ISSUES PAPER

CANCER TREATMENT AND CARE IN DEVELOPING COUNTRIES

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Pioneering Healthcare Solutions in the Developing World

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FACTS AND FIGURES

In 2008, it was estimated that more than 12 million new cases of cancer were identified worldwide, with around 7.6 million people dying of the disease *(1).* At current rates of growth these figures could rise to around 20 million new cases and 13 million deaths a year by 2030 *(2).* While the common assumption is that cancer mainly affects people in high-income countries, the reality is that more than half of all new cases – and over 60% of the deaths – now occur in the poorer regions of the world, where cancer is now one of the leading causes of death *(3)*.

Cancer now kills more people each year in developing countries than either AIDS, tuberculosis or malaria. The individual risk of developing cancer is still higher in industrialised countries than in the developing world. But the gap is closing as more and more people in low- and middle-income countries[1] move to towns and cities and adopt unhealthy modern lifestyles characterised by high fat and low-roughage diets, too little exercise, drinking alcohol, smoking and obesity. Furthermore, people in developing countries are tending to live longer, and the chance of developing cancer increases with age. However, more than one in four cancers in the developing world is not related to lifestyle but is linked to chronic infection. By comparison, less than one in twelve cancers in the developed world is infection-related *(4).* For example:

* Around 80% of liver cancer cases, which are strongly associated with hepatitis B and C viruses, occur in the low- and middle-income countries. In developing countries, more than half of liver cancer cases are associated with hepatitis B, despite the fact that there is an effective vaccine against this virus *(5).*

* Stomach cancer, caused in the majority of cases by the bacterium *helicobacter pylori*, is one of the commonest cancers in low- and middle-income countries, especially Asia. China alone accounts for 42% of cases. In the developed world access to screening and antibiotics has contributed to an 80% decline in stomach cancer over the past 50 years *(6).*

* AIDS has exacerbated the situation by increasing people's susceptibility to infection as their immune systems falter. Kaposi sarcoma, caused by the herpes virus, is the commonest cancer among men in sub-Saharan Africa *(7)*, for example, and there has been a 40-fold increase in this cancer among Uganda's children since the AIDS epidemic began. The rising incidence of cervical and colorectal cancers associated with the human papilloma virus (HPV) in sub-Saharan Africa has also been attributed to the AIDS epidemic *(8)*, as has a sharp increase in cancers of the lymphatic system among black gold miners in South Africa. However, in places where antiretroviral treatment for HIV is widely available, the incidence of these cancers declines *(9)*.

80% of patients in developing countries already have incurable disease when they are first diagnosed *(10)*

A wide disparity in death rates

In the developing world cancer is a silent crisis. It goes largely unreported, and elicits little of the attention it deserves from health authorities preoccupied with other pressing health problems. Efforts at prevention and early detection are extremely limited, as are diagnostic and treatment services. Moreover, lack of awareness means that the great majority of

[1] Low income countries are those with annual GNP per capita of less than $765 US. Middle income countries are those with annual GNP per capital of less than $9300 US. *(11)*

people do not seek medical help until their cancer is incurable. Survival rates are therefore exceptionally poor, compared with the developed world. By 2020, for example, cancer is expected to kill more than twice as many people worldwide as it did at the turn of the millennium -- but in low- and middle-income countries the death rate will be more than five times greater than in the industrialised world.

