or other cancer surgeons), pathologists, radiologists, radiation oncologists, medical oncologists, specialist nurses (gynaecological oncology nurses or oncology nurses) and palliative care specialists. If available, pharmacists, social workers and psychologists should also participate and address issues such as social support, transportation difficulties and financial constraints. The team can meet one-two hours weekly or bi-weekly on a fixed schedule to review patient cases together and plan their treatment based on stage of disease, overall state of health, available resources and best evidence.

A sample flow of an MDT meeting can be as follows:

- > Patient's history, physical and gynaecologic examination findings, laboratory findings, co-morbidities and general health status are presented by the physician in charge of the patient (e.g. gynaecologic oncologist).
- > Pathology slides are reviewed by the pathologist and imaging results by the radiologist for the patient under discussion.
- > Further diagnostic, treatment and care options and decisions are discussed among the MDT.
- > Discussion and consensus reached by the MDT are documented in the patient record using a standardized reporting method, so that they can be easily tracked. If no consensus is reached, then this situation should also be documented along with the different treatment options presented. This should be based on local clinical practice guidelines.

Very often, concerns are raised about the benefits of MDT in LMICs, particularly in settings with high patient loads and severe shortages of workforce. Nevertheless, the MDT model of care has been demonstrated to be feasible and effective in LMICs (22). It may even be of more value in a setting of low resources, where there is limited expertise available in individual hospitals and decisions are primarily made by physicians working in relative isolation. A variety of platforms are now widely available to improve communication and interaction between health care providers. For example, remote conferencing systems allow for real-time discussion of diagnostic findings and images (23). They require varying infrastructures, but these systems may help overcome regional limitations and provide a bridge for further coordination of services.



CASE STUDY: PROJECT ECHO® VIRTUAL TUMOUR BOARDS

Virtual tumour boards using the Project ECHO (Extension for Community Healthcare Outcomes) model provide a potential solution for closing disparities in oncology specialists between low-resource and high-resource settings in the United States and globally. Project ECHO was developed in 2003 at the University of New Mexico (UNM), to improve both provider capacity and access to specialty care for medically underserved populations. Project ECHO links multidisciplinary specialist teams with local clinicians through regularly scheduled telementoring sessions, in which the participants use videoconferencing via the Zoom platform to co-manage patient cases. Specialists share their expertise via mentoring, guidance, feedback and didactic education. This approach has helped to support clinicians in LMICs to develop the skills, confidence and knowledge to treat women with cervical dysplasia and cancer in their own communities. Project ECHO is different from “telemedicine”, where the specialist assumes the care of the patient, but instead involves “telementoring”, where the LMIC clinician retains responsibility for managing the patient, operating with increasing independence as their skills and self-efficacy grow.

APPLICATION IN THE INTERNATIONAL GYNAECOLOGIC ONCOLOGY SOCIETY (IGCS) PROGRAM

To address the lack of specialists providing cervical cancer prevention and treatment in LMICs, the IGCS developed a Global Gynaecologic Oncology Fellowship Program. This comprehensive programme provides structured support and training in gynaecologic oncology to physicians in countries in which no formal training programme exists by pairing them with gynaecologic oncology mentors from high-income settings. The programme includes a structured web-based curriculum, self-study, regular assessments, hands-on surgical training, regular visits by the international mentors to the training site, and a 3–6-month visit by the trainee to the international mentor’s home institution. Project ECHO tumour boards

are an important component of the programme and allow for a virtual connection to complement in-person visits. The videoconferences occur monthly via Zoom for one hour. The first 45 minutes involve case presentations (without patient identifying information) by the LMIC providers and the specialists provide feedback. This is followed by a 15-minute didactic presentation from a participating faculty member or guest lecturer. The IGCS fellows are responsible for case presentations. The local mentors, international mentors and other specialists (radiation oncology, pathology, radiology, medical oncology) join remotely from multiple countries for a multidisciplinary discussion. There are currently 12 IGCS fellowship training sites around the globe (Bahamas, Ethiopia, Fiji, Guatemala, Jamaica, Kenya, Mozambique, Nepal, Qatar, Uganda, Viet Nam, Zambia) with 30 fellows and 26 international and local mentors. As of December 2019, the programme had held 136 Project ECHO sessions with more than 300 providers participating.

CHALLENGES

International and local participants of Project ECHO must consider local LMIC context and resources in care delivery. The standard of care in the United States and other high-resource settings is not feasible in many regions, and creative solutions for providing basic services, given limited resources, provide a basis for many Project ECHO discussions. In addition, cultural differences and difficulty initiating change can create challenges and often require unique, region-specific strategies for care delivery. Regular videoconferences help to build trust and encourage development of partnerships by exchanging information and knowledge. Project ECHO videoconferences require internet connections, and in some regions, this is a major challenge. Some alternative strategies have been developed, including additional phone connections if the internet connection is unstable.

3.3 IMPLEMENTATION AND SCALE-UP

3.3.1 DEVELOPING GUIDELINES FOR CERVICAL CANCER MANAGEMENT

Development of evidence-based clinical practice guidelines or protocols contribute to reducing variations in cancer care delivery, improve quality of care and increase patient safety. Guidelines can be seen as a solution to the enormous volume of scientific information that challenges individual physicians to keep up with medical advances and to make unbiased judgements of evidence.

National guidelines/protocols should consider the health system context, including the availability of trained health care professionals, medicines and medical devices. They can be developed by (24,25):

- > preparation of new guidelines through rigorous systematic review to answer clinical questions;
- > adaptation of existing high-quality guidelines; or
- > adoption of a specific guideline with no change if adherence to them is feasible in national context.

Developing new guidelines requires significant time and cost and so may be unrealistic in resource-limited settings. Likewise, adopting guidelines may yield limited relevance. Adaptation may thus be the most pragmatic and appropriate approach for LMICs (25). Adaptation of existing quality guidelines can be done by following the steps shown in Figure 3.6 (26).

STEP 1. AGREEMENT AND APPOINTMENTS

The process starts with the Ministry of Health issuing an agreement to develop guidelines and appointing a technical working group. The group should be multidisciplinary and include experts in clinical management of cervical cancer, PHC delivery, programme management as well as health information systems. Patient representatives should also be involved as much as possible.

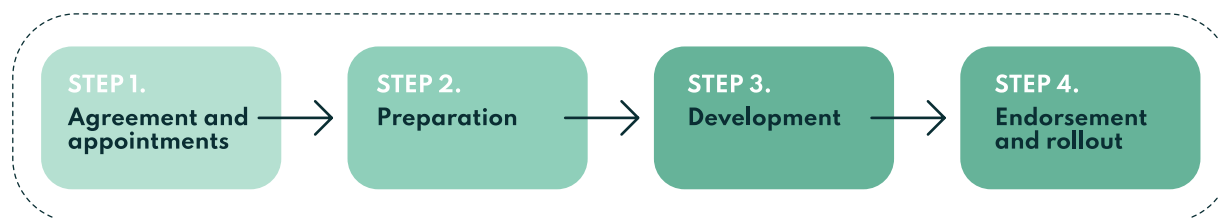
STEP 2. PREPARATION

The technical working group will then perform a desktop review of international guidelines that could be used for adaptation. It must be noted that guidelines in the same area of practice are not always consistent and there are many factors that can influence guideline conclusions. The most common factors include the composition of guideline panellists, the methodology of evidence review and interpretation, and the procedures to reach agreement on recommendations.

The quality of the chosen guidelines should also be assessed to ensure that they are credible, developed using high-quality methods and recent enough to reflect the current knowledge base. Various tools exist to assess the trustworthiness, transparency and quality of guidelines, for example, the Appraisal of Guidelines for Research and Evaluation (AGREE-II) Instrument (27). AGREE-II allows assessment of the quality of practice guidelines in six domains: (i) scope and purpose, (ii) stakeholder involvement; (iii) rigour of development; (iv) clarity and presentation; (v) applicability; and (vi) editorial independence. Training on the use of the AGREE-II Instrument is required before starting guidelines appraisal. Free resources exist for maintained databases of guidelines reviewed by experienced guideline appraisers (28). When using these resources, attention must be paid to the cut-off criteria for defining quality guidelines.

FIGURE 3.6

Steps for adapting guidelines



SOURCE: WHO 2018 (26).

Table 3.1 provides an overview of major regional cervical cancer management guidelines developed by international professional organizations. As of September 2020, there is one guideline that uses the new FIGO 2018 staging system; others use the FIGO 2009 staging system and updates are under way.

It is also advisable to compile and examine all national and local documents related to cervical cancer (e.g. cervical cancer screening guidelines) to ensure harmonization and to avoid conflicting recommendations.

TABLE 3.1

Available international guidelines for cervical cancer management

	NCCN Guidelines Cervical Cancer	ESGO-ESTRO-ESP Guidelines for Management of Patients with Cervical Cancer	ESMO Cervical Cancer: Clinical Practice Guidelines for diagnosis, treatment and follow-up	ASCO Management and Care of Women with Invasive Cervical Cancer
Year updated as of September 2020	2020	2018	2017, partially updated in 2020 in regard to radical hysterectomy performed by laparoscopy or robot-assisted surgery	2016
Staging system used	FIGO 2018	FIGO 2009	FIGO 2009	FIGO 2009
Resource stratification	✓ Has a separate NCCN Framework Cervical Cancer (Basic, Core, Enhanced)	—	—	✓ Basic, Limited, Enhanced, Maximal
Diagnostic and staging workup	✓	✓	✓	✓
Treatment by stage	✓	✓	✓	✓
Fertility sparing treatment	✓	✓	✓	✓
Treatment during pregnancy	✓	✓	—	—
Palliative care	✓ Has a separate NCCN guideline for palliative care	✓	✓ Has a separate ESMO guideline for palliative care	✓ Has a separate ASCO resource-stratified guideline for palliative care
Survivorship care	✓ Has a separate NCCN guideline for survivorship	✓	✓	✓
Treatment for relapse	✓	✓	✓	✓

Languages	English	Arabic, English, Greek, Italian, Portuguese, Russian, Spanish, Turkish	English	English
Website	https://www.nccn.org/professionals/physician_gls/default.aspx	https://guidelines.esgo.org/cervical-cancer/guidelines/recommendations/	https://www.esmo.org/guidelines/gynaecological-cancers	https://www.asco.org/research-guidelines/quality-guidelines/guidelines/gynecologic-cancer

ASCO: American Society for Clinical Oncology; ESGO: European Society of Gynaecological Oncology; ESMO: European Society for Medical Oncology; ESP: European Society of Pathology; ESTRO: European Society for Radiotherapy and Oncology; FIGO: International Federation of Gynaecology and Obstetrics; NCCN: National Comprehensive Cancer Network (USA)

STEP 3. DEVELOPMENT

Through meetings of the technical working group, consensus guidelines are designed and developed. It is crucial to identify potential challenges for implementation and make necessary contextualized changes. Once guidelines are developed, they should go through a rigorous review by an expanded group of experts and be revised in response to the reviewers' comments.

STEP 4. ENDORSEMENT AND ROLLOUT

The final step is the endorsement by the appropriate authorities and the rollout of the consensus guidelines in phases (by region or over time) or at a pan-national-level. Rollout includes capacity-building workshops, onsite trainings and development of derivative documents to encourage the successful implementation of the guideline. Implementation should be closely monitored so that periodic timely updates can be introduced.



PHOTO: Shyam Shrivastava



CASE STUDY: INDIA

ENSURING QUALITY CARE THROUGH CONSENSUS GUIDELINES AND INSTITUTIONAL REVIEW

The National Cancer Grid (NCG) of India is an initiative of the government through the Department of Atomic Energy, created in 2012. The NCG is a large network of cancer centres, research institutes, patient groups, professional societies and nongovernmental organizations across the country. It has a mandate to establish uniform standards of patient care for prevention, diagnosis and treatment of cancer; provide specialized training and education in oncology; and facilitate collaborative basic, translational and clinical research in cancer. Between the member centres, approximately 700 000 new patients with cancer are treated annually, which is about 60% of all of India's cancer burden. To ensure standardized service delivery and quality assurance, the NCG has not only developed Consensus Guidelines, but also a mechanism of adherence through institutional peer review.

UNIFORM STANDARDS OF CARE

The NCG evidence-based guidelines on management of common cancers have been endorsed by all participating centres and are periodically modified; as new evidence is generated, NCG guidelines continue to address the challenges of delivering standardized care in the context of India's highly diverse health care system. The second edition of the NCG guidelines considers available resources, dividing guidelines into "optional" (which reflect the state of the art, without cost considerations) and "optimal" (which take value into account while making treatment recommendations) (28). The resource-stratified guidelines for cancer management were jointly developed by experts from all regions of India through a consensus process between June 2019 and October 2020 and incorporated into the revised edition. The optimal guidelines are being adopted by the Pradhan Mantri Jan Arogya Yojana (PMJAY), which is the largest government-funded health care insurance scheme, covering 500 million of India's population.

The linking of pre-authorizations for care to evidence-based guidelines ensures that quality care is provided to the vast majority of patients with cancer in the country.

INSTITUTIONAL PEER REVIEW

Institutional peer review has been proven to have improved outcomes in patient care and costs of treatment. Sustained improvement in infrastructure, systems and processes of patient care is viable by a continuous cycle of peer review, identification of gaps, remedial measures (short-, medium- and long-term) and completion of the review cycle by re-evaluation by a follow-up peer review. The NCG offers institutional peer review to all members on a voluntary basis. The purpose is to identify strengths, gaps, and opportunities for improvement that are then shared with centres as a peer review report. One of the key elements on which institutions are assessed is level of adherence to the NCG guidelines. Several institutions have been peer reviewed by a diverse external group of experts drawn from NCG centres. The review starts with a 6-month period of electronic communication between the expert group and the centre where various volume, process and quality metrics are shared. Then, the expert group has a 2–3-day site visit of the centre with in-depth interviews and inspection of the facilities. The review culminates in a final day debriefing to the leadership of the centre and a detailed report submitted to them. Further follow-up to evaluate the implementation of the peer review suggestions and recommendations are carried out later. While a formal objective evaluation of the outcomes of the peer review reports has not been done yet, most centres have reported considerable improvement in functioning based on changes effected by peer review.

