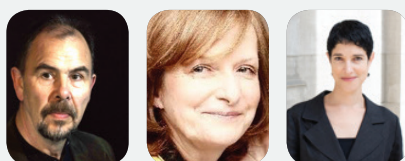


The Commonwealth and cervical cancer: Time for collective action

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A significant proportion of deaths from cervical cancer occur in Commonwealth countries where the effectiveness of strategies to prevent or treat the disease is variable, particularly in the low- and middle-income member countries. The global campaign to eliminate cervical cancer provides the Commonwealth with a unique opportunity to act collectively in the prevention, treatment and research of cervical cancer.

The Commonwealth is a voluntary association of 53 independent countries that work together to pursue common goals promoting development, democracy and peace. It has a combined population of 2.4 billion; equivalent to around one third of the global population. Significantly for cancer control, the Commonwealth is a heterogeneous, multicultural, multilingual grouping that includes both advanced and developing economies, encompasses every climate and continental region (Africa: 19 countries; Asia: 7; the Caribbean and Americas: 13; Europe: 3; and the Pacific: 11) and the extremes of topography and demography. In its councils, the Pacific nation of Nauru, the smallest Commonwealth member country, with a population of about 10,000, has the same voting power as India, its most populous member country with over 1.2 billion people.

Cervical cancer is a mostly preventable disease and its elimination is generally regarded as “low-hanging fruit” in discussions around Sustainable Development Goals. Nevertheless, in 2018, 13 women died every hour in the Commonwealth from cervical cancer and over 425,000 women were living with cervical cancer. Commonwealth member countries carry a 34% share of the global cervical cancer incidence burden (191,685 new cases) and 38% of global cervical cancer mortality (118,708 deaths). Globocan estimates indicate that by 2030 the Commonwealth’s share will have increased to 38% of global incidence (265,627 new cases) and 42% of global mortality (168,012 deaths (1).

The principal cause of most cases of cervical cancer is infection with oncogenic human papilloma virus (HPV). HPV infection is transmitted through skin to skin contact, which includes most sexual activity for men and women. Infected cells lining the cervix gradually develop pre-cancerous lesions

that later may turn into cancer. There are around 200 different types of HPV virus, of which 15 types are classified as high risk for cancers (HR-HPV type). Of all the HR-HPV types HPV16 and HPV 18 are the most commonly associated with invasive cervical cancer (2) and are responsible for about 70% of all cervical cancer cases worldwide. There is growing evidence of HPVs also being a relevant factor in other anogenital cancers (i.e., anus, vulva, vagina and penis) as well as head and neck cancers.

After infection with HPV the most common risk factors for cervical cancer are a weakened immune system and smoking. The immune system is important in destroying cancer cells and slowing their growth and spread. Human immunodeficiency virus (HIV) damages a woman’s immune system and puts them at higher risk for HPV infections. In women with HIV, a cervical pre-cancer might develop into an invasive cancer faster than it normally would.

Women in Commonwealth countries with high prevalence of HIV – for example, South Africa, Tanzania and Zambia (3,4,5,6,7) – are therefore especially at risk and this is reflected in their higher age-standardized incidence and mortality rates from cervical cancer.

Smoking is also a risk factor for the development of cervical

RISK FACTORS FOR CERVICAL CANCER

- HIV infection
- Weakened immune system (HIV)
- Smoking
- STDs (Chlamydia, Herpes simplex)
- Age <17 at first full term pregnancy
- Multiple sexual partners
- Multiple pregnancies
- Diet low in fruit and vegetables
- Overweight

cancer. Women who smoke are about twice as likely as non-smokers to get cervical cancer while the time since quitting is associated with a two-fold reduced risk (8). Tobacco by-products have been found in the cervical mucus of women who smoke (9). Researchers believe that these substances damage the DNA of cervix cells and may contribute to the development of cervical cancer (10). Other risk factors include chlamydia infection, a diet low in fruit and vegetables, excess weight and having multiple pregnancies. If a woman is younger than 17 years at first pregnancy, she is also more inclined to developing cervical cancer later in life than women who have waited to get pregnant until they were 25 years or older (11).

