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## Cervical cancer-associated suffering: Estimating the palliative care needs of a highly vulnerable population

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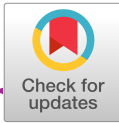
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# Cervical Cancer-Associated Suffering: Estimating the Palliative Care Needs of a Highly Vulnerable Population



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## abstract

**PURPOSE** To enable design of optimum palliative care for women with cervical cancer, we studied the most common types of suffering and their severity, prevalence, and duration.

**METHODS** We first reviewed the literature on the major types, severity, prevalence, and duration of suffering associated with cervical cancer. We then conducted a modified Delphi process with experts in cervical cancer care to supplement the literature. For each type of suffering, we distinguished between decedents (those who die from cervical cancer in a given year) and nondecedents (those who have cervical cancer in a given year but do not die). By applying the suffering prevalence and duration estimates to the number of decedents, nondecedents, and family caregivers in 2017, we were able to estimate their palliative care needs and the intensity of palliative care needed to respond adequately to this suffering.

**RESULTS** There is a high prevalence among decedents of moderate or severe pain (84%), vaginal discharge (66%), vaginal bleeding (61%), and loss of faith (31%). Among both decedents and nondecedents, there is a high prevalence of clinically significant anxiety (63% and 50%, respectively), depressed mood (52% and 38%, respectively), and sexual dysfunction (87% and 83%, respectively). Moderate or severe financial distress is prevalent among decedents, nondecedents, and family caregivers (84%, 74%, and 66%, respectively). More than 40% of decedents and nondecedents are abandoned by their intimate partners. Most patients experience some combination of moderate or severe physical, psychological, social, and spiritual suffering. In total, 258,649 decedents and 2,558,857 nondecedents needed palliative care in 2017, approximately 85% of whom were in low- and middle-income countries where palliative care is rarely accessible.

**CONCLUSION** Among women with advanced cervical cancer, suffering is highly prevalent and often severe and multifaceted.

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## INTRODUCTION

Cervical cancer, a preventable disease, is one of the gravest threats to women's well-being and lives worldwide. It is the fourth most common cancer in women globally and disproportionately afflicts the poor. One woman dies from it every 2 minutes, and the limited available data suggest that women with cervical cancer typically experience suffering that is more complex and severe than that caused by other serious illnesses.<sup>1-4</sup> To stop the unnecessary suffering and death from cervical cancer, the WHO developed the Global Strategy to Accelerate the Elimination of Cervical Cancer as a Public Health Problem, which was adopted by the 73rd World Health Assembly in August 2020.<sup>5</sup>

The strategy outlines a comprehensive roadmap toward elimination within the current century that entails achievement of the 90-70-90 targets associated with three main pillars of the strategy: (1) primary prevention through human papilloma virus (HPV) vaccination, (2) screening with high-precision tests and treatment of precancerous lesions, and (3) management of invasive cervical cancer, including palliative care. But while palliative care is an essential part of comprehensive cancer care, design and implementation of optimum palliative care for women with cervical cancer requires better understanding of the suffering it engenders.<sup>6</sup>

In this paper, we identify the most common and severe types of suffering of people affected by cervical cancer,

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## CONTEXT

### Key Objective

Cervical cancer disproportionately afflicts the poor and appears to cause worse suffering than most other serious illnesses. We studied the major types, prevalence, severity, and duration of suffering associated with cervical cancer as a necessary prerequisite to designing optimum palliative care.

### Knowledge Generated

Among women with cervical cancer in 2017, there was a high prevalence of moderate or severe pain, malodorous vaginal discharge, vaginal bleeding, anxiety, depressed mood, sexual dysfunction, and financial distress, and more than 40% experienced abandonment by intimate partners. Patients' primary family caregivers also experienced psychosocial distress. More than 3 million patients and primary family caregivers needed palliative care in 2017, 85% of whom were in low- or middle-income countries.