3.3.2 ENSURING COMPETENCE IN CANCER WORKFORCE

Cancer patient management is specialized health care and involves complex diagnostic, staging and treatment procedures, all requiring sophisticated decision-making and highly technical skills. The principle of multidisciplinary underpins cancer care and it has been proven to increase quality through enhanced patient assessment and management practices (20).

Most often, cancer management is provided by professionals who have completed postgraduate specialist training. Additionally, in many clinical environments, the operation, quality control, calibration and management of medical devices are devolved by the clinician to highly

trained health associate professionals: technical, scientific and biomedical engineering staff. These staff require relevant education and training in both academic and clinical settings. A good example of multidisciplinary is in radiology where medical imaging technicians operate imaging equipment under the direction of radiologists, medical physicists determine the radiation dose to the patient from the imaging procedure and biomedical engineers manage the relevant inventory of medical equipment and medical devices (see Section 2.1.2.2).

Titles of professionals and definitions of the role of clinical, technical, scientific and biomedical engineering

staff may vary from country to country. A detailed list of occupations and their respective roles in cancer management is described elsewhere (30). Tables 3.2

and 3.3 summarize some common core health work-force groups in management of cervical cancer.

TABLE 3.2

Core clinical professionals in the management of cervical cancer

ISCO-8 group and code	Specialty	Selected key functions
Specialist medical practitioner (2212)	Gynaecologic oncologist	Counsels, performs surgical procedures, including complex pelvic surgery for gynaecological cancers, including cervical cancer. Integrates palliative care with cancer treatment.
	Anaesthesiologist	Counsels, provides anaesthesia and post-operative pain management.
	Radiologist	Interprets medical imaging studies (e.g. conventional radiology, CT, MRI, ultrasound). Responsible for the medical aspects of medical imaging procedures and installations, including justification and optimization of studies.
	Anatomic pathologist/cytopathologist	Performs gross and microscopic analysis of tissue and cytology specimens with diagnosis.
	Radiation oncologist	Counsels, establishes curative or palliative treatment plan, including dose prescription, delineation of target volumes and organs at risk, plan evaluation and selection, monitors and manages toxicity; responsible for clinical quality assurance. In some countries radiotherapy and systematic treatment are provided by clinical oncologists.
	Medical oncologist	Counsels, prescribes curative or palliative chemotherapy, ensures safe administration and manages toxicity. In some countries, radiotherapy and systematic treatment are provided by clinical oncologists.
	Specialist palliative care physician	Counsels, provides relief from pain and other distressing physical and psychological symptoms, establishes symptom management plan prior to hospital discharge.
Nursing professional (2221)	Surgical nurse	Directly participates in the surgical field, handling sterile instruments or equipment. Works hand-in-hand with anaesthetist and surgeon to provide perioperative patient care.
	Oncology nurse	Counsels, ensures safe administration of chemotherapy and early detection of toxicity, manages simple toxicity, assesses patient response to treatment and manages vascular access devices.
	Specialist palliative care nurse	Nursing care for specific purposes of palliative care.
Other health professional (2262)	Oncology pharmacist	Ensures safety in compounding, preparing and dispensing of chemotherapy medicines.

SOURCE: Adapted from WHO 2017 (30).

TABLE 3.3

Technical, scientific and engineering professionals in the management of cervical cancer

Group	Specialty	Description
Technical	Biomedical laboratory scientist (pathology laboratory technician)	A technologist with direct responsibility for tissue assessment, processing, sectioning and staining, as well as for quality control procedures.
	Radiographer	A technologist with direct responsibility for the administration and quality control of imaging procedures in radiology.
	Nuclear medicine technologist	A technologist with direct responsibility for the administration and quality control of imaging procedures in nuclear medicine.
	Radiation therapist	A technologist with direct responsibility for the daily administration and quality control of radiotherapy procedures to cancer patients.
	Pharmaceutical technician	A technician with direct responsibility for reconstitution of chemotherapy medicines for administration under supervision of a pharmacist.
Scientific	Medical physicist	A health professional with specialist education and training in the concepts and techniques of applying physics in medicine and competent to practise independently in radiology, nuclear medicine or radiotherapy medical physics. Responsibilities in equipment commissioning, radiation safety and protection, radiation dosimetry, dose optimization and quality management.
Engineering	Biomedical engineer	Biomedical engineering is the profession responsible for innovation, research and development, design, selection, management and safe use of all types of medical devices, including single-use and reusable medical equipment, prosthetics, implantable devices and bionics, among others (31).
	Maintenance engineer	A technician or engineer with specialist training in the maintenance and repair of particular medical equipment.

SOURCE: Adapted from WHO 2017 (30).

Successful scaling-up of quality cancer management services largely depends on rapid expansion of a competent health workforce, equipped with an optimal skill mix (17). The specialized nature of cancer care aggravates challenges that are particular to LMICs, namely the shortage and uneven geographical distribution of the health workforce, the lack of supporting specialities (such as general surgeons and urologists), limited education and training capacity and inadequate knowledge transfer capacity (32). Relying only on traditional models of specialist training like those in high-income countries has limited applicability in LMICs, as such training is resource- and time-intensive. Therefore, countries develop strategies to bridge the existing gaps in training and address the inefficiency

of the existing cancer health workforce through innovative solutions for the near-term, while incrementally investing in local education and training for long-term sustainability (17,33).

Optimization of the existing workforce can also be achieved with the use of digital technologies for health, which employ routine and innovative forms of information and communications technology to address health system needs (34). Solutions such as telementoring, online platforms for clinical case discussions, e-Learning and virtual simulation may help to enhance efficiency and effectiveness of current providers (35–41).

Task-shifting is based on the principle that some medical procedures can be efficiently delivered by non-physician care providers, including mid-level health care workers. This has been effectively demonstrated, for example, in midwives successfully delivering screening and treatment of pre-invasive cervical cancer and in cancer nurses providing palliative care services (42,43). The reorganization of existing services can be facilitated by a responsible health administrator who adopts the model of supportive supervisor (44). The supervisor leads the organization of the health care services, focusing on improving performance and building relationships, and serves as a tutor, coach and mentor to support the workforce through regular follow-up. When planning for the expansion of cancer services, relevant health workforce needs should be accounted for and included in the NCCP (45). Identification of existing gaps can be done through workforce planning projections.

The WHO Global Strategy on Human Resources for Health: Workforce 2030 was developed in recognition of the central role of human resources in productive functioning of a health system (46). It provides a blueprint to address existing workforce challenges in four major domains: (i) education and training; (ii) inflow and outflow of the workforce; (iii) maldistribution/inefficiency of the existing workforce; and (iv) regulatory aspects. It also emphasizes the importance of strengthening data on human resources for health. The strategy outlines policy options that can be considered, taking into account the national context. Table 3.4 provides a summary of selected policy options, including for cervical cancer health workforce capacity-building.

TABLE 3.4

Summary of selected policy options for strengthening the health workforce

Strategic area of action	Select policy options
Optimize the existing workforce (performance, quality, impact)	<ul style="list-style-type: none"> ➤ Promote decent working conditions in all settings. ➤ Optimize health worker motivation, satisfaction, retention, equitable distribution and performance. ➤ Adopt transformative strategies in the scale-up of health worker education. ➤ Harness, where feasible and cost effective, information and communication technology (ICT) opportunities. ➤ Strengthen the capacity and quality of educational institutions and their faculty through accreditation of training schools and certification of diplomas awarded to health workers. ➤ Optimize health workforce performance through a fair and formalized employment package, within an enabling and gender-sensitive working environment. ➤ Governments to collaborate with professional councils and other regulatory authorities to adopt regulation.
Anticipate and align investment in future workforce requirements and plan the necessary changes	<ul style="list-style-type: none"> ➤ Invest in the education and training, recruitment, deployment and retention of health workers to meet national and subnational needs through domestically trained health workers. ➤ Consider opportunities to strengthen the skills and employment agenda within countries. ➤ Increase investments to boost market-based demand and supply of the health workforce and align them more closely with population health needs.
Strengthen individual and institutional capacity to manage human resources for health (HRH) policy, planning and implementation (e.g. migration and regulation)	<ul style="list-style-type: none"> ➤ Strengthen technical and management capacity in ministries of health and other relevant sectors and institutions to develop and implement effective HRH policies, norms and guidelines. ➤ Strengthen the institutional environment for health workforce education, deployment, retention and performance management. ➤ Align incentives for health workforce education and health care provision with public health goals and population needs.
Strengthen data, evidence and knowledge for cost-effective policy decisions	<ul style="list-style-type: none"> ➤ Invest in the analytical capacity of countries for HRH and health system data. ➤ Establish national health workforce registries of the competent and practising, rather than those that have simply completed a training programme. ➤ Exploit “leapfrogging” opportunities through the adoption of ICT solutions.

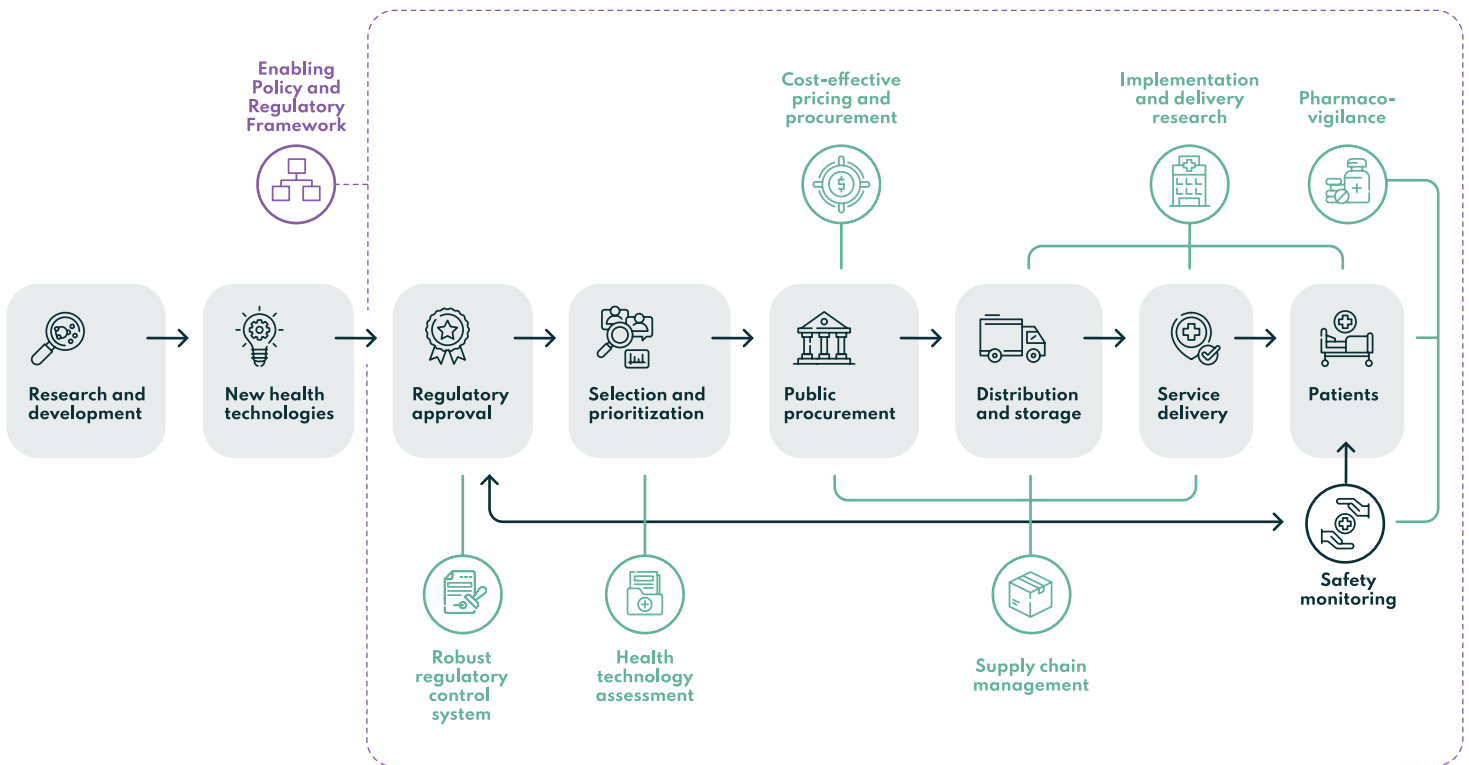
SOURCE: WHO 2016 (46).

3.3.3 IMPROVING ACCESS TO MEDICINES AND MEDICAL DEVICES

Effective cancer management requires access to essential medicines, diagnostics and medical devices.

Medicines and equipment lifecycle frameworks (or “value chains”) are useful tools to understand and address common barriers affecting access (Figure 3.7 and Figure 3.8). Given the rapidly evolving global markets in health care products, understanding these frameworks especially benefits essential functions such as public procurement within supply chain management.