Cervical cancer incidence and mortality in the Commonwealth

Cervical cancer is the fourth most frequent cancer in women, with an estimated global incidence of 569,847 new cases in 2018 and – most critically for domestic family budgets – the second most frequent female cancer in the 16–49 year age range. In that year 1,474,265 women were living with cervical cancer (five-year prevalence). Cervical cancer is also the fourth most frequent cause of cancer deaths in women. Globocan 2018 reports 311,365 deaths from cervical cancer worldwide; more than 85% of which occurred in low- and middle-income countries (1).

The Globocan 2018 data presented in Table 1 shows that within the Commonwealth cervical cancer is the leading female cancer in 10 member countries, the second-most common female cancer in 16 member countries, and the leading, or second-highest cause of death from cancer, in females in 29 member countries. The five Commonwealth member countries with the highest number of cervical cancer cases and deaths are India, Nigeria, Tanzania, Bangladesh and South Africa. The data reveals the strong association between national wealth and cervical cancer. Of the 26 Commonwealth countries where it is the leading or the second-most common female cancer, none are classified as high-income countries by the World Bank and only seven as “Upper-Middle Income”. The same pattern applies to mortality. Of the 29 Commonwealth member countries where cervical cancer is either the leading or the second-most common cause of female cancer deaths, only one is a high-income economy and seven are upper-middle income countries. The Globocan data suggests that the Commonwealth’s incidence of cervical cancers will rise by 38% in the 13 years between 2018 and 2030 in line with population growth, and that the number of deaths from cervical cancer will increase by 42% (from 118,708 p.a. to 168,012 p.a.) in the same period. These total figures mask the wide disparity between the increases predicted for the high-income countries (e.g., the UK’s 13% increase in mortality) and that expected in

the lower-middle and low-income countries (Nigeria 45% and Mozambique 47% respectively).

Prevention of cervical cancer

There are two ways cervical cancer can be prevented: 1) by immunizing girls, boys and young women at an early age against the infections that can cause premalignant lesions that may develop into malignancy and 2) by finding and destroying the precancerous lesions before they can become cancerous. The first strategy calls for vaccination with corresponding community education and social mobilisation as key components to enhance uptake; the second for screening and treatment of precancerous lesions (“screen and treat”) across the life course of the women. The most efficient formula for cervical cancer prevention (P) is a combination of the two strategies: Vaccination (V) plus Screen and Treat (ST), or P= V + ST.

➔ Primary prevention of cervical cancer by vaccination (V)

Human papilloma virus (HPV) infection through skin to skin contact – predominantly sexual – is the principle cause of almost all cervical cancers, with HPV 16 and HPV 18 being linked to 70% of all cervical cancers. There are three barriers to eliminating cervical cancer by vaccination:

- 1) Politics: Historically, resource allocation on LMIC health agendas has been skewed towards communicable diseases, maternal and neonatal mortality and nutritional poverty rather than non-communicable diseases (NCDs), such as cancer.
- 2) Uninformed or misinformed public and professional knowledge about cervical cancer and a low level of awareness about the dangers of HPV infection and how it can be prevented. Five common issues have been identified: medical misconceptions about the HPV vaccination; fear of the unknown; need for prior desensitisation to resolve cultural barriers; a rural-urban divide in health awareness; and economic concerns associated with access to the HPV vaccination.
- 3) Cost - The cost of HPV vaccines and of immunization: HPV vaccines are available to GAVI countries and to all PAHO member countries in the Caribbean and Americas region at a discount through the PAHO Revolving Fund, although for some of the Commonwealth’s small countries this price may still be unaffordable. Additional costs – of storage, transportation, delivery and promotion – are also incurred.