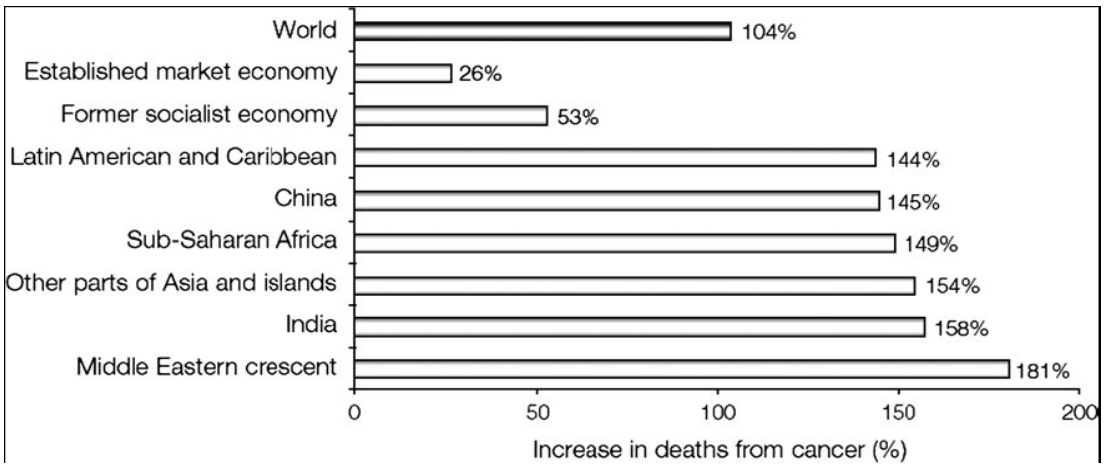

Figure 1: Predicted changes in the mortality of cancer by the year 2020 *(12)*

The commonest cancers

In low- and middle-income countries the three most commonly diagnosed cancers in men are lung, stomach and liver, and in women they are breast, cervix and stomach.
Most of Axios's work thus far has been in the field of women's cancers. This paper will focus on cancer of the breast and cervix, where the organisation has gained special insights and expertise.

Breast cancer

In 2007, there were 593,233 new cases of breast cancer in the developing world – just under half of all new cases that occurred worldwide *(13)*. The lifetime risk of developing breast cancer is still highest in the developed world – particularly the US, Australia, and northern and western Europe – and lowest in parts of Asia and Africa. But over the past 25 years the incidence rates have been rising in low- and middle-income countries, where it is now the most commonly diagnosed cancer in women and the second leading cause of cancer death among women *(14).* Reports from sub-Saharan Africa suggest that breast cancer in men is not as rare as generally assumed, with rates of 4% of patients in Uganda and 6.7% in Tanzania being males, compared to about 1% generally in Europe and the USA *(15).*

Every hour of every day in 2007, nearly 30women in the developing world are estimated to have died of breast cancer.

It is not clear why incidence should be rising in the poorer regions of the world, though longer life expectancy could be an important factor as a woman's risk of breast cancer increases with age. The adoption of modern, urbanised lifestyles could also be significant, as poor diet, physical inactivity and obesity, as well as daily consumption of alcohol are known to play a part in breast cancer. Women who choose not to breastfeed their babies, postpone childbearing until they are over 30 or who remain childless are also at increased risk *(16).*

Early detection is the single most important factor in surviving breast cancer as it is easier and less costly to treat than advanced disease and there are more options. In the USA, for example, 98% of women whose breast cancer is diagnosed and treated early are still alive 5 years later, compared with 84% of women whose disease has spread to the lymph nodes before treatment starts, and 28% of those whose cancer has spread to distant organs *(17).* Many developing countries cannot afford mass screening programmes with mammography, but lack of public knowledge and awareness among doctors also mean that many women are not diagnosed till their breast cancer is advanced. Evidence from Africa and Asia shows that treating late stage breast cancer is up to 9 times more costly than treating early disease *(18).* In sub-Saharan Africa around 32% of women diagnosed with breast cancer are still alive five years later, compared with 81% of such women in the USA *(19).*

Cervical cancer

Cervical cancer is the second most commonly diagnosed cancer and the leading cause of cancer deaths in women in the developing world *(20)*. Public health screening programmes using the Pap smear test have cut the incidence of cervical cancer dramatically in the developed world because it is detected and treated early, often in the precancerous stage. Limited screening in the poorer regions of the world means that they account for over 80% of all new cases. In 2007, an estimated 473,430 women in developing countries were diagnosed with the disease *(21).*

Coverage of cervical screening in developing countries together averages 19%, compared with 63% in the developed world *(22)*

The incidence of cervical cancer in the developing world as a whole is 30 per 100,000 women. But this figure masks wide variations – the disease affects 69 per 100,000 women in Tanzania, 55 per 100,000 in Bolivia, and 25 per 100,000 in Cambodia, compared to 10 per 100,000 in the USA and Europe *(23, 24)*.

The main cause of cervical cancer is infection with the human papilloma virus (HPV), a sexually transmitted organism that destroys the regulatory machinery within the cells of the cervix, and which is extremely common among sexually active individuals. However, the infection usually clears up spontaneously within a few years, and only a small percentage persists and progresses to cancer. Of the 40 or so types of HPV known to infect the genital tract, 15 have been found to put women at significant risk for cervical cancer -- with just two types, HPV 16 and 18, responsible for over 60% of cases *(25).*

Cervical cancer is one of the easiest cancers to treat successfully if it is diagnosed early – and particularly if abnormal cells are detected before they become cancerous. The five-year survival rate for women in the USA who receive treatment early is 92%. But in Africa, where the majority of women do not discover they have cervical cancer until the disease is advanced, fewer than 3 in 10 patients are still alive five years after their diagnosis. In the developing world as a whole, more than 272,000 women died of this disease in 2007, while in the developed world there were around 42,000 deaths from cervical cancer *(26).*