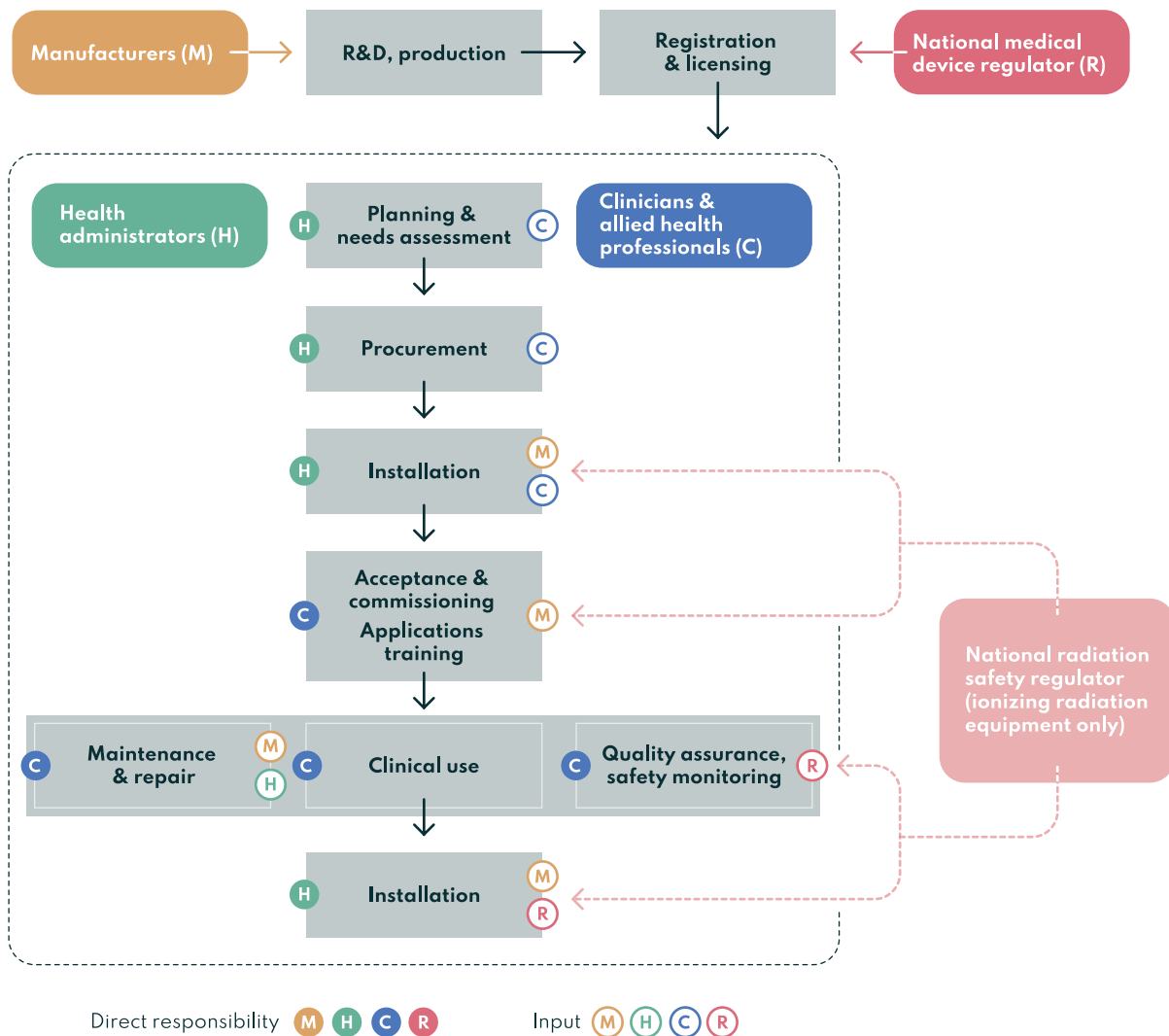
FIGURE 3.7
Lifecycle of a medicine



SOURCE: Adapted from the Access and Delivery Partnership (47).

FIGURE 3.8

Lifecycle of medical equipment



R&D: research and development

A country's national essential medicines list and essential devices list should be developed considering local context, including disease epidemiological data, cost-effectiveness and availability of resources (48). The WHO *Model lists of essential medicines, Model list of essential in vitro diagnostics, List of priority medical devices for cancer management*, and *Priority assistive products list* provide global guidance and can be consulted when developing adapted national lists (30,49–51). All lists should be periodically reviewed and updated if needed. It is also important to ensure alignment between national lists, national cancer control priorities as outlined in the NCCP, national cancer practice guidelines and benefit packages. National procurement practice should be in agreement with developed national guidance.

The prioritization and pricing of particular medicines and health technology within a cancer benefit package or cancer care system may be systematically evaluated through a formal health technology assessment (HTA) process, separately or together with a cost-effectiveness analysis. New cancer technologies (including both medicines and devices in the HTA framework) are of increasingly marked concern to public health systems due to their high cost and/or potential harms. HTA can provide a careful weighing of their introduction using explicit analytical methods with pre-specified criteria for adoption or recommendation of the technology. HTA may also be applied at different points of the lifecycle of the technology to assess its value, including for potential disinvestment. Anticipatory or early HTA for

novel medicines and technology might be performed to explore a break-even price or range of prices that is tolerated by government. It could help prepare countries in aligning budgets and in preliminary discussions with donors and manufacturers, such as in negotiating prices. The country context of clinical effectiveness, cost-effectiveness, health insurance (or reimbursement) structure, demand, and legal, ethical, social and patient concerns may all be considered in determining both intended and unintended consequences of using the technology. While HTA processes are well developed in a few upper-middle-income countries, they are still in a nascent stage in most LMICs (52). HTA is considered an important contributor to UHC, as recognized by WHA resolution 67.23, and LMICs may receive technical support and guidance from WHO and international HTA organizations in capacity strengthening and institutional development (53,54).

3.3.3.1 ACCESS TO MEDICINES

Maximizing access to medicines requires appropriate management to ensure that the correct medicines are selected, procured in the right quantities, distributed to facilities in a timely manner, and handled and stored safely and in a way that maintains their potency and reduces harm when disposal is necessary.

1. SELECTION AND PRICING

Affordability of medicines is an important factor in access to cancer treatment, and ensuring affordability will be crucial in accelerating cervical cancer elimination. Efficient selection and procurement directly affect the pricing of medicines and, therefore, contributes to their affordability. The selection of medicines must be based on clearly defined criteria that reflect a “best value for money” approach and consider clinical effectiveness, quality and price of medicines. WHO recently acknowledged ESMO-MCBS as a tool to aid the selection of cancer medicines for inclusion in the WHO *Model lists of essential medicines*. The scale not only recognizes the value of direct endpoints, such as overall survival, health-related quality of life and medicines safety profile, but also scores the endpoints according to their absolute and relative gains according to clinical indication (i.e. tumour site and treatment intent). Priority must be given to cancer medicines with high clinical benefit scores, whenever available. ESMO-MCBS high scores are scores A and B for curative intent and scores 4 and 5 for non-curative intent (55,56).

Apart from cancer medicines, access to other categories of medicines is pivotal for management of invasive cervical cancer. Table 3.5 lists examples of medicines that are included in the WHO *Model lists of essential medicines* (50). Individual countries may consider more expansive lists, resources permitting.

In many LMICs, medicine prices are often higher than international reference prices, and supply to the public sector can be lower than to the private sector (57). Although most current medicines (including cancer medicines used for cervical cancer treatment) are off-patent, and therefore available in many countries via multiple generic suppliers, LMICs disproportionately purchase more expensive branded generics rather than unbranded generics compared to high-income countries (58). Besides inefficient selection and procurement, excessive markups, taxes and duties, and weak or fragmented demand for the medicines also contribute to unaffordable prices. Thus health systems must strengthen their institutional capacities and leverage their negotiating power. This latter may involve engagement with or developing a regional pooled procurement initiative (59).

Finally, health systems must ensure that any favourable pricing achieved results in savings to the end user. Up to 90% of low-income populations purchase medicines through out-of-pocket payments, making medicines the largest household expenditure item after food (60). Consequently, it is essential that governments control markets and that generic medicines are promoted to improve affordability (59). Similarly, national health insurance can be designed to provide financial protection, for example, through assistance in paying or reimbursing of cancer drug costs (see Section 3.3.4).

2. PROCUREMENT AND SUPPLY MANAGEMENT

Efficient and effective procurement and supply management activities are fundamental for consistent and reliable access. This needs to be backed up by administrative and regulatory policies that enable procurement of sufficient quantities to reduce cost inefficiencies, ensure the reliability and security of the distribution system and encourage the appropriate use of these health products. When procuring centrally for distribution to health facilities, the following must be considered:

- > available financing
- > stock on hand at all levels of distribution system
- > consumption rate and orders expected for delivery
- > expected losses through expiration or damage
- > availability/appropriateness of donations
- > desired stock at the end of each planning period (safety and working stock at all levels).

With the proliferation of new and very costly cancer medicines, developing a national essential medicines list is increasingly important to guide procurement and stocking of the most required and best-value medicines. Once the package of health products has been selected, forecasting and supply planning are needed to determine the quantity required in the short-, medium- or long-term.

TABLE 3.5

Examples of medicines used in cervical cancer management

Categories	Examples
General anaesthetics and oxygen	isoflurane, nitrous oxide, oxygen, ketamine, propofol
Preoperative medication and sedation	atropine, midazolam, morphine
Anticoagulant	enoxaparin, heparin sodium
Cytotoxic medicines	cisplatin, carboplatin, paclitaxel, fluorouracil
Analgesic	ibuprofen, paracetamol, fentanyl, morphine
Antifibrinolytic	tranexamic acid
Antiemetic	dexamethasone, metoclopramide, ondansetron, haloperidol
Antidiarrhoeal	loperamide, glucose with sodium chloride
Anti-constipation	lactulose
Antidepressant	amitriptyline, fluoxetine
Anxiolytic	diazepam, amitriptyline, fluoxetine, haloperidol
Antiulcer	omeprazole, ranitidine
Antianaemia	packed red blood cells, ferrous salt
Diuretic	furosemide
Antibiotics	metronidazole, cefazolin, gentamicin, ampicillin, ciprofloxacin, amoxicillin + clavulanic acid, amikacin
Antifungal	fluconazole, nystatin

SOURCE: WHO 2019 (50).

Considerations also include expiration dates of currently available medicines, distribution time and funding. Stock-outs of cancer medicines must be avoided as they result in sub-optimal care and compromised treatment outcomes, with persisting stock-outs having a cascading disruptive impact on cycles of chemotherapy and related management (61). Stock-outs also adversely affect the budgeting and financing of cancer medicines.

Medicine procurement and supply chains exist in a complex international ecosystem, and inefficient chains are barriers to access and coverage, contributing to increased costs, lack of availability and increased opportunities for substandard and falsified medicines to leak into distribution systems. Distribution is the trans-

port of a medicine from the store to another destination (port, customs, warehouse, hospital, patient). Sometimes it represents the most challenging stage of the supply chain, since particular attention is needed to maintain all of the conditions specified on the medicine's label, such as temperature and dryness. Data standardization is a key element of a strong supply chain, necessary for monitoring and providing ongoing management in the detailed movement of health products.

3. STORAGE AND INVENTORY MANAGEMENT

Proper storage of a medicine is essential for its correct preservation and administration to patients and to prevent diversion of controlled medicines. Unless the medicine reaches the patient in good condition, waste and loss

occurs. Storage areas must be large enough to allow the orderly arrangement of medicines, and should be clean and dry, with a stable temperature. Adequate lighting for all operations must be provided, even when protecting medicines from direct sunlight. Some products, such as several controlled narcotics and psychotropic medicines, need a special access-controlled area, while flammable liquids require a location separate from the main store-room. To prevent fire damage, smoke detectors and a fire extinguisher need to be available in every storage area. Ideally, cytotoxic medicines storage areas should have negative air pressure in relation to surrounding areas. Spill kits must be readily available to ensure proper handling of accidental cytotoxic spills (62). Staff should be properly trained to perform spill clean-ups to ensure safety and minimize personnel exposure.

When it is not possible to have a dedicated room for storage, a cupboard or cabinet that can be controlled and secured should serve as “the store”. Essentially, there should be enough personnel who are well trained in good storage practice, regulations, procedures, safety and hygiene.

The goal of an inventory is to have an accurate record of all goods held at any given moment. Importantly every item must be numbered, to allow prompt identification. A good inventory becomes an indispensable tool of forecasting and budgeting, determining staffing, identifying needs, managing service contracts and developing replacement and disposal policies for items no longer needed.

4. PRESCRIBING, DISPENSING AND USE

Important steps in the value chain of medicines involves their appropriate prescribing, dispensing and use. Even if all of the steps in selection, procurement and supply management were performed effectively and efficiently, the lack of trained personnel and poor prescribing and dispensing practices will inhibit access of the right medicine at the right time to the right patient.

Physicians must be aware of cervical cancer medicines on the national essential medicines list and prescribe according to their availability and in accordance with national standards and guidelines. Only those certified to prescribe medicines should do so. Governments must ensure that prescribing follows national policy and is in accordance with regulatory controls. Pharmacists have an important role in confirming the appropriate use and dosing when dispensing prescriptions, and ensuring that patients take the medicines as indicated. Pharmacists also need to manage their inventory effectively, preventing stock-outs and ensuring security and safety of the medicines (63,64).

Chemotherapy medicines should only be prepared and administered by health care professionals who have been specially trained (62). Cytotoxic medicines require special safety considerations for handling and administration. Health care facilities need to comply with special requirements for heating, ventilation and air-conditioning systems to avoid accidental exposure risks. Mixing and preparation of cytotoxic medicines require a dedicated area (biologic safety cabinets) with laminated air flow and must be done in appropriate personal protective equipment (PPE). Once prepared, cytotoxic drugs should be transported to a patient with all precautions for preventing contamination in the event of breakage. A checklist for safe handling of hazardous drugs pre-, during and post-administration is available in Annex 7.

5. SAFE DISPOSAL

Expired medicines and wastes from use of medicines, especially cytotoxic medicines, are hazardous wastes; their safe disposal requires special handling and must be guaranteed. Any materials that come into contact with chemotherapy can also be considered hazardous waste. With proper procurement, there will be limited expiration and waste of the medicines themselves, although with weight-based dosing often there is some excess left in the vial.