➔ Secondary prevention of cervical cancer by screening and treatment of precancerous lesion (ST)

Prevention by screening and treatment is possible because cervical cancer is preceded by a long latent period when

Table 1 : Cervical Cancer Incidence, Mortality and Prevalence 2018 – 2030

	World Bank	Incidence	Cervix Ca	Incidence	Est. 2018	Deaths	Cervix Ca	Deaths
	Class 2018	2018	rank	2030	Prevalence	2018	rank	2030
Australia	HI	924	13	1,047	3,438	331	16	410
Bahamas	HI	29	4	35	85	23	2	30
Bangladesh	LMI	8,068	2	11,481	17,702	5,214	3	7,629
Barbados	HI	38	4	43	106	27	3	33
Belize	UMI	46	2	68	122	25	1	37
Botswana	UMI	333	1	479	852	166	1	249
Brunei	HI	52	4	66	168	14	4	21
Cameroon	LMI	2,356	2	4,998	4,566	1,546	2	2,333
Canada	HI	1,434	13	1,586	5,049	586	15	714
Cyprus	HI	45	11	55	143	18	14	24
eSwatini (formally Swaziland)	LMI	380	1	539	774	238	1	351
Fiji	UMI	124	2	145	354	94	2	121
Gambia	LI	184	1	284	310	132	1	208
Ghana	LMI	3,151	2	4,761	6,857	2,119	1	3,235
Guyana	UMI	124	2	150	298	64	1	81
India	LMI	96,922	2	128,291	225,689	60,078	2	81,113
Jamaica	UMI	486	3	569	1340	361	2	452
Kenya	LMI	5,250	2	8,335	10,963	3,286	1	5,478
Lesotho	LMI	477	1	595	876	346	1	430
Malawi	LI	4,163	1	6,621	7,770	2,879	1	4,587
Malaysia	UMI	1,682	3	2,402	4,898	944	4	1,436
Malta	HI	11	16	12	34	7	22	9
Mauritius	UMI	120	3	147	342	56	3	75
Mozambique	LI	4,291	1	6,308	6,965	3,376	1	4,956
Namibia	UMI	236	2	344	544	135	1	200
New Zealand	HI	190	12	214	677	72	17	88
Nigeria	LMI	14,943	2	21,528	29,601	10,403	2	15,085
Pakistan	LMI	5,601	3	8,075	11,659	3,861	3	5,621
Papua New Guinea	LMI	1,024	2	1,406	2,075	663	2	931
Rwanda	LI	1,304	1	2,048	2,410	921	1	1,472
Saint Lucia	UMI	15	3	18	40	12	2	16
Samoa	UMI	10	6	12	27	6	5	7
Sierra Leone	LI	299	2	431	474	242	2	350
Singapore	HI	429	7	697	1,318	208	8	313
Solomon Islands	LMI	55	2	78	114	39	1	55
South Africa	UMI	12,983	2	16,240	34,170	5,595	1	7,322
Sri Lanka	LMI	1136	2	1404	3183	643	2	844
Tanzania	LI	9,772	1	15,213	19,332	6,695	1	10,449
Trinidad and Tobago	HI	140	4	156	414	97	2	120
Uganda	LI	6,413	1	10,342	12,337	4,301	1	6,961
United Kingdom	HI	3,430	12	3550	12,575	1,033	17	1,169
Vanuatu	LMI	21	2	28	46	13	2	17
Zambia	LMI	2,994	1	4,826	6,407	1,839	1	2,980
		191,685		265,627	437,104	118,708		168,012
% increase 2018 - 2030				38.5				42
WORLD		569,847		691,129	1,474,265	311,365		394,561
Commonwealth % of World totals		34%		38%	30%	38%		43%

persistent HPV infection leads to the development of asymptomatic precancerous lesions. Left untreated or undetected, these precancerous lesions may develop into cancer over a 5 – 30 year period whereas, if detected, they can be removed, preventing the development of cancer in the future and saving costly interventions. Systematic screening of women with an organized population-based approach has contributed to the reduction in cervical cancer incidence by up to 80% in developed countries.

Precancerous lesions can be detected by (i) performing cytological (Pap) smears; (ii) visual inspection with ascetic acid (VIA); or (iii) HPV testing. While all three modalities are considered by WHO to be “very cost-effective interventions” or “Best Buys” (13), WHO does not recommend starting or scaling-up cytology-based screening in countries that have not yet done so. Rather, the emphasis is on HPV as the primary screening modality, although costs are currently prohibitive in many countries. Screening levels remain variable throughout the Commonwealth and dependent on the availability of resources and infrastructure. Screening and pre-cancer treatment algorithms are being optimized (14,15) in many countries with the availability of HPV testing, the known difficulties with accuracy and quality assurance for VIA (12) and challenges in taking VIA as a primary screen, and cryotherapy as the primary pre-cancer treatment method to scale.