THE CHALLENGES

Cancer is a low priority in the developing world where health services are generally set up to treat infectious diseases, which are the greatest burden, rather than to manage chronic conditions. A 2002 survey by the World Health Organization (WHO) of 167 countries showed that less than half – and only 15% in sub-Saharan Africa – had cancer policies or plans in place. And everywhere except Europe and the Americas implementation of such plans as did exist was poor, with less than a third of countries in Africa and less than half in South-East Asia having national guidelines for prevention and management of cancer *(27)*.

Only 5% of global resources for cancer are spent in the developing world *(28)*.

Most countries have very poor understanding of the nature and extent of the problem they face, since precious few maintain registers of cancer patients or have surveillance and epidemiological research programmes in place to guide decision-making. In sub-Saharan Africa, for example, cancer registries cover only 8% of the population, while coverage in Asia and Latin America is 7% and 10% respectively *(29)*.

Other challenges in responding to the cancer epidemic include:

* *Poor health infrastructure*. Though the picture varies considerably from one county to another, many people in the developing world – especially those living in remote rural areas -- have limited access to clinics and health centre, and the number of doctors and nurses to serve populations is woefully inadequate *(see table 1).* There are acute shortages of laboratory facilities, equipment and technicians to provide screening programmes; and radiotherapy services for treating cancers fall far short of need, with some African countries lacking such services altogether *(30)*.

Table 1: Health professionals per 100,000 people in selected countries

COUNTRY	DOCTORS	NURSES
Lesotho	5	62.6
Malawi	2	56.4
Mozambique	2.6	20
South Africa[2]	74.3	393
Rwanda	5	42
Sierra Leone	3	23
USA	247	901
UK	222	1,170
WHO minimum standard	20	100

Source: World Development Indicators, 2007, World Bank. World Health Report 2006

* *Scarcity of specialist skills.* Ethiopia, for instance, had only one oncologist for a population of 60 million in 2005, and Cambodia only one haematologist (a specialist in blood disorders) in 2006 *(31)*. Everywhere, pathologists able to provide accurate diagnoses and staging of cancers are in short supply.

* *The high cost of drugs and diagnostics.* Cancer therapies, especially the newer and more effective drugs, can be extremely expensive. These therapies are currently beyond the

[2] According to *Medecins Sans Frontieres*, some two thirds of doctors and half of all nurses in South Africa work in the private sector, and are concentrated in urban areas.

reach of public health systems in low- and middle-income countries, and are unaffordable to all but the very richest individuals in these countries. The high cost of cancer drugs and diagnostics is one of the most important reasons why less than half of those in need of cancer treatment in the developing world have access to it *(32).* To date, there have been only small and very limited efforts to make these lifesaving therapies available, through drug access initiatives similar to those that have brought treatment to people living with HIV/AIDS in the developing world.

* *The need for personalised treatment regimens and long-term follow-up of patients*, which may require considerable reorientation of health services, education of health staff, and changes in how records are kept.

* *Lack of awareness and knowledge about cancer* among the general public. People need education to encourage them to go for screening if available, to seek timely treatment for signs and symptoms, and to overcome fear and stigma associated with the disease. The healthcare community also needs to be educated about cancer, as many health workers have little knowledge or experience of working with this and other chronic diseases.

WHAT CAN BE DONE?

A major obstacle to action is fatalism: there is a widespread assumption that tackling cancer is not feasible in the poorer regions of the world because it requires sophisticated facilities and equipment and expensive drugs that are difficult to administer. Similar assumptions delayed the delivery of antiretroviral treatment for HIV and AIDS in developing countries until pioneering teams from UNAIDS and WHO proved in a four-country pilot programme in Chile, Cote d'Ivoire, Uganda and Viet Nam that the drugs could be delivered safely and effectively in all kinds of conditions. The same is true for cancer: something can be done to prevent, detect and treat the disease virtually everywhere.