Cytotoxic waste, which can contain substances with genotoxic properties, must be segregated from other waste in a secure location and collected in safe sealed plastics or leak-proof containers, properly labelled with the hazard symbol designating “cytotoxic waste” (62). Then, it can be chemically degraded or incinerated with safe air pollution control. As these methods may still be in development in low-resource settings, the waste can be safely packaged and returned to the original supplier or encapsulated as a last resort.

General pharmaceutical waste and sharps must also be segregated from other waste and must be correctly discarded according to local/national regulations. WHO has guidance for specific disposal methods for each type of waste (65,66).

TABLE 3.6

Examples of major medical devices for cervical cancer management

Services	Examples
Gynaecologic examination	speculum, colposcope, gynaecologic biopsy set
Pathology	fume hood chamber, tissue processor, tissue embedding unit, microtome, hot plate, binocular light microscope, autostainer
Medical imaging	digital radiography system, CT system, CT phantom, CT quality control devices, MRI system, system quality assurance device, ultrasound
Surgery	anaesthesia unit, hysterectomy set
Radiotherapy	linear accelerator or Cobalt-60 teletherapy unit, remote after-loading BT unit, imaging system, treatment planning system
Chemotherapy	thermometer, vital signs monitor, oxygen therapy flowmeter, resuscitation trolley equipped with medicines and defibrillator, infusion pump, biological safety cabinet
Palliative care	nebulizer, pulse oximeter, sphygmomanometer, oxygen therapy flowmeter, wheelchair, crutches, air mattress

SOURCE: WHO 2017 (30).

3.3.3.2 ACCESS TO MEDICAL DEVICES

A medical device is defined as an article, instrument, apparatus or machine that is used in the prevention, diagnosis or treatment of illness or disease, or for detecting, measuring, restoring, correcting or modifying the structure or function of the body for some health purpose (67). WHO follows the convention that in vitro diagnostics are a subset of medical devices. Medical equipment requires calibration, maintenance, repair, user training and decommissioning. For cervical cancer management, medical devices are required in the areas of clinical assessment, medical imaging, surgery, pathology, radiotherapy, systemic therapy and palliative care (Table 3.6) (30).

1. NEEDS ASSESSMENT

WHO has developed guidance on needs assessment for medical devices (67). The general approach in performing a needs assessment is to examine what is available in the facility, region or country, and to compare it with what should be available, considering the particular demand and situation of the catchment area or target group in consultation with users. In cervical cancer, the WHO *List of priority medical devices for cancer management* acts as the standard for which medical devices and equipment should be available (30). The identified

gap determines the overall need. It is necessary to review the existing financial and human resources needed to address the identified gaps, and if resources are constrained, then priorities will need to be assigned. Accurate demand forecasting ensures that health facility/hospital needs can be fulfilled, and allows industry to plan their production cycles and decrease supply chain costs. Certain medical devices can take a long time to manufacture and their transportation cycle may be longer than other health products.

2. SPECIFICATION

Specification of medical devices involves the process of describing and itemizing the required functional performance and features of a medical device. WHO has developed a process for creating specifications of medical devices, including those specifically for cervical cancer control (68–71).

3. PROCUREMENT

After specifications are made, procurement services are required for supplier solicitation, tender, bid evaluation, contract preparation and award of supply. The procurement process can involve (72):

- > providing inputs, including procurement policies, a procurement plan, specifications, financial approval and a decision on the method of procurement;

- > asking for bids and issuing tender documents;
- > receiving and opening bids;
- > evaluating bids and comparing them to specifications;
- > awarding contract or placing orders;
- > arranging transport to the end user in consultation with supplier; and
- > scheduling payments.

Medical equipment, depending on level of complexity, will also generally require installation, acceptance and commissioning, and these aspects must be planned for in the procurement phase. Acceptance is the process of testing the performance of the equipment by the supplier and end user to ensure that specifications are met. Normally, final payment is not made until acceptance is satisfactorily completed. Successful acceptance also signals the start of the warranty period. Service and maintenance of medical equipment under warranty is typically the responsibility of the vendor. Commissioning is the process of preparing the equipment for safe and effective patient procedures. It may involve characterizing the performance of the equipment, testing it under simulated conditions, having staff trained in safe use of the equipment, and developing policies and procedures and work instructions for staff.

4. REGULATION

In many countries, medical device regulatory bodies have been established to protect the public from unsafe and ineffective medical devices. Within the medical device regulatory framework, medical devices cannot be sold or purchased unless the device is already registered with the medical device regulator. In the absence of a local medical device regulatory framework, a national body must be accountable for the listing and delisting of products for sale and use (or more usually for importation).

Post-market surveillance is a set of activities undertaken by the device manufacturer to collect feedback on the actual use of devices, to analyse such data and to identify the need for any actions. Adverse events, where serious harm happened or may have happened to the patient, user or another person, are an important type of feedback. The outcome of the analysis of post-market surveillance data can also highlight opportunities for the manufacturer to improve their medical device. Vigilance is the process whereby the manufacturer reports certain adverse events to the national regulatory authority (NRA) and keeps it updated on the actions taken in relation to the adverse event.

WHO guidance on post-market surveillance and market surveillance of medical devices, including in vitro diagnostics, is forthcoming (73). The International Organization for Standards (ISO) has published *ISO/TR 20416 Medical devices – Post-market surveillance for manufacturers* that may also be used (74). Users of medical devices are encouraged to be aware of the need to detect/observe, document and then report any feedback they deem necessary. Common product problems are summarized in Box 3.1.

Medical equipment involving ionizing radiation will also be subject to radiation regulation as well as medical device regulation. Examples are BT after-loaders and medical linear accelerators used in the practice of radiotherapy and CT scanners used in medical imaging. National legislation, standards and regulations will cover all aspects in ensuring the safe practice of ionizing radiation devices in medicine. Ionizing radiation regulation can involve the following aspects for the hospital:

BOX 3.1

Most common medical devices problems

- > **Patient-device incompatibility**, interaction between the patient's/client's anatomy and the medical device that affects patient/client.
- > **Material integrity problem**, including broken, cracked, degraded, deformed, disintegrated, split/cut/torn, scratched materials/components.
- > **Use of device problem**, including device handling, improper or incorrect procedure or method, misassembled by users, off-label use.
- > **Misdiagnosis**, including false-positive and false-negative test results.

- > seeking a licence from the radiation regulator to import ionizing radiation equipment;
- > arranging transport of ionizing radiation equipment with licensed carriers;
- > undergoing staff training in radiation safety;
- > obtaining radiation use/operation licences for specialized staff operating ionizing radiation equipment from the radiation regulator;
- > providing security for radiation sources within the hospital; and
- > developing a radiation management plan that is approved by the radiation regulator that sets out all departmental practices in ensuring radiation safety for the patient, staff and members of the public.

Further information on the framework for ionizing radiation regulation and safe practice can be found in IAEA and WHO publications (30,75,76).

5. MAINTENANCE AND LIFECYCLE

After the warranty period of major medical equipment expires, responsibility for service and maintenance passes from the vendor/manufacturer to the facility. Maintenance provisions for medical equipment must be put in place by the facility to ensure continuity of service over its expected lifetime. Maintenance can be provided by contracts with suppliers or through an in-house engineering service or through a mixture of both.

In negotiating a maintenance contract with suppliers, the following should be considered:

- > inclusion of spare parts;
- > inclusion of all safety, hardware and software updates and upgrades during the lifetime of the equipment;
- > inclusion of a regular service schedule specifying the number of days of service per year and whether the service is performed during work hours or out of hours;
- > access to help desk and remote diagnostics;
- > whether major parts, e.g. the X-ray tube for a CT scanner, are included or excluded in the contract;
- > whether front-line maintenance by trained in-house maintenance engineers is included or excluded; and
- > penalties for not meeting pre-agreed levels of uptime, e.g. 95% uptime (defined as time available for clinical service as a percentage of normal operating hours) could be stipulated with a penalty of reduced maintenance contract cost in the following year.

Maintenance contracts should also be considered for the facility's operational software. Maintenance contracts are advantageous in including all software updates and upgrades, access to a help desk and repair of hardware faults.

Funding of a facility providing cancer services includes recognition of the need for ongoing replenishment of consumables. Consideration for funding of equipment replacement needs to be based on the expected lifecycle of equipment.

As with medicines, inventory management of medical devices is essential for continuous supply (77). An up-to-date inventory also aids in developing budgets, determining relevant staffing levels, managing service contracts and planning for spare parts and consumables orders.

At the end of the lifecycle of medical devices and medical equipment, arrangements will need to be in place for disposal and decommissioning. Decommissioning of medical equipment may be complex in requiring services for deconstruction and scrapping. Decommissioning of ionizing radiation sources may involve special procedures for repatriation or storage of sources and dealing with induced radioactivity in materials. The national radiation regulator will need to be involved in the decommissioning of ionizing radiation sources.

6. DONATIONS OF MEDICAL DEVICES

The health sectors of many LMICs may rely significantly on donations of medical devices and medical equipment. Although these donations are generally made with good intentions, the outcomes are not always positive if the donations are not properly planned and coordinated (78). A distinction is made between donation of *new* medical devices and *used* medical devices.

In consideration of the donation of *new* medical devices and medical equipment, the following points are relevant:

- > intended recipients should be actively engaged in the process, including prioritizing equipment needs, reviewing specifications and evaluating bids based on appropriateness for the setting;
- > donations of medical equipment are to be done in accordance with a country's regulations and policies pertaining to the donation, importation, marketing and use of medical devices;
- > use of local markets for equipment procurement is advantageous;
- > procurement of basic devices can have a far greater impact on public health than more sophisticated devices; and
- > if the recipient is not able to sustain the costs of installation, service and supplies required to operate and maintain the medical equipment offered, then the donor may want to consider an alternative donation package that includes the operation and maintenance costs, especially considering that the purchase costs of medical equipment may only represent about 20% of the total costs incurred during the life of the equipment.

Because donations of *used* medical devices and equipment present their own challenges, the following points can be made:

- > used equipment, like new equipment, requires user training, maintenance, spare parts and manuals for service and operation; however, unlike for new equipment, the manufacturer is less willing to provide support for used, donated equipment, leaving the recipient with little or no recourse when the equipment breaks down;
- > manufacturers may not be willing or able to provide parts, maintenance and consumables for used equipment, particularly if the equipment is already of advanced age or if the model is out of production; and
- > refurbished equipment from reputable suppliers may be a better alternative to used equipment.

3.3.4 SUSTAINABLE FINANCING

Sustainable financing of cancer services, including cervical cancer, is a challenge for all countries, and especially LMICs. It requires strong political will and efficient multisectorial collaboration, based on a profound understanding of the benefits of investing in cancer control and prioritizing good-value-for-money services. Additionally, it must be aligned with general health care system financing under the principles of UHC, which call on expanding financing of core services to cover more population as opposed to expanding financing of select advanced services for few individuals and to provide protection against impoverishment resulting from private out-of-pocket payments (10,79,80).

The most sustainable financing approach is to use domestic public sources of funds, but general government revenues (direct expenditures or through mandatory health insurance) is a major source of NCD funding in only 71% of low-income countries as opposed to 100% of high-income countries (6). In most LMICs direct taxation for revenue generation is limited by the relatively smaller segment of the population employed in the formal economy, and indirect taxation is not well used for expanding the fiscal space for health care expenditures (81). For example, earmarked taxes from tobacco consumption remain a relatively uncommon source of revenues; only 26% of low-income countries report financing based on this source. On the other hand, 58% of low-income countries and 85% of lower-middle-income countries rely on international donors as a major source of funds. Given the large funding gap in scaling-up

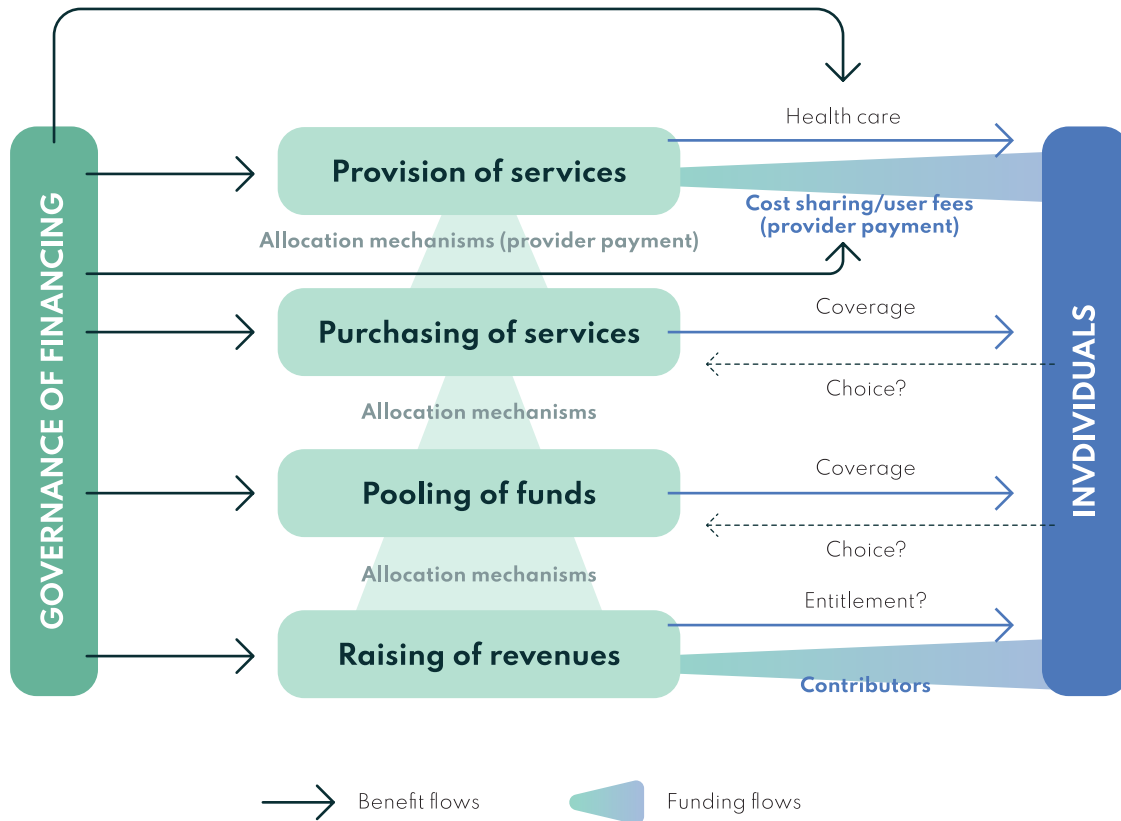
coverage of basic and essential health care services under a UHC framework, including for cancer services, it is anticipated that in the near-term external and private sources of funds will remain important in LMICs (82–85).