Most high-income Commonwealth member countries have population-based screening programmes, with Australia recently replacing cytology with HPV DNA detection tests to screen women aged 25 to 74 years every five years and New Zealand and the UK following in this direction. A recent report predicts that in the coming two decades Australia could eliminate cervical cancer as a major public health issue, which the authors suggest is the same as the accepted annual incidence for a “rare” cancer, that is <4 cases/100 000 per year, by 2021-2035 (16).

Elsewhere, screening coverage is variable. Although the Commonwealth member countries in the Caribbean and Latin America region have all implemented opportunistic conventional cytology-based cervical cancer screening programmes, screening has achieved limited success there due to the lack of an organized population-based approach, poor quality control and low population coverage. Despite its lack of resources, Belize has demonstrated that screening for cervical cancer and precancerous lesions can be combined with delivering STD counselling. India shares one-fourth of the global burden of cervical cancer. The Fourth National Family Health Survey (NFHS-4) (17), a nationally representative survey including 699,686 Indian women aged 15–49 years that was conducted at the district level during 2015–2016 found

that lifetime cervical cancer screening prevalence was low (29.8%) and varied by geographic region, ranging from 10.0% in the Northeast Region to 45.2% in the Western Region.

Opportunistic screening programmes provide free Pap smear services to the women at all the public health facilities in Malaysia and at the women’s wellness clinics in Sri Lanka. In South Africa, the national programme has had little impact on disease burden; by 2014 it had reached only 14% of the target population. In comparison, a screening pilot study has been successfully scaled-up to 75 government-run health facilities across Zambia’s 10 provinces and supported by rigorous quality assurance.

Treatment of cervical cancer

Treatment for invasive cervical cancer is dependent on ‘Stage’ as defined by the International Federation of Gynaecology and Obstetrics (FIGO). For Stage 1A cancers, surgery is the preferred treatment. 74% of cervical cancer cases will need this modality at some point in the management pathway (18). Current capacity and capability for delivering the range of pelvic procedures that are required to manage cervical cancer from a surgical perspective varies widely across Commonwealth countries.

For high-income populations in some upper middle-income member countries, surgical availability and outcomes mirrors that found in the high-income countries. However, this only covers some 6% of women with cervical cancer in Commonwealth countries. For the remainder, access remains both geographically and financially poor (19), reflecting the reality that women with cervical cancer need to travel an average of 100km to access a health facility capable of carrying out a surgical biopsy, a major contributor to late presentation (20,21). In many Commonwealth LMICs a scarcity of appropriately trained pelvic surgeons, the shortage of operating rooms, and a low operating volume can conspire to deliver an often unsafe surgical environment (22).

For Stage 1 tumours greater than 4cms in size and for all other Stages, the standard primary treatment is concurrent chemotherapy and radiation, although for Stage 4, disease treatment is determined by performance status. Several challenges to the equitable provision of radiotherapy services in LMI Commonwealth countries have been identified, with many populations having little or no access to publicly-funded radiotherapy services. These general barriers to the provision and delivery of radiotherapy include the lack of: adequate human and financial resources; equipment that meets IEC standards or equivalent national device standards; preventive maintenance and repair contract and funds and quality assurance (QA) equipment, treatment planning systems and simulation equipment for assuring

Figure 1: Reports of research published in 2016 relevant to cervical cancer control in Commonwealth member countries, listed by institutional/country affiliation of first authors