It is estimated that more than a third of cancers are preventable and another one third are potentially curable provided they are detected early *(33).*

For example, mass screening with mammography for breast cancer is not feasible in the poorer regions of the world. But there is evidence that manual examination of the breast by a nurse can be equally effective at saving lives. And where laboratory facilities, equipment and expertise for conducting Pap smears are not available, screening for cervical cancer can be carried out by visual inspection using acetic acid (vinegar) or Lugol iodine. Such screening can be done by specially trained nurses in the most basic primary health care settings. The benefits are great: research shows that screening a woman once only between the ages of 35 and 40 reduces her lifetime risk of cervical cancer by 25-36% *(34).*

Vaccines to protect against infection with HPV 16 and 18 have recently become available, and one manufacturer, Merck, has a donation programme for developing countries, which is managed by Axios. Three doses of the vaccine need to be given to adolescent girls before they become sexually active. But even if the vaccine is widely administered the decline in incidence rates for cervical cancer will not become apparent for another 20 years.

If detected early, cervical cancer can be treated in a primary healthcare facility too, using cryotherapy. This is a minimally invasive procedure that uses extreme cold to freeze and destroy diseased tissue. Cryotherapy is simple, inexpensive, does not require electricity, and is 95% effective *(35)*. Nurses can be trained to use the acetic acid screening technique and cryotherapy in 5-10 days *(36)*. Breast cancer however does require referral to a hospital and specialist services for treatment. For screening programmes to be ethical, acceptable to the public and successful, treatment must always be available for people who discover they have cancer.

The World Health Organization has made cancer in developing countries a priority and produced guidelines to assist countries to establish national cancer control programmes that are relevant to their settings. Successful initiatives in a number of countries show what can be achieved, even in the poorest of settings.

The Sudan, for example, is ranked 147th out of 177 countries in the 2007 Human Development Index, and has established a cancer control programme against formidable odds. It is the biggest country in Africa and one of the most diverse, with 80% of its 39 million people living in rural areas or nomadic, and widespread illiteracy *(37)*.

The Sudan has chosen to focus on three cancers – breast, cervical and oral – because they are major killers and there is good evidence that screening is effective, affordable and sustainable, and treatment is feasible. The cornerstone of the programme is education of the general public and of the healthcare community. Radio is the principal tool for public education, backed up by posters, TV, information booklets and other media and by

discussions in public places. There is a common perception that cancer is transmissible, which leads to patients being shunned by family and friends and inhibits people from accessing screening or acknowledging early symptoms. 78% of cancer patients are first seen with late stage disease *(38)* which has a poor prognosis and is long, difficult and costly to treat, often requiring a combination of surgery, radio- and chemotherapy. The aim of public education is to raise awareness, encourage vigilance and dispel myths. Training programmes for healthcare professionals are designed to spread understanding of the risk factors and possible preventive measures, to train them in screening and to impress upon them the importance of recognizing early signs and referring patients for appropriate care.

The Sudan's programme has not yet been fully evaluated, but there is evidence already of patients being diagnosed earlier and of more patients receiving treatment. There is some evidence also of a decline in alcohol and tobacco consumption, which are major risk factors for oral and breast cancer particularly.

In Cambodia, a Boston-based non-governmental organisation, Partners Telemedicine, is piloting a project that uses the internet and email to connect patients in two extremely remote villages in Cambodia with specialists in a hospital in Phnom Penh and in Boston who can provide expert opinions and advice *(39)*. A satellite dish provides access to the internet using electricity supplied by solar panels and generators.

Operation Village Hope has been working since 2001 in the two communities who scarcely, if ever, see a doctor in their health centres. Every month a Cambodian nurse travels hours from Phnom Penh to visit each village for two days. He examines and photographs patients whose medical details and images, if necessary and with appropriate consent, are emailed to distant experts who respond by the next day. The system has proved effective for a range of health problems that can be treated locally and relatively easily. It has helped with the detection of cancer also, but is unable to overcome serious logistic and financial constraints in relation to cancer treatment: this still requires travel to Phnom Penh and is not free. A full course of treatment for breast cancer, for example, is approximately US$1,200 – far more than most people earn in a year.

In Ethiopia, Axios, with support from the drug company AstraZeneca, and in close collaboration with the Ethiopian Ministry of Health, has a breast cancer pilot project aimed at building the country's capacity to manage all aspects of the disease. When the project began in January 2005 there were no data on breast cancer patients, no mammography, no treatment or care guidelines, only one cancer specialist and one radiotherapy unit for the whole country, and precious few cancer drugs. By late 2008, Tikur Anbessa Hospital in Addis Ababa had become a centre of excellence and referral for women with breast cancer. Guidelines for treatment and care had been developed, state-of-the-art equipment had been installed, procurement systems for drugs and lab supplies had been set up, and staff trained in various disciplines to run the programme. AstraZeneca has made some of the life-saving cancer drugs available free to patients. In parallel, an Ethiopian Cancer Association has been set up, with its main tasks being to raise public awareness and to establish a cancer registry and gather data *(40)*. By end 2008, 3,634 patients had been screened, diagnosed, and treated at Tikur Anbessa, and were being followed up as necessary.