### Relevance

Cervical cancer generates suffering that is highly prevalent, severe, and varied, especially among the global poor. It is medically and morally imperative to assure access by the global poor to cervical cancer prevention, early diagnosis and treatment, and appropriate palliative care.

including patients and their primary family caregivers, most of whom are poor and live in low- or middle-income countries (LMICs) where access to palliative care remains rare.<sup>7</sup> We also identify the prevalence and duration of this suffering using a method pioneered by the Lancet Commission on Palliative Care and Pain Relief.<sup>8</sup> Our hypothesis was that moderate and severe suffering is more prevalent and multifaceted among women with cervical cancer than among people with other cancers or serious illnesses.<sup>9</sup>

### Epidemiology

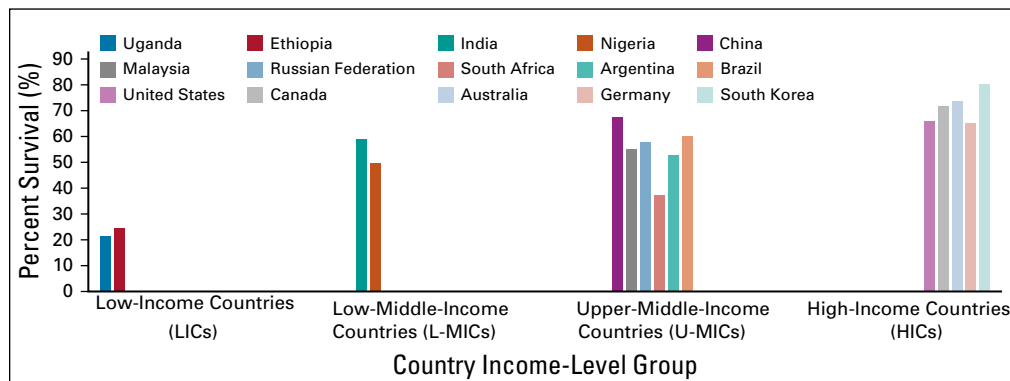
The International Agency for Research on Cancer (IARC) estimates that, in 2018, 570,000 women were diagnosed with cervical cancer and 311,000 women died of it. More than 85% of cases occurred in LMICs or among poor and marginalized communities in high-income countries (HICs), and it was the most common cause of cancer-related death in sub-Saharan Africa.<sup>10</sup> Globally, in 2018, the average age at diagnosis of cervical cancer was 53 years, and the average age at death was 59 years. China and India together had more than a third of the global cervical cancer cases (106,000 in China and 97,000

in India) and deaths (48,000 in China and 60,000 in India).<sup>10</sup>

Five-year survival for women with cervical cancer varies widely by country income level (Fig 1). Although data on 5-year survival are scant from low-income countries (LICs) and lower-middle-income countries (L-MICs), it appears that a minority of patients survive for 5 years in these countries where 3.6 of the world's 7.7 billion people live.<sup>11,12</sup> Available data indicate that 5-year survival in LICs may range from 3% to 23%. The differences in survival are due in part to the late diagnosis of cancer in these countries and the lack of access to adequate treatment including external beam radiotherapy and brachytherapy.<sup>13</sup> Each increase in disease stage at diagnosis is known to decrease 5-year survival.<sup>12,14</sup> But even in HICs, more than a third of patients die within 5 years.

Among cervical cancers, around 70% are squamous cell carcinomas, 25%-30% of carcinomas are adenocarcinomas, and there is a small percentage of noncarcinomas.<sup>5</sup> Almost all cervical carcinomas are associated with chronic HPV infection, which is also associated with increased risk of vaginal and vulvar cancer in women, penile cancer in

**FIG 1.** Five-year survival with cervical cancer of any stage (%) by country income level. HIC, high-income country; LIC, low-income country; L-MIC, low-middle-income country; U-MIC, upper-middle-income country. Sengayi-Muchengeti et al,<sup>12</sup> Arbyn et al,<sup>10</sup> Allemani et al,<sup>11</sup> Hong et al,<sup>32</sup> National Cancer Institute,<sup>33</sup> Cancer Australia,<sup>34</sup> Canadian Cancer Society.<sup>35</sup>



men, as well as anorectal cancer and oropharyngeal cancer in both men and women. Additional risk factors for cervical cancer include chronic immunosuppression, first- and second-hand exposure to tobacco smoke, prolonged use of oral contraceptives, increasing parity, as well as increased numbers of sexual partners or a single sexual partner who has multiple sexual partners. Women living with HIV infection are at increased risk for chronic HPV infection and are six times as likely to develop HPV-associated cervical cancer compared with HIV-negative women.<sup>15</sup> This accounts in part for the high prevalence of cervical cancer in sub-Saharan Africa.<sup>13</sup> Use of highly active antiretroviral therapy partially reduces the risk of HPV-associated neoplasia.<sup>16</sup>