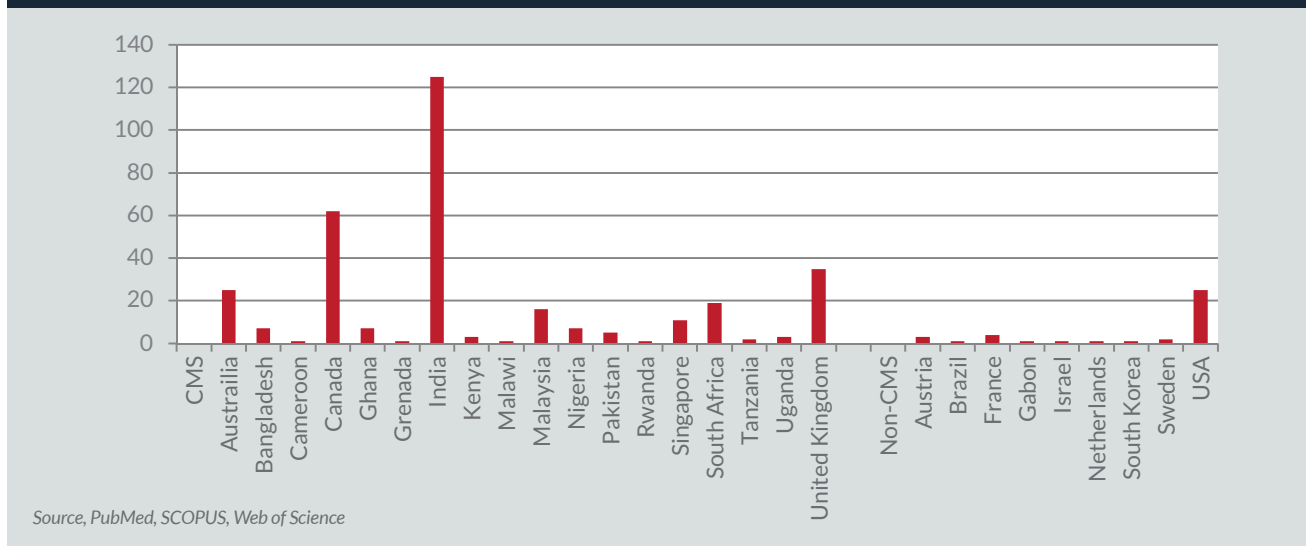
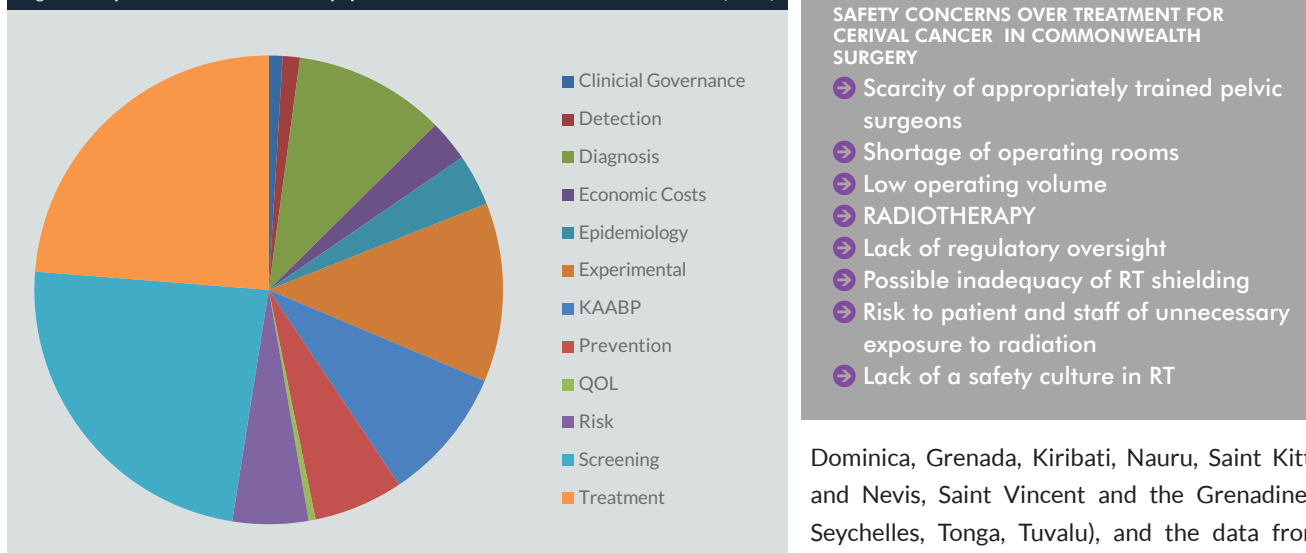


Figure 2: Topics addressed in research papers on cervical cancer in the Commonwealth (2016)



optimized radiotherapy treatments. There is concern over the availability of brachytherapy equipment in countries with no regulatory authority as the IAEA Code of Conduct on the Safety and Security of Radioactive Sources (23) would prevent the exportation of sources to countries without adequate regulatory oversight. In some countries the lack of regulatory authority with expertise in authorization and inspection of radiotherapy may be putting the patient, worker and public at risk to unnecessary exposure to radiation.