Sustainable financing must, therefore, include non-traditional ways of securing funding and of using existing or new funds. Strategies for innovative and diverse cancer control financing include engaging in multi-party strategic partnerships, pooling resources at regional or global levels, leveraging global health financing facilities, instituting government incentives (e.g. payments for meeting performance criteria), expanding fiscal interventions and enabling voluntary contributions from patients (1,86,87). For example, national health insurance through upfront contributory pooled schemes that will assist paying off cancer drug costs at the time drugs are required could be promoted. Increasing national capacity to perform HTA would promote more rational uses of domestic funds, especially in middle-income countries that can no longer rely on external funding and where increased demand for new services and medical products exerts increasing pressures on national budgets. Regardless of the type of measure, sustainability is enhanced by tailoring solutions specifically to the country context, keeping in mind also that progressive measures improve equity in accessing cancer services (88,89).

Previously, financing cervical cancer management has received relatively less attention compared to prevention and screening interventions, rightly so given the high cost-effectiveness and relatively equitable distribution of benefits of interventions such as HPV vaccination (90). However, the new challenge of scaling-up management concurrently with prevention and screening to accelerate cervical cancer elimination means that finding solutions for funding management services will need to become more prominent and more urgent. The investment case for the Elimination Strategy estimates that scaling-up all three pillars of prevention must be financed at the estimated rate of US\$ 0.40 per person per year from 2020 to 2030 in low-income countries and at US\$ 0.20 per person per year in lower-middle-income countries (91). About 40% of financing would go towards secondary and tertiary prevention. However, it must be emphasized that by 2050 each dollar of this investment will return US\$ 3.20 to the global economy due to increased workforce participation. When all societal benefits are counted, including the intrinsic value of being alive and the broad economic benefits, US\$ 26 is returned.

FIGURE 3.9

Health financing arrangements



SOURCE: Adapted from WHO 2017 (94).

To ensure that the projected health, economic and societal benefits of eliminating cervical cancer flow fully to nations and to women, governance of health financing for cervical cancer control must be effectively implemented. Figure 3.9 shows how governance-driven core health financing functions of revenue raising, pooling and purchasing leads to provision of services to benefit the entire population. Ineffective financing governance leads to mismatches between the cost of services and the revenues raised for them, resulting in shortfalls made up by out-of-pocket payments or the creation of parallel informal systems of payment (92). The purchasing function, when not well governed, is especially vulnerable to risks of corruption (93).

Decisions on what to purchase from the array of management services can be assisted with an explicit national health financing policy that specifically includes governance, such as that for Ghana.^f

An example of the implementation of national universal health insurance law through a financing policy with strong governance principles for strategic purchasing is illustrated in Egypt (95).

3.3.5 STRENGTHENING SURVEILLANCE AND INFORMATION SYSTEMS

High-quality, timely data are the required outputs of the diverse cancer information systems needed for planning, decision-making, improving outcomes, ensuring accountability and safeguarding the quality of cancer management services (96). Surveillance and information systems are intimately related to the monitoring and evaluation functions of a robust and high quality cervical cancer control programme (see Section 3.4).

^f Ghana Health Financing Strategy. 2015 (<https://www.moh.gov.gh/wp-content/uploads/2016/02/Health-Finance-Strategy-160203045304.pdf>, accessed 23 July 2020).

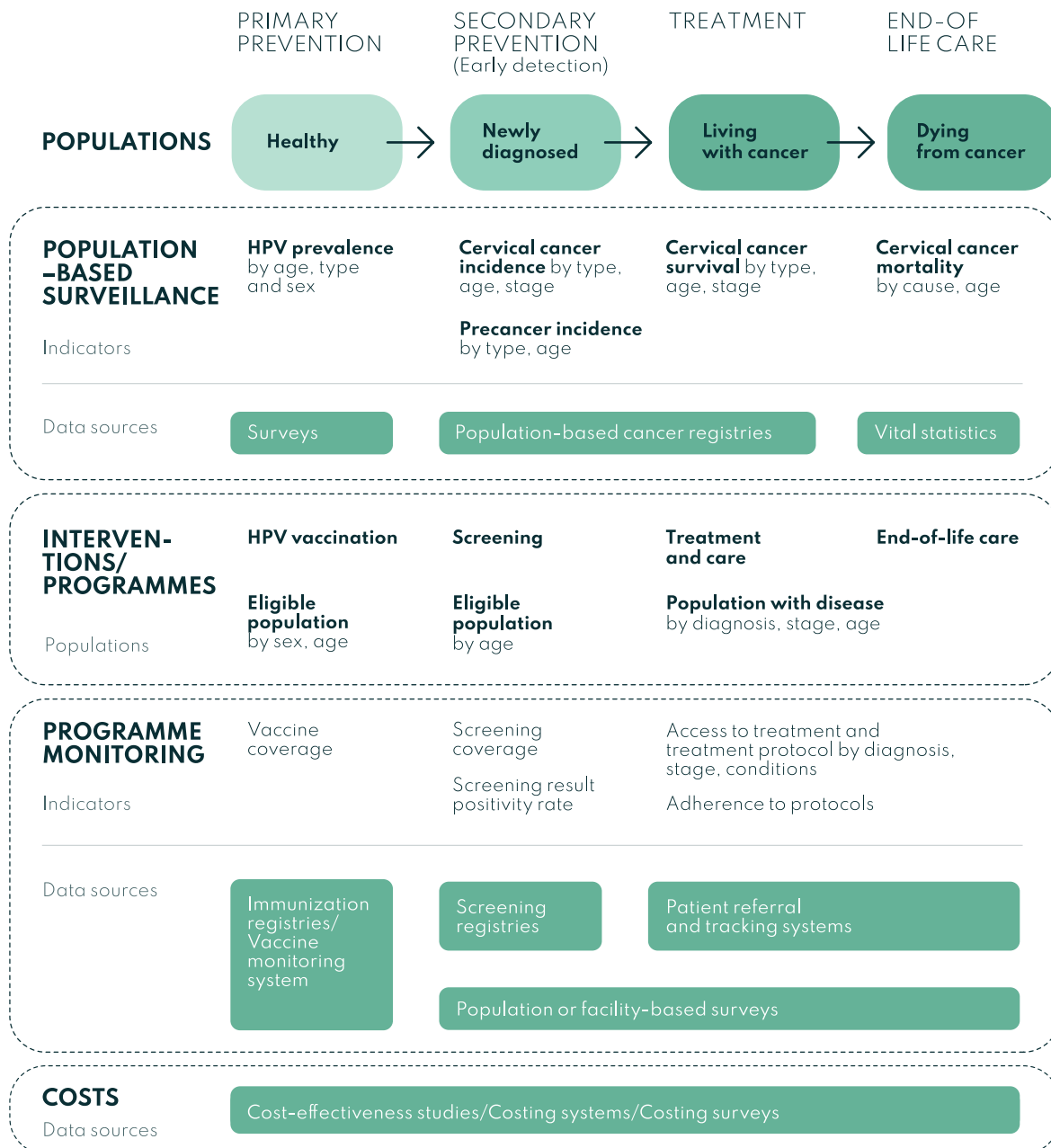
3.3.5.1 CERVICAL CANCER INFORMATION SYSTEMS

It is fundamental that robust surveillance and information systems are available and functioning at the national or subnational level both to establish the baseline situation and to monitor and evaluate the impact of the broad interventions and activities implemented to scale-up cancer services (see Section 3.4).

Figure 3.10 illustrates a framework for data collection, indicator development and the different strategies required to obtain such information. It is essential to note that effective actions all along the cancer continuum rely on the functioning of multifaceted information systems, with linking between systems whenever possible (e.g. linkage of screening information systems with PBCs). These systems require government leadership in planning and adequate investment.

FIGURE 3.10

Critical interlinked components of surveillance and monitoring for cervical cancer control



SOURCE: Adapted from Piñeros et al. 2020 (97).

3.3.5.2 POPULATION-BASED SURVEILLANCE

PBCRs are a continual system of data collection, storage, validation and analysis that permits the dissemination of incidence and survival data for each of the major types of cancer, by stage of disease at diagnosis. As with any other public health surveillance strategy, the recording and reporting of PBCR data should be undertaken in a standardized way. Compliance to international registry standards developed through the professional organization of registries, the International Association of Cancer Registries (IACR), would ensure maximum comparability.

Pertinent to invasive cancer management, PBCR data inform future planning of cancer services and health workforce and benchmarking of the effectiveness of cancer care delivery in different regions and countries through the comparisons of the survival of cancer patients.

Currently, there are more than 500 PBCRs worldwide, although their pace of development has been much slower in LMICs than in high-income countries. On the global scale, only one in three countries has high-quality incidence data at present.

In many LMICs, hospital-based registries are the main source of cancer data. They can provide valuable information on local patterns of care and quality of care, and with investment in their development, can provide high-quality data to PBCRs or become the nucleus of new PBCRs. A guidance document from the International Agency for Research on Cancer (IARC) and WHO provides technical advice to planners and health specialists in LMICs wishing to develop and implement PBCRs as information systems to inform cancer control policy (98). The Global Initiative for Cancer Registry Development can also directly assist countries in developing PBCRs through support from regional partners as part of the established IARC Regional Hubs.⁹

The freely available CanReg5 software from IACR and IARC can help countries to ensure the quality of processing cancer registry data by facilitating capture, quality verification and analysis of registry data.

3.3.5.3 VITAL REGISTRATION

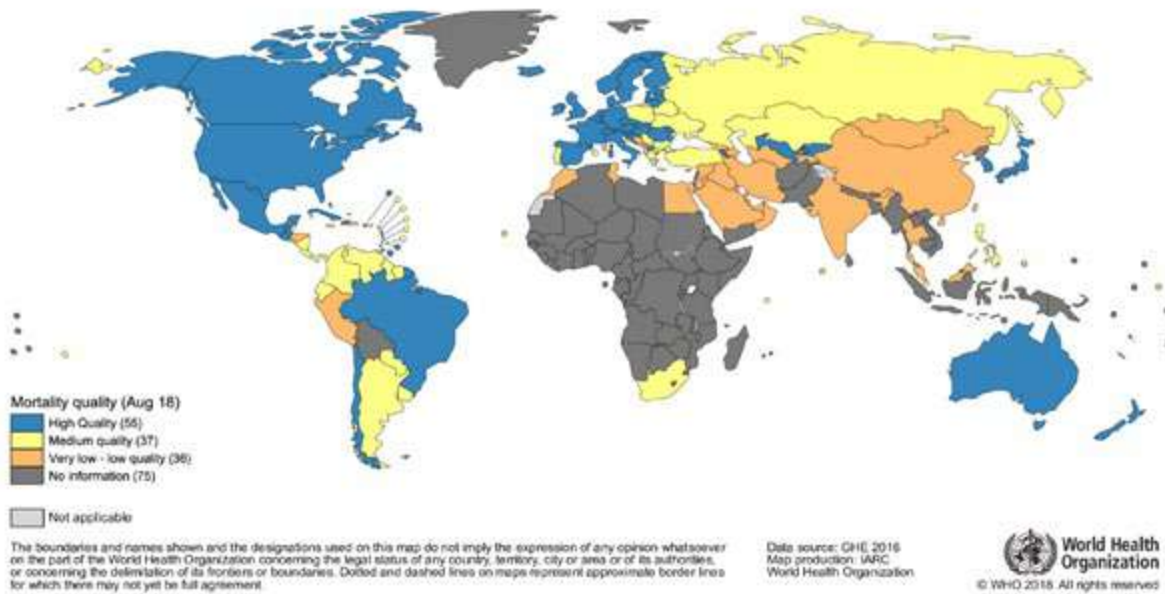
A well-functioning civil registration and vital statistics (CRVS) system registers all births and deaths in a defined geographic area or population, issues birth and death certificates, and compiles and disseminates vital statistics, including cause of death information. Despite the well-documented benefits of CRVS, many countries do not have adequate systems in place; it is estimated that two thirds of deaths are never registered and are thus not counted in the vital statistics system (Figure 3.11). The development of CRVS requires a holistic approach, taking into consideration all events (including births, marriages, deaths, cause of death and issuance of national unique personal identification numbers), their supporting information systems and associated legislation.

Cause of death data are a key data source for the cervical cancer elimination initiative as a means to evaluate cervical cancer mortality in a population. The evolution of cervical cancer mortality trends is particularly relevant to monitor the effectiveness of the cervical cancer screening programmes. In countries where there is no nationwide death registration, governments should prioritize establishing vital registration, beginning in a well-defined geographic area or population. Training of health care professionals to systematically record and code cause(s) of death is urgently needed in many countries. Standardized coding methods are important when analysing deaths due to cancers of the uterus. Unspecified cancers of uterine origin (ICD-10 C55) represent a significant percentage of all reported deaths, some of which should be properly attributed to cancer of the cervix uteri (ICD-10 C53) in the corresponding time periods (99).