Prophylactic HPV vaccination, given before onset of sexual activity, conveys almost 100% protection against HPV infection with the subtypes covered by the vaccine. However, as of 2020, less than a quarter of LICs and < 30% of L-MICs have introduced the HPV vaccine into their national immunization schedules, while more than 85% of HICs have done so.<sup>15</sup> Screening for HPV-associated cervical neoplasia, followed by ablative or excisional treatment, has been shown to decrease the incidence of invasive cervical cancer. But striking disparities between countries of different income levels also exist in access to cervical cancer screening, diagnosis, and treatment services. Combined basic capacity for pathology, cancer surgery, radiotherapy, and chemotherapy is accessible only in about 13% of LICs. The other 87% of LICs lack one or more of these services.

## METHODS

We first conducted a review of the literature on the major types, prevalence, and duration of suffering because of cervical cancer. We began with a PubMed search using the search terms uterine cervical cancer suffering, uterine cervical cancer pain, and uterine cervical cancer palliative care. All English-, French-, and German-language papers reporting quantitative or qualitative data on the types, severity, prevalence, or duration of suffering associated with cervical cancer, all meta-analyses of such reports, and all reviews of these topics were used for the study. Similar papers noted on the PubMed website and in the reference list of the downloaded papers were also used. For each paper, we also noted the World Bank country income classification of the country or countries from which data were obtained. All quantitative data on the types, severity, prevalence, or duration of suffering associated with cervical cancer were used to populate preliminary tables. In creating these tables, we adhered to the standard distinction in the palliative care literature between four categories of suffering: physical, psychological, social, and spiritual. Although these categories of suffering cannot be clearly distinguished in clinical practice, we do so heuristically here to better understand the ways women with cervical cancer suffer and thus what would constitute optimum palliative care. When there was more than one study

reporting data on the prevalence or duration of any specific type of suffering, we calculated a mean for use in the preliminary tables.

In light of the dearth of quantitative data, especially from LMICs, on the specific types of suffering within each category and of prevalence and duration of each type of suffering, we also convened an expert panel of experienced providers of care for women with cervical cancer to review, comment on, and supplement our literature review. The expert panel consisted of two clinicians from each of the six WHO regions and included 10 medical doctors, one nurse, and one social worker. One member was from an LIC, five were from L-MICs, four were from upper-middle-income countries, and two were from high-income countries. We used a two-round modified Delphi Process to achieve consensus among members of the expert panel for refining and completing the preliminary tables on the types, prevalence, and duration of physical, psychological, social, and spiritual suffering experienced by women with cervical cancer and their primary family caregivers.<sup>17</sup> Whereas the first round of a standard Delphi Process would have entailed asking each participant to identify the most common and severe types of suffering and their prevalence without providing any data or suggestions, we modified the first round by providing participants with the preliminary tables populated with available data from the literature on the most common and severe types of suffering, their prevalence, and their duration, to help inform their responses. For each type of suffering, we asked the participants to distinguish between decedents (those who die from cervical cancer in a given year) and nondecedents (those who have cervical cancer in a given year but do not die). We also asked participants to estimate the prevalence and duration of most types of psychological, social, and spiritual suffering of primary family caregivers.

To determine the total number of patients with cervical cancer per year who have one or more types of moderate or severe suffering and therefore require palliative care, we began with data on the number of deaths from cervical cancer in 2017 from the Institute for Health Metrics and Evaluation (IHME), the total prevalence of cervical cancer in 2017 from the IHME, and the 5-year prevalence data from IARC.<sup>18,19</sup> The number of nondecedents was calculated as the sum of all patients with cervical cancer within 5 years of diagnosis and 50% of patients who survived longer than 5 years. We used the IHME data from 194 countries and territories. For the 16 countries for which no data from IARC were available, we imputed 5-year survival using the average from each country's World Bank income group. To calculate the number of family caregivers with moderate or severe psychological, social, or spiritual suffering and thus in need of palliative care, we assumed that each decedent had only one primary family caregiver at risk of some type of suffering.