Cervical cancer research in the Commonwealth

Epidemiological data from population-based registries and scientific data from clinical trials and studies are two of the foundation stones of evidence-based cancer control. The International Agency for Research on Cancer’s Globocan 2018 database does not include data from 10 Commonwealth small countries with LMI economies (Antigua and Barbuda,

Dominica, Grenada, Kiribati, Nauru, Saint Kitts and Nevis, Saint Vincent and the Grenadines, Seychelles, Tonga, Tuvalu), and the data from some of the remaining 43 Commonwealth

countries that are presented in Table 1 may be underpowered. An African Cancer Registry Network (24) has been established to improve the effectiveness of cancer surveillance in sub-Saharan Africa by providing expert evaluation of current problems and technical support to remedy identified barriers, with the long-term goal of strengthening health systems and creating research platforms for the identification of problems, priorities, and targets for intervention. AFCRN works with cancer registries in Botswana, The Gambia, Ghana, Kenya, Malawi, Mauritius, Mozambique, Namibia, Nigeria, Seychelles, South Africa, Swaziland, Uganda, and Zambia and acts as the African Regional Hub for cancer registration as part of IARC’s Global Initiative for Cancer Registry Development in Low and Middle Income Countries framework.

The incomplete and of variable quality of the data reported by their cancer registries is compounded by the difficulties in retrieving reports of cancer research conducted in low-

or middle-income Commonwealth member countries. An electronic search of four bibliographic databases (Pubmed, Embase, African journals Online and WHO's African Index Medicus) conducted in 2017 by INCTR UK for evidence published between 2000 and 2016 relevant to cervical cancer and other HPV-linked cancers in sub-Saharan Africa identified 1,656 reports of research, of which 1,414 (85%) reports related to populations or patients in African Commonwealth countries (25). A second sample search of PubMed; SCOPUS and Web of Science, for reports of cervical cancer research relevant to Commonwealth members published in 2016 (the most recent complete year) identified 370 reports from 18 Commonwealth countries and 9 non-Commonwealth countries (Figure 3), of which 45 reports (12%) were by first authors located in African countries.

The most frequently researched topics were Screening (100 publications) and Treatment (100 publications) Experimental medicine (52 publications, of which 36 had first authors in India), Diagnostics (44 publications) and Prevention (26 publications). Knowledge, Awareness, Attitude, Behaviour and Practice (KAABP) issues relating to cervical cancer were addressed in 39 publications (Figure 4). Twelve papers considered cost and resource management in the management of cervical cancer, but only two papers looked at the quality of life of patients receiving treatment for cervical cancer.

Discussion

Because the majority of cervical cancers start with pre-cancerous changes caused by HPV infection, the high mortality rate from cervical cancer can be reduced through a comprehensive approach that includes prevention, early diagnosis, effective screening and treatment programmes. For the foreseeable future, cervical cancer prevention will require both HPV vaccination and screening, providing opportunities to improve primary healthcare systems and reduce cancer disparities (26). Allocation of resources and the provision of skilled healthcare professionals are essential for effective cervical cancer control. Included in the package of care should be access to HPV vaccination for girls aged 9–12 years. Similarly, screening programmes should be initiated for women over 30 years, aiming for the widest coverage and ensuring that all women with abnormal cytologies be offered either further assessment or treatment with follow-up. Zambia's successful roll out of screening serves as an example of achievement through political will.

Surgery and radiotherapy are essential components of effective cancer treatment; it is not possible to offer comprehensive cancer care without them. The increase in the number of women screened for cervical cancer is driving a huge demand that is not being matched by investment in

the surgical supply side to manage both malignant disease and benign pelvic pathology that is incidentally picked up (27). 80% of Commonwealth cervical cancer patients require radiotherapy as part of their treatment protocol (28). Health systems in LMI Commonwealth countries do not yet have adequate RT facilities to provide these services.