⁹ Global Initiative for Cancer Registry Development (<https://gicr.iarc.fr/>, accessed 25 September 2020).

FIGURE 3.11

Global availability of mortality data



SOURCE: WHO 2018 (100).

3.3.5.4 DATA MANAGEMENT IN INFORMATION SYSTEMS

Data management of information from multiple systems requires thoughtful planning and implementation, continual monitoring and periodic adjustment (101–103). For each information system, there must be standardization of indicators, data collection procedures, and systems specified (104). Each information source should develop and operate according to an SOP. The information systems should be staffed by qualified personnel who have been trained on the data collection and management SOPs. Supervision of data collection and management operations and personnel is necessary to provide frequent feedback and data quality checks. National guidelines for effective administration of health management information systems (HMIS) data should

be consulted, and similarities and differences in the HMIS and cervical cancer information systems must be noted. Issues of data ownership and stewardship need to be clearly articulated beforehand to facilitate effective data management, analysis and reporting, and to avoid conflicts arising after data collection begins.

While information systems at health care facilities are managed by hospital personnel, it is critical to ensure that the cervical cancer control programme itself collects necessary hospital data on individual women using unique identifiers, to enable data linkage with cancer and death registries for detailed evaluation of outcomes and impact. Countries that currently collect only aggregated data in HMIS will need to upgrade data systems that captures disaggregated data. Publicly available software include District Health Information Software 2 (DHIS2) and OpenMRS systems.^{h,i}

^h District Health Information Software 2 (DHIS2) (<https://www.dhis2.org/>, accessed 25 September 2020).

ⁱ OpenMRS (<https://openmrs.org/>, accessed 25 September 2020)

3.4 MONITORING AND EVALUATION (M&E)

3.4.1 ROLE OF M&E

M&E are distinct but highly complementary activities. Monitoring is the systematic and continuous process of observing, collecting, and storing inputs, activities, outputs, outcomes, and impacts of a project or programme, to ensure that activities are taking place as planned and are consistent with objectives (105–107). In contrast, evaluation is the periodic analysis of the activities and outcomes to determine the effectiveness or success of the project or programme in meeting the stated objectives. Evaluation makes judgments about the performance of projects or programmes in order to improve its quality, effectiveness, timeliness and impact, allowing a course of correction, if warranted.

The iterative nature of M&E, exchanging respective data inputs and outputs in feedback loops, is the foundation of an evidence-based approach to decision-making (101,106). For this reason, the M&E plan and its associated indicators should be determined before programme implementation (101,107). M&E plans articulate elements in the process of implementation to be monitored and evaluated, in order to continually improve programme quality, equity, efficiency and effectiveness (101,108,109). Specifying indicators at the outset makes clear the programme objectives, activities, and expectations regarding the timeliness and quality of the programme to be implemented at each level of care.

3.4.2 IMPLEMENTING HIGH-QUALITY M&E

As women enter the cervical cancer care pathway at diverse points in the health care system (see Section 2.1), the ideal M&E plan would specify indicators for monitoring at each level of care, as well as at the population level (see Figure 3.10). Policy-makers, programme managers and other stakeholders should jointly determine the indicators to be monitored within their own country context. Agreeing on a standardized set of indicators allows a country to compare progress in cervical cancer management across different geographic areas and across facilities. A recent evaluation of national health information systems in Mozambique provides an example of cataloguing important indicators and necessary data sources to identify gaps (110).

M&E at the population level requires national government commitment and investment in health surveillance and service delivery systems (111). A first step is to establish a central coordinating function to support the country's cancer management scale-up activities as a part of its national cancer or NCD control plan. The M&E system should enable evaluation of workforce availability, competencies, retention plans, infrastructure and supply chain to deliver essential components of invasive cervical cancer management, adherence to treatment guidelines, patient referral systems to ensure follow-up and access to care, affordability of care and patient financing and reimbursement plans, and integration across various levels of care.

As health information systems and related databases vary by the level of care and, in some cases, vary within a single facility, an effective M&E plan requires maximum interoperability to track patient information and outcomes across multiple facilities and information systems (103,112). A central office responsible for cervical cancer control should communicate and implement the M&E plan, and develop an efficient and secure system to receive, reconcile, manage, analyse and report the data being monitored, as well as provide timely feedback to programme managers at various levels. Electronic health management data platforms offer more advantages compared with paper-based data collection, as data collating and analysis are less time consuming and error prone. Different open source platforms can be used for this purpose (113,114).

The use of a national unique personal identification number by diverse information sources is critical in enabling linkage of data on individual patients across information systems. This allows assessment of patient outcomes and the impact of scale-up of services on cervical cancer survival and mortality, as well as outcomes such as quality and timeliness of care.

It is important that the M&E plan clearly documents the availability and quality of health information systems needed for monitoring at all levels of care, and treatment response (115–119). Additional information to be specified are indicator definition, information systems and data sources, reporting frequency, and targets (102).

3.4.3 POPULATION-LEVEL MONITORING

The tools and methods by which population-level monitoring is carried out include examination of population-based cancer and death registries, population-based studies, data aggregation from facility-based surveys and hospital-based information systems, surveys of health care providers and patients, and data extraction from health or hospital insurance systems.

The core cervical cancer specific indicators, cervical cancer incidence and mortality, can be developed at the population level based on data accumulated and aggregated appropriately from lower level sources. Hospital cancer registries and other sources can report cases of newly diagnosed invasive cervical cancer to the PBCR that covers the city or province (98). An important source of case finding for the PBCR is hospital-reported death due to cervical cancer. The reported deaths should be verified against patient logs and pathology records for information on primary cancer diagnosis.

Tracking outcome indicators, such as stage-specific incidence, 5-year cervical cancer survival and proportion of cancers diagnosed at early stage, is useful in judging the overall effectiveness of a health system in management of cervical cancer. It also allows determining the effectiveness of early detection programmes. Comparison and benchmarking against other countries with a similar epidemiological case mix may be made, too (120). Disaggregation of incidence and survival data by age, race, ethnicity, migratory status, disability and geographic location helps understanding of inequities in access to health care and informs equity-oriented strategies and action plans.

M&E of the Elimination Strategy will specifically require monitoring progress towards 90% coverage of women who are appropriately managed according to the stage of their disease (Table 3.7). This requires compiling data from all relevant sources to report the total number of cervical cancer cases receiving appropriate treatment based on stage of disease as a proportion of all diagnoses of invasive cervical cancer.

TABLE 3.7

Key outcome indicators at the population level

Indicator	Information systems involved	Reporting source
Cervical cancer incidence (new cases of cervical cancer) by stage and histology	PBCRs; hospital-based cancer registries; hospital and health care information systems; pathology information systems	PBCRs
Stage-specific 5-year overall survival	PBCRs; death registration system (vital statistics system); patient follow-up information	PBCRs; specific population-based studies
Cervical cancer mortality (death due to cervical cancer)	Death registration system with cause of death	Vital statistics official system
Proportion of women diagnosed with invasive cervical cancer appropriately managed, by stage of disease according to clinical guidelines	PBCRs; hospital and health care information systems; administrative databases	National cervical cancer control initiatives (including accountability mechanism specific to the cervical cancer elimination initiative) Population-based studies

3.4.4 FACILITY-LEVEL MONITORING

M&E at the facility level relies on medical records, in paper-based forms or in electronic databases, and on individual cervical cancer cases diagnosed and/or treated at that facility. Monitoring also involves capturing data beyond patient registers on various aspects of quality of care, such as timeliness of services, quality of clinical care, patient satisfaction, proportion of patients completing planned treatment, occurrence of adverse events and adherence to follow-up care at the same or other health facilities.

Measuring quality of cancer care gained significant attention among policy-makers and the health professional community during the last decade. The demand for quality is driven by needs for ensuring patient safety, improving clinical outcomes of cancer treatment, using available resources effectively and shifting towards performance-based budgeting of health care providers (2,121–123). Public reporting against clinical quality performance indicators (QPIs) is adopted as mandatory or on a voluntary basis in some countries (117,124). One of the benefits is that it allows benchmarking by participating health care providers at the peer and national levels.

Recently, national and international professional organizations have published standardized sets of QPIs for cervical cancer (117,118,124,125). Examples are given in Annex 8. It must be emphasized that QPIs have to be developed and adapted while taking into account the national context, as they are closely linked to national clinical practice guidelines.

In addition to measuring objective clinical quality of care, measuring patients' perceived quality of care and perceived responsiveness to their expectations are also important in evaluating care at the facility level (126). Recommendations for delivering high-quality cancer care include developing a national quality reporting programme for cancer care, strategies to reduce disparities in access to care, and engaging patients and their caregivers in decision-making on cancer treatment and end-of-life decisions (5). Providing patients and caregivers with information about cancer prognosis, treatment benefits and harms, palliative care, psychosocial support, and costs is a critical component of quality cancer care.



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annexes

ANNEX 1 FIGO 2009 AND 2018 STAGING AND TNM CLASSIFICATION OF MALIGNANT TUMOURS SYSTEMS

The following table compares the FIGO 2009 and 2018 staging systems. Major changes are shown in stages IA, IB and IIIC with beige shading.

2009 FIGO STAGE	2018 FIGO STAGE	TNM
I: Carcinoma is strictly confined to the cervix	I: Carcinoma is strictly confined to the cervix	
<p>IA: Invasive carcinoma that can be diagnosed only by microscopy, with deepest invasion ≤ 5 mm and largest extension ≤ 7 mm</p> <p>IA1: Measured stromal invasion of ≤ 3 mm in depth and horizontal extension of ≤ 7 mm</p> <p>IA2: Measured stromal invasion of >3 mm and not >5 mm with an extension of not >7 mm</p>	<p>IA: Invasive carcinoma that can be diagnosed only by microscopy, with maximum depth of invasion ≤ 5 mm^a</p> <p>IA1: Measured stromal invasion ≤ 3 mm in depth</p> <p>IA2: Measured stromal invasion >3 mm and ≤ 5 mm in depth</p>	<p>T1a N0 M0</p> <p>T1a1 N0 M0</p> <p>T1a2 N0 M0</p>
<p>IB: Clinically visible lesions limited to the cervix uteri or pre-clinical cancers greater than stage IA</p> <p>IB1: Clinically visible lesion ≤ 4 cm in greatest dimension</p> <p>IB2: Clinically visible lesion >4 cm in greatest dimension</p>	<p>IB: Invasive carcinoma with measured deepest invasion >5 mm (greater than Stage IA); lesion limited to the cervix uteri with size measured by maximum tumour diameter^b</p> <p>IB1: Invasive carcinoma >5 mm depth of stromal invasion, and ≤ 2 cm in greatest dimension</p> <p>IB2: Invasive carcinoma >2 cm and ≤ 4 cm in greatest dimension</p> <p>IB3: Invasive carcinoma >4 cm in greatest dimension</p>	<p>T1b N0 M0</p> <p>T1b1 N0 M0</p> <p>T1b2 N0 M0</p> <p>T1b3 N0 M0</p>
II: Carcinoma invades beyond the uterus, but not to the pelvic wall or to the lower third of the vagina	II: Carcinoma invades beyond the uterus, but has not extended onto the lower third of the vagina or to the pelvic wall	
<p>IIA: Without parametrial invasion</p> <p>IIA1: Clinically visible lesion ≤ 4 cm in greatest dimension</p> <p>IIA2: Clinically visible lesion >4 cm in greatest dimension</p>	<p>IIA: Involvement limited to the upper two thirds of the vagina without parametrial invasion</p> <p>IIA1: Invasive carcinoma ≤ 4 cm in greatest dimension</p> <p>IIA2: Invasive carcinoma >4 cm in greatest dimension</p>	<p>T2a N0 M0</p> <p>T2a1 N0 M0</p> <p>T2a2 N0 M0</p>
<p>IIB: With obvious parametrial invasion</p>	<p>IIB: With parametrial involvement but not up to the pelvic wall</p>	<p>T2b N0 M0</p>
III: Tumour extends to the pelvic wall and/or involves lower third of the vagina and/or causes hydronephrosis or non-functioning kidney	III: Carcinoma involves the lower third of the vagina and/or extends to the pelvic wall and/or causes hydronephrosis or non-functioning kidney and/or involves pelvic and/or para-aortic lymph nodes	
<p>IIIA: Tumour involves lower third of the vagina, with no extension to the pelvic wall</p>	<p>IIIA: Carcinoma involves the lower third of the vagina, with no extension to the pelvic wall</p>	<p>T3a N0 M0</p>
<p>IIIB: Extension to the pelvic wall and/or hydronephrosis or non-functioning kidney</p>	<p>IIIB: Extension to the pelvic wall and/or hydronephrosis or non-functioning kidney (unless known to be due to another cause)</p>	<p>T3b N0 M0</p>

	IIIC: Involvement of pelvic and/or paraaortic lymph nodes (including micrometastases); ^a irrespective of tumour size and extent (with r and p notations) ^d IIIC1: Pelvic lymph node metastasis only IIIC2: Paraaortic lymph node metastasis	AnyT N1 M0
IV: Carcinoma has extended beyond the true pelvis or has involved (biopsy proven) the mucosa of the bladder or rectum	IV: Carcinoma has extended beyond the true pelvis or has involved (biopsy proven) the mucosa of the bladder or rectum	
IVA: Spread of the growth to adjacent organs	IVA: Spread of the growth to adjacent organs	T4 AnyN M0
IVB: Spread to distant organs	IVB: Spread to distant organs	AnyT AnyN M1

FIGO: International Federation of Gynaecology and Obstetrics; **TNM:** tumour node metastasis

- ^a Imaging and pathology can be used, where available, to supplement clinical findings with respect to tumour size and extent, in all stages. Pathological findings supersede imaging and clinical findings.
- ^b The involvement of vascular/lymphatic spaces should not change the staging. The lateral extent of the lesion is no longer considered.
- ^c Isolated tumour cells do not change the stage but their presence should be recorded.
- ^d Adding notation of r (imaging) and p (pathology) to indicate the findings that are used to allocate the case to Stage IIIC. For example, if imaging indicates pelvic lymph node metastasis, then the stage allocation would be Stage IIIC1r, and if confirmed by pathologic findings, it would be Stage IIIC1p. The type of imaging modality or pathology technique used should always be documented. When in doubt, the lower staging should be assigned.