By applying the suffering prevalence and duration estimates from the modified Delphi Process to the calculated number of decedents, nondecedents, and family caregivers, we were able to estimate the number of decedents, nondecedents, and family caregivers who experienced each type of suffering in 2017. We then also estimated the intensity of palliative care needed to respond adequately to this suffering, measured as the number of days when contact with a palliative care provider is needed either in inpatient or outpatient settings or in the home, to apply the essential package of palliative care recommended by WHO and described elsewhere.<sup>6,20,21</sup> We generated estimates of the palliative care need by patients with cervical cancer and

their family caregivers globally, regionally, for each country, and for each country income group.

## RESULTS

The results of the modified Delphi Process are shown in Table 1. Cervical cancer and its treatment result in an average prevalence of pain among decedents that is higher (mild 96%; moderate-severe 84%) than among patients with any other illness that commonly generates a need for palliative care, including malignant neoplasms in general.<sup>8</sup> Nearly two thirds of decedents suffer from moderate or severe malodorous vaginal discharge (66%) and vaginal bleeding (61%). Among nondecedents, prevalence of mild

**TABLE 1.** Global Burden of Suffering Associated With Cervical Cancer, Measured by the Prevalence of Moderate or Severe Physical, Psychological, Social, and Spiritual Suffering of Patients and Family Caregivers and by the Average Duration of Each Type of Suffering

Type of Suffering	Decedents		Nondecedents		Family Caregivers	
	Prevalence (%)	Duration (months)	Prevalence (%)	Duration (months)	Prevalence (%)	Duration (months)
<b>Physical suffering</b>						
Pain (mild)	96	5	42	7	NA	NA
Pain (moderate or severe)	84	4	30	4	NA	NA
Dyspnea	16	1	6	1	NA	NA
Fatigue	71	5	44	6	NA	NA
Weakness	58	4	37	4	NA	NA
Nausea or vomiting	26	1	20	2	NA	NA
Diarrhea	11	1	20	3	NA	NA
Constipation	37	4	28	4	NA	NA
Incontinence of urine	23	2	28	4	NA	NA
Incontinence of stool	17	2	20	3	NA	NA
Malodorous vaginal discharge	66	5	49	4	NA	NA
Bleeding	61	2	53	3	NA	NA
Dry mouth	31	3	NA	NA	NA	NA
Leg edema	39	3	22	5	NA	NA
<b>Psychological suffering</b>						
Anxiety or worry	63	5	50	8	51	7
Depressed mood	52	5	38	6	28	6
Post-traumatic stress disorder	28	3	27	5	14	3
Confusion or delirium	26	1	NA	NA	NA	NA
Sexual dysfunction	87	6	83	11	NA	NA
Complicated grief	NA	NA	NA	NA	11	7
<b>Social suffering</b>						
Stigma and discrimination	52	4	39	8	13	4
Financial difficulties	84	6	74	9	66	9
Abandonment by intimate partner	46	5	41	9	NA	NA
<b>Spiritual suffering</b>						
Loss of meaning	49	4	27	5	12	4
Anger toward higher power	31	2	21	5	18	4
Belief higher power causing illness	26	3	20	5	17	4

Abbreviation: NA, not applicable.

pain is 42%, moderate or severe pain 30%, moderate or severe malodorous vaginal discharge 49%, and moderate or severe vaginal bleeding 53%. These symptoms contribute to a high prevalence of moderate or severe psychological suffering among both decedents and nondecedents, including anxiety (63% and 50%, respectively), depressed mood (52% and 38%, respectively), and sexual dysfunction (87% and 83%, respectively). Moderate or severe financial distress also is highly prevalent among decedents (84%) and nondecedents (74%) and it affects nearly two thirds of family caregivers (66%). More than half of the decedents and more than a third of nondecedents feel stigmatized or socially isolated (52% and 39%, respectively), and more than 40% are abandoned by their intimate partner (46% and 41%, respectively). Nearly half of the decedents experience loss of meaning in life (49%), and nearly one third suffer a loss of faith (31%). Most patients experience some combination of moderate or severe physical, psychological, social, and spiritual suffering.