Policy-makers require reliable evidence in order to make informed decisions (29). Without reliable and robust data from population-based registries, Health Ministries cannot know whether their vaccination and screening programmes are succeeding or failing. Similarly, progress in healthcare is based on the evidence from painstaking and rigorous research that provides an insight into the impact of interventions on specific communities where country-level data disaggregation has formerly been poor. Its size, geographical spread, economic diversity and heterogeneous genetic composition gives the Commonwealth unique advantages in research into the causes of cancer and various strategies for its control, in different healthcare settings and as the testing ground for anticancer policies and treatments (30).

The identification of 370 reports published in one year provides a helpful freeze-frame picture of what was being researched in the area of cervical cancer at the time, but it cannot begin to represent the full magnitude of the Commonwealth's contribution to research in this area. A more substantial body of reports of scientific research studies relevant to the populations of low- or middle-income Commonwealth countries lies scattered across the international literature in a multitude of regional databases, online journals and libraries; a large reservoir of scientific wealth generally unread and unreferenced because it is expensive to find in terms of time and cost. Ignorance is not strength. Creating and sharing a knowledge base of the research conducted across the Commonwealth into the prevention and treatment cervical cancer is a prerequisite for evidence-based cancer control. Healthcare interventions and policy strategies that prove to be effective across the diversity of the Commonwealth member countries offer gains for the global economy.

Conclusions

In his Call to Action to Eliminate Cervical Cancer on 19 May 2018, WHO Director-General Dr Tedros Adhanom Ghebreyesus emphasized that most women who die of cervical cancer live in the low- or middle-income countries that are the least prepared for managing the increasing burdens of cancer and other non-communicable diseases. Collective action by the Commonwealth countries to address the deficits outlined in this article will represent a good investment by governments, given the impact of cervical cancer on premature death and disability, with its long-lasting

“Cervical cancer strikes women in the prime of life. These women are raising children, caring for their families and contributing to the social and economic fabric of their communities. Nine in 10 women who die from cervical cancer are in poor countries. This means some of the most vulnerable women in our world are dying unnecessarily. That cannot be fair or just. But it doesn’t have to be this way. Cervical cancer is one of the most preventable and treatable forms of cancer, as long as it is detected early and managed effectively.”

Call to Action to Eliminate Cervical Cancer
Dr Tedros Adhanom Ghebreyesus, WHO Director-General
 19 May 2018

social, financial and economic consequences for the affected women, their immediate families and their wider community. The establishment of a Commonwealth Cancer Fund would be a useful innovation.

Addressing the issue of cervical cancer can illuminate the way to move forward and to protect health systems from the high expense and ravages of malignant diseases. This is a unique leadership opportunity for the Commonwealth to act as a global and regional catalyst for pulling together major stakeholders involved in the fight against, not just cervical cancers, but all cancers. If taken, it will have an impact extending far beyond the boundaries of its member countries. ■

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Therese Lethu is a global health specialist with more than 25 years of experience working with organizations such as WHO, the Global Business Coalition (GHHealth) and the French Ministry of Foreign Affairs, with a focus on Africa. Thérèse’s expertise is very much related to helping fight non-communicable diseases, especially cervical cancer, as one of the most preventable forms of cancer. She founded a Swiss-based NGO, Global Health Objectives, to advocate for accelerating the elimination of cervical cancer according to the global strategy of WHO.

Dr Ophira Ginsburg is a medical oncologist and global women’s health researcher with technical and policy expertise in non-communicable diseases prevention and management. She is the Director of the High-Risk Cancer Genetics Program and Associate Professor in the Section for Global Health, Department of Population Health at New York University School of Medicine. Formerly based at the University of Toronto, from 2015 to 2016 she was a Medical Officer at WHO, and continues to serve as a consultant to several UN agencies, providing technical assistance to Member States on national cancer control planning and policies. She is leading a new study funded by the US National Institutes of Health (“Cancer Moonshot” programme), to improve access to cancer genetics services through primary care clinics in the New York area.

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