SOURCES:

- Pecorelli S. Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium. *Int J Gynaecol Obstet.* 2009;105(2):103–4.
- Pecorelli S. Corrigendum to Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium: [Int J Gynaecol Obstet. 2009; 105: 103–04]. *Int J Gynaecol Obstet.* 2010;108(2):176.
- Bhatla N, Berek JS, Cuello Fredes M, Denny LA, Grenman S, Karunaratne K et al. Revised FIGO staging for carcinoma of the cervix uteri. *Int J Gynaecol Obstet.* 2019;145(1):129–35.
- Corrigendum to Revised FIGO staging for carcinoma of the cervix uteri [Int J Gynaecol Obstet 2019;145(1):129–35]. *Int J Gynaecol Obstet.* 2019;147(2):279–80.

ANNEX 2 **MINIMUM REQUIREMENTS FOR PATHOLOGY REPORTING FOR CERVICAL CANCER**

1. Description of the specimens submitted for histological evaluation.
2. Macroscopic description of specimens (biopsy, loop/cone, trachelectomy, hysterectomy), including specimen dimensions (three dimensions), number of tissue pieces for loop/cones, and maximum and minimum length of vaginal cuff and the parametria in two dimensions.
3. Macroscopic tumour site(s), if the tumour is visible grossly, in trachelectomy and hysterectomy specimens.
4. Tumour dimensions, including two measurements of horizontal extent and depth of invasion or thickness (tumour dimension should be based on a correlation of the gross and histological features). When multifocal separate tumours are present, each should be described and measured separately, and the largest used for tumour staging. Specimens from prior conization and subsequent conization, trachelectomy or hysterectomy should be correlated for estimation of the tumour size. This is important because different specimens might have been reported at different institutions. It should also be recognized that simply adding up the maximum size of tumours in separate specimens may significantly overestimate the maximum tumour dimension.
5. Histological tumour type and tumour grade.
6. The presence or absence of lymphovascular space involvement (LVSI).
7. Coexisting pathology (squamous intra-epithelial lesion/cervical intra-epithelial neoplasia, adenocarcinoma in situ, stratified mucin-producing intra-epithelial lesion).
8. Minimum distance of uninvolved cervical stroma.
9. Margin status (invasive and pre-invasive disease, specify the margin(s)).
10. Lymph node (LN) status, including sentinel lymph node (SLN) status, the total number of nodes found, the number and location of positive LNs, and the presence of extra-nodal extension. Micrometastasis (>0.2 mm and up to 2 mm) are reported as pN1 (mi). Isolated tumour cells no greater than 0.2 mm in regional nodes should be reported as pN0 (i+).
11. Pathologically confirmed distant metastases.
12. Provisional pathological staging pre-tumour board/multidisciplinary team meeting.

SOURCE: Cibula D, Pötter R, Planchamp F, Avall-Lundqvist E, Fischerová D, Haie-Meder C et al. The European Society of Gynaecological Oncology/European Society for Radiotherapy and Oncology/European Society of Pathology Guidelines for the Management of Patients with Cervical Cancer. *Virchows Arch.* 2018;472(6):919–36. doi: 910.1007/s00428-00018-02362-00429.

MACROSCOPIC TUMOUR SITE(S) (select all that apply)

- No macroscopically visible tumour
- Indeterminate

- Ectocervix
- Anterior
 - Posterior
 - Left lateral
 - Right lateral
 - Circumference of cervix

- Endocervix
- Anterior
 - Posterior
 - Left lateral
 - Right lateral
 - Circumference of cervix

- Vagina
- Uterus
- Lower uterine segment
 - Corpus

- Parametrium
- Left
 - Right

Other organs or tissues, specify

BLOCK IDENTIFICATION KEY

(List overleaf or separately with an indication of the nature and origin of all tissue blocks)

TUMOUR DIMENSIONS

(If separate tumours specify the dimensions for each tumour)

- Tumour dimensions cannot be determined

Horizontal extent mm x mm At least*

Depth of invasion mm At least*

OR Not assessable

If not assessable record:

Thickness mm

* It is advisable to include "at least" for the tumour measurements in loop or cone excisions when tumour is present at a resection margin/s. If not applicable, delete "at least".

HISTOLOGICAL TUMOUR TYPE

HISTOLOGICAL TUMOUR GRADE

- Not graded/applicable
- G1: Well differentiated
- G2: Moderately differentiated
- G3: Poorly differentiated
- GX: Cannot be graded

LYMPHOVASCULAR INVASION

- Not identified
- Indeterminate
- Present

COEXISTENT PATHOLOGY

(Required for loop/cone excisions/trachelectomies only and recommended for other specimens)

Squamous intraepithelial lesion (SIL) (CIN)

- Not identified
- Present

↓
GRADE

- Low-grade SIL (LSIL) (CIN 1)
- High-grade SIL (HSIL) (CIN 2/3)

Adenocarcinoma in-situ (AIS)/High-grade cervical glandular intraepithelial neoplasia (HG CGIN)

- Not identified
- Present

Stratified mucin-producing intraepithelial lesion (SMILE)

- Not identified
- Present

Other possible precursor lesions

- Not identified
- Present

- Lobular endocervical glandular hyperplasia
- Adenocarcinoma in situ of gastric type
- Other, specify

EXTENT OF INVASION

- Not applicable

Vagina

- Not involved
- Involved

- Upper two thirds
- Lower third

Lower uterine segment

- Not involved
- Involved

Endometrium

- Not involved
- Involved

Myometrium

- Not involved
- Involved

Parametrium

- Not involved
- Involved

- Left
- Right

Fallopian tube

- Not involved
- Involved

- Left
- Right

Ovary

- Not involved Not applicable
 Involved
 ▼ Left
 Right

Bladder

- Not involved Not applicable
 Involved, *specify compartment*
 ▼

Rectum

- Not involved Not applicable
 Involved, *specify compartment*
 ▼

Other organs or tissues

- Not involved Not applicable
 Involved, *specify*
 ▼

PATHOLOGICALLY CONFIRMED DISTANT METASTASES

- Not identified
 Present, *specify site(s)*
 ▼

ANCILLARY STUDIES

- Performed Not performed
 ↓
 HPV testing, *specify details*

 Immunohistochemistry, *specify details*

 Other, *specify details*

MARGIN STATUS

For carcinoma

HYSTERECTOMY/TRACHELECTOMY SPECIMEN

Margin	Involved	Not involved	Distance from tumour (mm)	Cannot be assessed
Ectocervical/vaginal cuff				
Endocervical [^]				
Radial/deep stromal				
Closest lateral	<input type="radio"/> Left <input type="radio"/> Right			

LOOP/CONE

Margin	Involved	Not involved	Distance from tumour (mm)	Cannot be assessed
Ectocervical				
Endocervical				
Radial/deep stromal				
Unspecified ^{^^}				

For preinvasive disease

Margin	HSIL				AIS				SMILE				Margin is not applicable to specimen	
	Involved	Not involved	Dist. from margin (mm)	Cannot be assessed	Involved	Not involved	Dist. from margin (mm)	Cannot be assessed	Involved	Not involved	Dist. from margin (mm)	Cannot be assessed		
Ectocervical/vaginal cuff														
Endocervical														
Radial/deep stromal														
Unspecified ^{^^}														

[^] This is required only for trachelectomy specimens.

^{^^} Use for loop/cone biopsies where it is not possible to say whether the margin is ectocervical or endocervical.

LYMPH NODE STATUS

Not submitted

^^^ If the actual number of lymph nodes examined or the number of positive nodes cannot be determined due, for example, to fragmentation, then this should be indicated in the response.

Lymph Node Type	Detail	Number of lymph nodes examined ^{^^^}	Number of positive lymph nodes ^{^^^}
Sentinel node(s)	Left		
	Right		
Regional nodes: pelvic	Left		
	Right		
Regional nodes: para-aortic			
Non-regional nodes: inguinal	Left		
	Right		
Other node group, specify			

PROVISIONAL PATHOLOGICAL STAGING PRE-MDTM

FIGO (2018 edition) (Reproduced with permission)

Stage I: The carcinoma is strictly confined to the cervix uteri (extension to the corpus should be disregarded)

- IA Invasive carcinoma that can be diagnosed only by microscopy, with maximum depth of invasion <5 mm^{*}
 - IA1 Measured stromal invasion <3 mm in depth
 - IA2 Measured stromal invasion ≥3 mm and <5 mm in depth
- IB Invasive carcinoma with measured deepest invasion ≥5 mm (greater than stage IA), lesion limited to the cervix uteri[†]
 - IB1 Invasive carcinoma ≥5 mm depth of stromal invasion and <2 cm in greatest dimension
 - IB2 Invasive carcinoma ≥2 cm and <4 cm in greatest dimension
 - IB3 Invasive carcinoma ≥4 cm in greatest dimension

Stage II: The carcinoma invades beyond the uterus, but has not extended onto the lower third of the vagina or to the pelvic wall

- IIA Involvement limited to the upper two-thirds of the vagina without parametrial involvement
 - IIA1 Invasive carcinoma <4 cm in greatest dimension
 - IIA2 Invasive carcinoma ≥4 cm in greatest dimension
- IIB With parametrial involvement but not up to the pelvic wall

Stage III: The carcinoma involves the lower third of the vagina and/or extends to the pelvic wall and/or causes hydronephrosis or non-functioning kidney and/or involves pelvic and/or paraaortic lymph nodes[‡]

- IIIA Carcinoma involves the lower third of the vagina, with no extension to the pelvic wall
- IIIB Extension to the pelvic wall and/or hydronephrosis or non-functioning kidney (unless known to be due to another cause)
- IIIC Involvement of pelvic and/or paraaortic lymph nodes, irrespective of tumor size and extent (with r and p notations)[‡]
 - IIIC1 Pelvic lymph node metastasis only
 - IIIC2 Paraaortic lymph node metastasis

Stage IV: The carcinoma has extended beyond the true pelvis or has involved (biopsy proven) the mucosa of the bladder or rectum. A bullous edema, as such, does not permit a case to be allotted to stage IV

- IVA Spread of the growth to adjacent organs
- IVB Spread to distant organs

^{*} Imaging and pathology can be used, when available, to supplement clinical findings with respect to tumor size and extent, in all stages.

[†] The involvement of vascular/lymphatic spaces does not change the staging. The lateral extent of the lesion is no longer considered.

[‡] Adding notation of r (imaging) and p (pathology) to indicate the findings that are used to allocate the case to stage IIIC. For example, if imaging indicates pelvic lymph node metastasis, the stage allocation would be stage IIIC1r and, if confirmed by pathological findings, it would be Stage IIIC1p. The type of imaging modality or pathology technique used should always be documented. When in doubt, the lower staging should be assigned.

TNM STAGING (UICC TNM 8th edition 2016)^{**}

TNM Descriptors

- m - multiple primary tumors r - recurrent
 y - post-therapy

Primary tumour (pT)

- TX Primary tumour can not be assessed
- T0 No evidence of primary tumour
- Tis Carcinoma in situ (preinvasive carcinoma)
- T1¹ Tumour confined to the cervix
 - T1a¹ Invasive carcinoma diagnosed only by microscopy; stromal invasion with a maximum depth of 5.0 mm measured from the base of the epithelium and a horizontal spread of 7.0 mm or less²
 - T1a1 Measured stromal invasion 3.0 mm or less in depth and 7.0 mm or less in horizontal spread
 - T1a2 Measured stromal invasion more than 3.0 mm and not more than 5.0 mm with a horizontal spread 7.0 mm or less
 - T1b Clinically visible lesion confined to the cervix or microscopic lesion greater than T1a/IA2
 - T1b1 Clinically visible lesion 4.0 cm or less in greatest dimension
 - T1b2 Clinically visible lesion more than 4.0 cm in greatest dimension
- T2 Tumour invades beyond uterus but not to pelvic wall or to lower third of vagina
 - T2a Tumour without parametrial invasion
 - T2a1 Clinically visible lesion 4.0 cm or less in greatest dimension
 - T2a2 Clinically visible lesion more than 4.0 cm in greatest dimension
 - T2b Tumour with parametrial invasion
- T3 Tumour extends to pelvic wall, involves lower third of vagina, causes hydronephrosis or nonfunctional kidney
 - T3a Tumour involves lower third of vagina
 - T3b Tumour extends to pelvic wall, causes hydronephrosis or nonfunctional kidney
- T4 Tumour invades mucosa of bladder or rectum or extends beyond true pelvis³

¹ Extension to the corpus uteri should be disregarded.

² The depth of invasion should be taken from the base of the epithelium, either surface or glandular, from which it originates. The depth of invasion is defined as the measurement of the tumour from the epithelial-stromal junction of the adjacent most superficial papillae to the deepest point of invasion.

³ All macroscopically visible lesions even with superficial invasion are T1b/IB.

⁴ Vascular space involvement, venous or lymphatic, does not affect classification.

⁵ Bullous oedema is not sufficient to classify a tumour as T4.

Regional lymph nodes (pN)

- NX Regional lymph nodes cannot be assessed
- N0 No regional lymph node metastasis
- N1 Regional lymph node metastasis

^{**} Reproduced with permission. Source: UICC TNM Classification of Malignant Tumours, 8th Edition, eds by James D. Brierley, Mary K. Gospodarowicz, Christian Wittekind. 2016, Publisher Wiley-Blackwell.