In total, more than 3 million people needed palliative care in 2017 because of the effects of cervical cancer: 258,649 decedent women with cervical cancer, an equal number of family caregivers, and 2,558,857 nondecedent women with cervical cancer (Table 2). L-MICs and upper-middle-income countries had the largest number of patients and family caregivers in need of palliative care, and 85% of people in need (more than 2.6 million) were in LMICs. Among the seven World Bank regions, the East Asia and Pacific region had the largest number of people

(patients and their primary family caregivers) in need of palliative care (33% of the global total) followed by the South Asia and sub-Saharan Africa regions (19% and 17% of the global total, respectively). The number of people with each common type of suffering because of cervical cancer is shown in Table 3. Globally, nearly 1 million women with cervical cancer suffered from moderate or severe pain in 2017, 85% of whom were in LMICs. More than 1.4 million suffered from moderate or severe malodorous vaginal discharge, 84% of whom were in LMICs. Nearly 2 million women suffered from moderate or severe sexual dysfunction, and nearly 2 million patients and family caregivers combined suffered from moderate or severe financial difficulties associated with the patient's cervical cancer.

To provide adequate palliative care globally for women with cervical cancer, in 2017, using the WHO essential package of palliative care, we estimated that an inpatient palliative care encounter would have been needed on 22,919 days, an outpatient encounter on 34,586 days, and a home visit on 35,038 days (Table 4). Of the total of 92,543 days when a palliative care encounter would have been needed, 78,576 of these encounters (85%) were needed in LMICs.

## DISCUSSION

To our knowledge, ours is the first quantitative study of the major types, severity, prevalence, and duration of suffering associated with cervical cancer. Our data indicate that women with cervical cancer experience physical, psychological, social, and spiritual suffering that is more prevalent, complex, and severe than the suffering

**TABLE 2.** Number of Decedent and Nondecedent Women With Cervical Cancer, and Their Family Caregivers, Who Needed Palliative Care in 2017, by Country Income Group and Region

Country Income Group or Region	Decedents	Nondecedents	Family Caregivers	People Needing PC—Total No.	%
By country income group <sup>a</sup>					
Low (LICs)	34,065	268,377	34,065	336,508	11
Lower-middle (L-MICs)	96,741	912,766	96,741	1,106,247	36
Upper-middle (U-MICs)	91,998	973,446	91,998	1,157,443	38
High (HICs)	35,845	404,268	35,845	475,957	15
Global	258,649	2,558,857	258,649	3,076,155	100
L&MICs	222,805	2,154,589	222,805	2,600,198	85
By region <sup>a</sup>					
East Asia and Pacific	79,260	862,848	79,260	1,021,369	33
Europe and Central Asia	30,362	322,186	30,362	382,909	12
Latin America and The Caribbean	32,271	312,642	32,271	377,184	12
Middle East and North Africa	4,280	47,080	4,280	55,641	2
North America	8,431	101,475	8,431	118,336	4
South Asia	53,968	487,657	53,968	595,593	19
Sub-Saharan Africa	50,077	424,969	50,077	525,124	17

Abbreviations: HIC, high-income country; LMIC, low-middle-income country; L&MIC, low- and middle-income country; LIC, low-income country; PC, palliative care; UMIC, upper-middle-income country.

<sup>a</sup>World Bank categories.

**TABLE 3.** Number of Decedent and Nondecendent Women With Cervical Cancer and Their Family Caregivers With Each Common Type of Moderate or Severe Suffering in 2017, by Country Income Group and Region (in Thousands)

Type of Suffering	By Income Group						By Region						
	LICs	LMICs	UMICs	HICs	Global	L&MICs	EAP	ECA	LAC	MENA	NA	SA	SSA
Physical suffering													
Pain (mild)	145	476	497	204	1,323	1,119	574	210	227	33	70	350	313
Pain (moderate or severe)	109	355	369	151	985	834	423	155	167	25	52	258	231
Dyspnea	22	70	73	30	195	165	84	31	33	5	10	51	46
Fatigue	142	470	494	203	1,310	1,106	578	212	228	34	71	350	313
Weakness	119	394	414	170	1,097	926	485	177	191	28	60	294	262
Nausea or vomiting	63	208	219	90	579	489	258	94	102	15	32	156	139
Diarrhea	57	193	205	85	540	455	246	90	97	14	31	148	132
Constipation	88	291	307	126	812	686	362	132	143	21	45	219	195
Incontinence of urine	83	278	294	121	776	655	350	128	138	21	44	211	188
Incontinence of stool	59	199	210	87	556	469	251	92	99	15	31	151	135
Malodorous vaginal discharge	154	511	538	222	1,425	1,203	634	232	250	37	78	383	342
Bleeding	152	506	533	220	1,412	1,192	630	230	249	37	78	381	339
Dry mouth	11	30	29	11	80	69	25	9	10	1	3	17	16
Leg edema	72	239	250	103	664	561	292	107	115	17	36	177	158
Psychological suffering													
Anxiety or worry	173	567	592	243	1,574	1,331	684	250	270	40	84	416	372
Depressed mood	129	424	444	182	1,179	997	514	188	203	30	63	313	280
Post-traumatic stress disorder	87	287	301	124	800	675	354	129	140	21	44	214	191
Confusion or delirium	9	25	24	9	67	58	21	8	8	1	2	14	13
Sexual dysfunction	252	842	888	367	2,349	1,982	1,054	385	416	62	131	636	567
Complicated grief	4	11	10	4	28	25	9	3	4	0	1	6	6
Social suffering													
Stigma and discrimination	127	419	439	181	1,166	985	514	188	203	30	63	312	278
Financial difficulties	250	821	858	353	2,282	1,929	997	365	394	58	123	606	541
Abandonment by intimate partner	126	419	441	182	1,168	986	523	191	206	31	65	316	281
Spiritual suffering													
Loss of meaning	93	305	319	131	849	718	369	135	146	21	45	224	201
Anger toward higher power	73	239	250	102	664	562	288	106	114	17	35	175	157
Belief higher power causing illness	68	224	234	96	623	527	271	99	107	16	33	165	148

Abbreviations: EAP, East Asia and Pacific region; ECA, Europe and Central Asia; HIC, high-income country; LMIC, low-middle-income country; L&MIC, low- and middle-income country; LAC, Latin America and Caribbean; LIC, low-income country; MENA, Middle East and North Africa; NA, North America; SA, South Asia; SSA, sub-Saharan Africa; UMIC, upper-middle-income country.

associated with most other serious illness.<sup>8</sup> As a result of inadequate availability of primary prevention, early diagnosis and treatment of cervical cancer, and social problems such as poverty and stigmatization, a disproportionate percentage of patients with cervical cancer and family caregivers in need of palliative care live in LMICs. Yet, access to palliative care to prevent and relieve this suffering also remains rare in LMICs.

Cervical cancer typically leads to multiple types of moderate and severe suffering for a variety of anatomic, physiologic, psychological, and social reasons. For purely anatomic

reasons, pain due to cervical cancer and its treatment is more prevalent and severe than pain because of many other cancers. The pelvic region is highly innervated, and major nerves and nerve plexuses, including the sacral plexus and inferior hypogastric plexus, are located in or near the pelvis. Thus, invasive cervical cancer often injures nerves by invasion or compression resulting in neuropathic pain that is more difficult to control than nociceptive pain.<sup>22</sup> Pelvic nerve injury and neuropathic pain also may result from surgery. In addition, peripheral neuropathic pain is a common adverse effect of paclitaxel and cisplatin, the



**TABLE 4.** Number of Days With a Palliative Care Provider Contact, Including Inpatient Days, Outpatient Encounters, and Home Visits, for Decedent and Nondecedent Women With Cervical Cancer and Their Family Caregivers in 2017, by Country Income Group and Region (in Thousands)