ANNEX 4 ESSENTIAL PACKAGE OF PALLIATIVE CARE FOR CERVICAL CANCER (EPPCCC)

The EPPCCC includes only the most basic interventions, medicines, equipment, social supports and human resources needed typically by women with cervical cancer or their family caregivers. It should be universally accessible by all people in need.

Intervention	Inputs			
	Medicines ^a	Equipment	Social supports ^b	Human resources ^c
Prevention and relief of pain or other physical suffering, ^d acute or chronic	Amitriptyline, oral Bisacodyl (senna), oral Dexamethasone, oral and injectable Diazepam, oral and injectable Diphenhydramine (chlorpheniramine, cyclizine, or dimenhydrinate), oral and injectable Fluconazole, oral Fluoxetine (sertraline or citalopram), oral Furosemide, oral and injectable Haloperidol, oral and injectable Hyoscine butylbromide, oral and injectable Ibuprofen (naproxen, diclofenac or meloxicam), oral Lactulose (sorbitol or polyethylene glycol), oral Loperamide, oral Metaclopramide, oral and injectable Metronidazole, oral (for vaginal insertion) Morphine, oral immediate release and injectable Naloxone, injectable Omeprazole, oral Ondansetron, oral and injectable ^f Oxygen Paracetamol, oral Petroleum jelly	Pressure-reducing mattresses Nasogastric drainage and feeding tubes Urinary catheters Opioid lock boxes Flashlights with rechargeable batteries (if no access to electricity) Adult diapers or cotton and plastic		Doctors (with basic palliative care training) Nurses (with basic palliative care training) CHWs (if available)

Prevention and relief of psychological suffering, ^e acute or chronic	Amitriptyline, oral Dexamethasone, oral and injectable ^f Diazepam, oral and injectable Diphenhydramine (chlorpheniramine, cyclizine or dimenhydrinate), oral and injectable Fluoxetine (sertraline or citalopram), oral Haloperidol, oral and injectable Lactulose (sorbitol or polyethylene glycol), oral	Adult diapers or cotton and plastic		Doctors (with basic palliative care training) Nurses (with basic palliative care training) Social workers, psychologists, grief counsellors, or trained and supervised lay counsellors CHWs (if available)
Prevention and relief of social suffering, acute or chronic			Cash transfers to cover housing, children's school tuition, transportation to health care facilities or funeral costs Food packages Other in-kind support: blankets, sleeping mats, shoes, soap, toothbrushes, toothpaste	Social workers CHWs (if available) Peer supporters
Prevention and relief of spiritual suffering				Local spiritual counsellors

CHW: community health worker

^a Based on the WHO *Model List of Essential Medicines*, 21st list, 2019 . Acceptable alternative medicines are in parentheses: ().

^b At least for patients living in extreme poverty and for one caregiver per patient.

^c Doctors may be oncologists, gynecologists, surgeons, general practitioners, family doctors, clinical officers or assistant doctors, or others.

^d Other physical suffering includes breathlessness, weakness, nausea, vomiting, diarrhea, constipation, incontinence, malodorous vaginal discharge and bleeding.

^e Psychological suffering includes anxiety, depressed mood, post-traumatic stress disorder (PTSD), confusion or delirium, sexual dysfunction and complicated grief.

^f Only in hospitals that provide cancer chemotherapy or radiotherapy.

SOURCES:

- WHO Model list of essential medicines, 21st list. Geneva: World Health Organization; 2019.
- Integrating palliative care and symptom relief into primary health care: a WHO guide for planners, implementers and managers. Geneva: World Health Organization; 2018.
- Knaul FM, Farmer PE, Krakauer EL, De Lima L, Bhadelia A, Kwete XJ et al. Alleviating the access abyss in palliative care and pain relief – an imperative of universal health coverage: the Lancet Commission report. *Lancet*. 2018;391(10128):1391–1454.
- Krakauer EL, Muhimpundu MA, Mukasahaha D, Tayari J-C, Ntirimira C, Uhgaze B et al. Palliative care in Rwanda: aiming for universal access. *J Pain Symptom Manage*. 2018;55(2s):S77–S80.

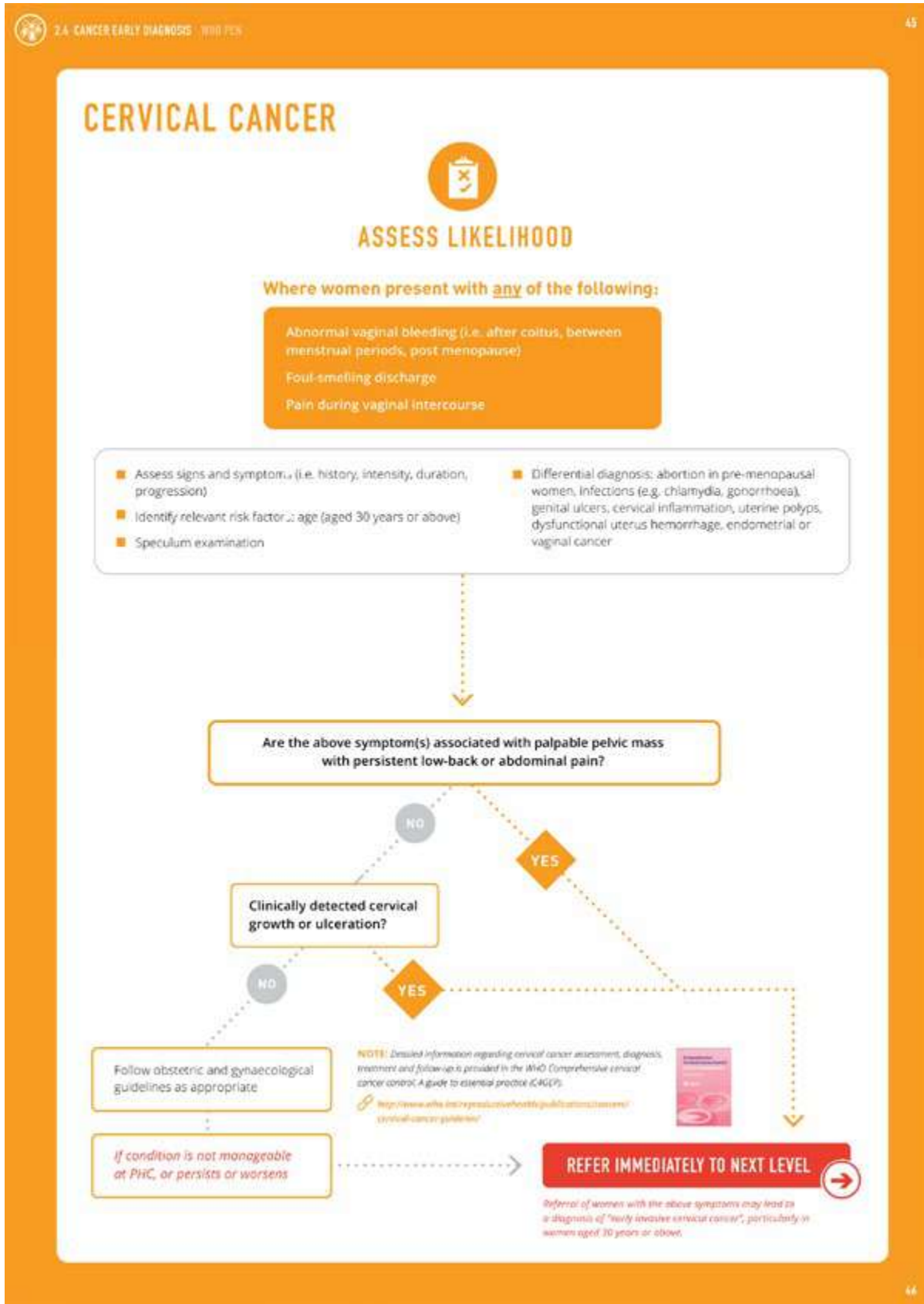
ANNEX 5 PATIENT REFERRAL FORM

Name of facility:		Referral form		Original/Copy			
Referred by:	Name:				Position:		
Initiating facility Name and address:				Date of referral:			
Telephone arrangements made:	YES	NO	Facility Tel No.	Fax No.			
Referred to facility Name and address:							
Client name							
Identity number				Age:		Sex:	
Client address							
Clinical diagnosis							
Clinical history							
Findings							
Treatment given							
Reason for referral							
Documents accompanying referral							
Print name, sign & date	Name:			Signature:	Date:		
<p>Note to receiving facility: On completion of client management please fill in and detach the referral back slip below and send with the patient or send by fax or mail.</p>							

Referral back from facility Name		Tel No.	Fax No.
Reply from (person completing form)	Name:		Date:
	Position:	Specialty:	
To initiating facility: (enter name and address)			
Client name			
Identity number		Age:	Sex:
Client address			
This client was seen by: (give name and specialty)			On date:
Patient history			
Special investigations and findings			
Diagnosis			
Treatment/operation			
Medication prescribed			
Please continue with: (meds, Rx, follow-up, care)			
Refer back to:			On date:
Print name, sign & date	Name:	Signature:	Date:

SOURCE: Management of health facilities: referral systems. World Health Organization (<https://www.who.int/management/facility/referral/en/>, accessed 25 September 2020).

ANNEX 6 WHO PEN PROTOCOL FOR CERVICAL CANCER



SOURCE: WHO package of essential noncommunicable (PEN) disease interventions for primary health care. Geneva: World Health Organization; 2020.

ANNEX 7 CHECKLIST FOR SAFE HANDLING OF HAZARDOUS DRUGS DURING ADMINISTRATION

Name: _____ Date of Review and Exam: _____

Yes No Initials

	Yes	No	Initials
Prior to Administration			
1. Gather equipment required for drug administration.			
2. Select appropriate gloves for hazardous drug administration.			
3. Select appropriate gown for hazardous drug administration.			
4. Identify situations when face shield/eye protection is required.			
5. Locate spill kit and mask.			
6. Obtain hazardous waste container.			
7. Receive drug(s) from pharmacy in sealed container.			
Administration			
1. Wash hands and don gown and gloves before opening drug delivery bag.			
2. Visually inspect the contents of the delivery bag.			
3. Don face shield, as indicated.			
4. Select IV equipment with locking connections.			
5. For IV infusions:			
• Place plastic-backed absorbent pad to protect patient from droplets.			
• Remove cap from IV tubing and connect to patient delivery site.			
• Tighten locking connections.			
• When complete, discontinue IV bag/bottle/tubing intact and re-cap patient delivery site.			
6. For IV push medications:			
• Wrap gauze around connection to catch drug droplets.			
• Tighten locking connection.			
• When complete, remove syringe from needleless connection.			
• Discard syringe and waste in a puncture-proof/leakproof container.			
7. For IM/SQ injections:			
• Attach needle to syringe.			
• Tighten locking connection.			
• When complete, do not re-cap needle.			
• Discard syringe-needle unit in puncture-proof/leakproof container.			
8. For oral drugs:			
• Don gloves.			
• Open unit dose package and place into medicine cup (avoid touching drug or inside of package).			
Post-Administration			
1. Don gown, gloves, and face shield, if indicated.			
2. Seal contact material in plastic bag for transport to hazardous waste container.			
3. Place sealed plastic bag in hazardous waste container.			
4. Remove PPE properly, seal it in a plastic bag, and dispose of it in the hazardous waste container.			
5. Close lid on waste container.			
6. Wash hands thoroughly after removal and disposal of PPE.			
7. Decontaminate equipment appropriately in the area.			

SOURCE: Safe handling of hazardous chemotherapy Drugs in limited-resource settings. Washington (DC): Pan American Health Organization; 2013.

ANNEX 8 **CLINICAL QUALITY PERFORMANCE INDICATORS FOR CERVICAL CANCER MANAGEMENT**

The following table is an example of the most commonly reported key quality performance indicators (QPIs) for cervical cancer management in the domains of preoperative care, perioperative care, non-operative care, patient reporting, and survival. QPIs must be adapted to national context and based on national clinical practice guidelines for management of invasive cervical cancer.

Examples of QPIs for cervical cancer

Preoperative	1	Proportion of patients who have their stage of disease assessed by magnetic resonance imaging (MRI) prior to first treatment.
	2	Proportion of patients for whom primary definitive surgery is not appropriate, who undergo positron emission tomography-computed tomography (PET-CT) imaging.
Perioperative	3	Proportion of patients with stage IBI cervical cancer, who undergo radical hysterectomy.
	4	Proportions of patients with surgically treated cervical cancer who have clear resection margins.
	5	Proportion of patients who have pelvic lymphadenectomy specimens that contain at least one examined lymph node in each common iliac, external and internal iliac and obturator area or proportion of patients who have successful bilateral identifications of sentinel nodes after a sentinel node procedure.
	6	Proportion of patients suffering pelvic recurrence after radical hysterectomy for cervical cancer.
Nonoperative	7	Proportion of patients undergoing radical radiotherapy for whom treatment time is no longer than 56 days.
	8	Proportion of patients undergoing radical radiotherapy, who receive concurrent platinum-based chemotherapy.
	9	Proportion of patients with locally advanced cervical cancer where intra-cavitary brachytherapy is incorporated into treatment.
Patient report	10	Proportion of patients whose American Society of Anesthesiologists (ASA) and/or World Health Organization (WHO) score is reported.
	11	Proportion of patients who have an operative report that contains all minimum required elements.
	12	Proportion of patients who have a pathology report that contains all minimum required elements.
	13	Proportion of recorded serious post-operative complications or deaths.
Survival	14	Proportion of patients who are alive 1/3/5 years after their diagnosis.

SOURCE: Bonte AS, Luyckx A, Wyckmans L, Trinh XB, van Dam PA. Quality indicators for the management of endometrial, cervical and ovarian cancer. *Eur J Surg Oncol.* 2019;45(4):528–37.



PHOTO: Groesbeck Parham