Population in Need of Palliative Care	Location	Average PC Contacts per Year on Average	By Income Group					By Region							
			LIC	LMIC	UMIC	HIC	Global	L&MICs	EAP	ECA	LAC	MENA	NA	SA	SSA
Decedents	Referral hospital <sup>a</sup>	Inpatient PC days (15)	511	1,451	1,380	538	3,880	3,342	1,189	455	484	64	126	810	751
		Outpatient PC encounters (5)	170	484	460	179	1,293	1,114	396	152	161	21	42	270	250
	District hospital	Inpatient PC days (14)	477	1,354	1,288	502	3,621	3,119	1,110	425	452	60	118	756	701
		Outpatient PC encounters (6)	204	580	552	215	1,552	1,337	476	182	194	26	51	324	300
	Community health center	Inpatient PC days (0.25)	9	24	23	9	65	56	20	8	8	1	2	13	13
		Outpatient PC encounters (4)	136	387	368	143	1,035	891	317	121	129	17	34	216	200
		Home PC visits (84)	2,861	8,126	7,728	3,011	21,727	18,716	6,658	2,550	2,711	360	708	4,533	4,206
Nondecedents	Referral hospital <sup>a</sup>	Inpatient PC days (3)	805	2,738	2,920	1,213	7,677	6,464	2,589	967	938	141	304	1,463	1,275
		Outpatient PC encounters (4)	1,074	3,651	3,894	1,617	10,235	8,618	3,451	1,289	1,251	188	406	1,951	1,700
	District hospital	Inpatient PC days (3)	805	2,738	2,920	1,213	7,677	6,464	2,589	967	938	141	304	1,463	1,275
		Outpatient PC encounters (4)	1,074	3,651	3,894	1,617	10,235	8,618	3,451	1,289	1,251	188	406	1,951	1,700
	Community health center	Outpatient PC encounters (4)	1,074	3,651	3,894	1,617	10,235	8,618	3,451	1,289	1,251	188	406	1,951	1,700
			Home PC visits (5)	1,342	4,564	4,867	2,021	12,794	10,773	4,314	1,611	1,563	235	507	2,438
Family caregivers		Home PC visits (two for needed bereavement support)	68	193	184	72	517	446	159	61	65	9	17	108	100
Total inpatient PC days			2,607	8,306	8,532	3,474	22,919	19,445	7,495	2,821	2,820	408	855	4,505	4,015
Total outpatient encounters			3,732	12,404	13,061	5,389	34,586	29,197	11,543	4,322	4,236	629	1,344	6,661	5,851
Total home PC visits			4,272	12,884	12,779	5,104	35,038	29,934	11,131	4,222	4,338	604	1,232	7,080	6,431
Total days with any PC contact			10,610	33,594	34,372	13,967	92,543	78,576	30,169	11,365	11,394	1,640	3,432	18,245	16,297

Abbreviations: EAP, East Asia and Pacific region; ECA, Europe and Central Asia; HIC, high-income country; LMIC, low-middle-income country; L&MIC, low- and middle-income country; LAC, Latin America and Caribbean; LIC, low-income country; MENA, Middle East and North Africa; NA, North America; PC, palliative care; SA, South Asia; SSA, sub-Saharan Africa; UMIC, upper-middle-income country.

<sup>a</sup>Referral hospital: cancer center or general hospital with oncology department.

chemotherapeutic agents used most commonly to treat cervical cancer. Radiotherapy to the pelvis may result in chronic inflammatory or nociceptive pain from vaginitis, cystitis, or proctitis as well as in sexual dysfunction, urinary incontinence, and diarrhea. Obstructive nephropathy and resultant end-stage kidney disease, common sequelae of cervical cancer, may result in dyspnea, pruritus, or delirium and may exacerbate edema and pain. Metal or hard plastic percutaneous nephrostomy drains, used in some places, severely limit patients' mobility and may increase risk of pain, leakage, dependence, and psychological distress. Fatigue and problems with memory and concentration often result from some combination of pain, chemotherapy, kidney disease, and depressed mood.

The high prevalence of psychological and social suffering among both decedents and nondecedents is due at least in part to the emotionally powerful meanings associated with the sex organs and sexual function, both of which are injured or ablated by invasive cervical cancer or its treatment. These meanings are informed by cultural values that often demean women deemed to have an unpleasant bodily odor and those whose sexual function does not reflect the cultural norm.<sup>3,23</sup> In some East Asian cultures, for example, a young woman's status in society and personal identity may depend heavily on the ability to bear children, which often is destroyed by cervical cancer or its treatment.<sup>24</sup> Women with both HIV infection and cervical cancer may be doubly stigmatized and at highest risk for psychological, social, or spiritual suffering.

WHO defines palliative care as care that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.<sup>25</sup> In our view, the essence of palliative care is prevention and relief of suffering, and the problems associated with life-threatening illness also may occur with non-life-threatening conditions. For example, women with early-stage, curable cervical cancer may suffer from abandonment, depression, or treatment-related acute pain, and long-term cervical cancer survivors may suffer from chronic pain. The specific types and severity of suffering vary by geopolitical situation, socioeconomic conditions, culture, and accessibility of disease prevention and treatment.<sup>26</sup> People in LMICs typically experience less healthy social conditions and greater morbidity and mortality than people in HICs, yet they typically have less access to disease prevention, diagnosis, and treatment. Palliative care should never be considered a substitute for these, but it is imperative that palliative care be universally accessible.<sup>26-28</sup>

Our measure of necessary palliative care intensity (days-when-a-palliative-care-encounter-is-needed) refines the measure used by the Lancet Commission on Palliative Care

and Pain Relief (days-in-palliative care).<sup>8</sup> Some patients may require a palliative care encounter every day, whereas others may require only one encounter per month. By the previous measure, a patient receiving palliative care once per month for 1 year would have 365 days in palliative care but only 12 days with a palliative care encounter. Thus, days-in-palliative-care is an inaccurate measure of needed palliative care intensity and is not useful for estimating human resource needed. Days-with-a-palliative-care-encounter is a more accurate and useful measure.

Our study has several limitations. First, our literature review was limited to papers in English, French, and German that reported quantitative or qualitative data on the types, severity, prevalence, or duration of suffering associated with cervical cancer. However, among the English-language papers that met these criteria, 10 were from China and four were from countries whose official language is Spanish. In addition, our PubMed search revealed only five such papers in the other four official languages of the United Nations, three in Chinese, and one each in Russian and Spanish. Furthermore, our expert panel included members from countries whose official languages are Russian, Spanish, Arabic, French, Farsi, and Vietnamese. Thus, we believe that our research reflects the global situation. Our literature review revealed a large publication bias in that the majority of data on the types, severity, prevalence, and duration of suffering associated with cervical cancer came from HICs, whereas the majority of suffering patients are in LMICs. In addition, the studies used various methods, and although we did not systematically review each published study for bias, some contained various degrees of selection, recall, or other biases. We addressed these problems by conducting a modified Delphi process with an expert panel from each WHO region and from countries of all income classifications. Delphi studies themselves are limited in that they rely on expert opinion. But, we believe our method produced the most reliable data to date on the suffering of a highly vulnerable population.

The scarcity of quantitative data on the suffering of women in LMICs with cervical cancer and other gynecologic cancers reflects a morally indefensible neglect of this vulnerable population. Our study provisionally fills this massive gap in knowledge with expert opinion, but rigorous quantitative study of this palliative care need is crucial.<sup>8</sup> As with all studies of highly vulnerable and seriously ill patients, short but clinically and ethically well-crafted, locally validated tools are needed to assess clinical outcomes of patients who receive any type of palliative care and those who do not. Although measures of outputs such as opioid accessibility and palliative care training programs are useful, they are never an adequate substitute for measures of patient outcomes such as quality of life, degree of pain control, or presence of depression. Because the specific types and severity of suffering vary, studies in different

settings are needed to guide development of optimum palliative care services for any given population.<sup>6,20</sup> Implementation science studies of integration of palliative care into healthcare systems at all levels, as urged by WHO, are necessary to make services for women with cervical cancer more integrated and people-centred.<sup>29</sup> In light of the particularly high prevalence in this population of severe pelvic pain, humiliating malodorous vaginal discharge, anxiety, depression, sexual dysfunction, financial difficulties, and spiritual distress, these problems should be the focus of intensive research on optimum palliative care in LMICs. Further research on task shifting to improve access to mental health care, including treatment of depression and PTSD in patients with cervical cancer and other serious and severely troubling illnesses, is also needed.<sup>30,31</sup>

In conclusion, the suffering of women with advanced cervical cancer, an illness mainly of the global poor, has been largely ignored by scientific research. By reviewing

the available literature and supplementing it with expert consensus, we found that the suffering of this population appears to be more prevalent, severe, and multifaceted than that associated with other cancers. Severe pelvic pain, malodorous vaginal discharge, sexual dysfunction, psychological distress, and financial insecurity are particularly prevalent. The high burden of suffering borne by women with cervical cancer makes it medically and morally imperative that there be universal access to HPV vaccination, screening, and treatment and that appropriate, effective, affordable, people-centered palliative care be integrated into all levels of systems of care for women with cervical cancer. This integration will require vigorous efforts from researchers, public health officials, oncologists, gynecologists, and primary care providers and should be part of the overall integration of palliative care into healthcare systems that is indispensable for achievement of universal health coverage.<sup>27</sup>

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