Not 'business as usual'

A number of pharmaceutical companies make certain drugs available free of charge to patients who cannot afford to pay for them in developing countries. Merck, for example, has donated drugs to fight river blindness in Africa, and vaccines against mumps, measles and rubella, and hepatitis B in developing countries *(41)*. But such programmes depend on

pharmaceutical companies' budgets for corporate social responsibility. Such budgets are pure expense budgets and are therefore vulnerable if the overall business is not doing well.

Now Axios – noting the lessons of AIDS and antiretrovirals, and recognising that the fastest growing markets for cancer and other chronic disease drugs are in low- and middle-income countries rather than the developed world – is proposing a new model of business for Big Pharma *(42)*. As an organisation that specializes in strategic advice and technical assistance to improve healthcare delivery in developing and emerging countries, Axios is brokering deals that promise to benefit both drug companies and poor patients in developing countries – a win-win for all parties. In the conventional business model, Pharma makes its money from selling its drugs at a uniform price to those who can afford them, predominantly in the developed world. But as governments in Europe and the US put ceilings on health care costs, this is a shrinking market. The model that Axios proposes works on the principle of differential pricing – charging individual patients only what they can afford – and relying on volume of sales to make more money than before. Applying the model involves painstaking market research and sophisticated computing as the strategy has to be tailored to fit the disease profile, population structure, and income distribution patterns in each individual country.

Besides computing the details, Axios helps with the operational design of the programme and in selecting and training local partners to administer it. As of December 2008, Axios was managing drug and diagnostic access programmes in 117 countries from which over 8 million people had already benefited.

AGENDA FOR ACTION

These few examples of activities aimed at responding to the cancer crisis in low- and middle-income countries give an indication of what is possible. But they represent only a drop in the ocean – the vast majority of people with cancer in the poorer regions of the world are still beyond the reach of services. There is a pressing need for developing countries to learn the lessons of experience and to adopt, adapt and expand what has been proven to work elsewhere.

To encourage this process and assist government with planning and budgeting, Axios and its partners in the fight against cancer have been developing models of treatment and care for different types of cancer in various socio-economic settings and putting a cost to them. They emphasise that cancer services should not be set up as stand-alone programmes but everything -- from screening and diagnosis to treatment for cancer -- should be integrated with general healthcare services, and the opportunity taken to build capacity and strengthen the health system as a whole.

Priorities for action in tackling the cancer epidemic include:

* *Education and awareness raising* among the general public and among health professionals. The family and community have a role to play in caring for people with cancer, especially those with terminal disease, and for this they need sound knowledge and understanding of cancer as well as information about what they can do.

* *Surveillance.* Countries need to establish and maintain cancer registries and to invest also in epidemiological research so that they have a clear picture of what they are dealing with, and can make informed decisions about how to respond.

* *Prevention and treatment of infectious diseases that cause cancer.* This means, for example, including hepatitis B vaccine in the schedule of immunizations for children, and considering a vaccination programme against HPV for adolescent girls and boys. It means improving hygiene where necessary to protect against infection with *H. pylori,* and providing antibiotic treatment for those who do become infected to reduce the risk of stomach cancer. Health departments should take steps also to encourage healthy diets and exercise, control the use of tobacco and alcohol, and protect the population from environmental pollutants.

* *Early detection.* The earlier cancer is detected, the easier and cheaper it is to treat. This relies on two things: cancer 'literacy' among the general public so that individuals seek timely treatment for signs and symptoms, and mass screening of people at risk. As described earlier, screening programmes for such cancers as breast and cervix need not be prohibitively expensive if low-tech options are adopted.

* *Effective treatment.* As with HIV and AIDS, successful treatment programmes for cancer in resource-poor settings have shattered the myth that such treatment is not feasible in the developing world. The pharmaceutical industry and governments alike need to commit themselves to the principle of equitable access to such treatment, and there are a growing number of innovative programmes and projects from which to draw lessons and inspiration for action. A much neglected aspect of cancer treatment, and one that needs urgent attention, is palliative care for the terminally ill. The experience and management of pain are culturally sensitive, and research is needed to provide information on which to build effective palliative care services that increase access to morphine which is very limited in most developing countries.

* *Training and Capacity building.* Training of physicians and public health professionals at all levels is a key component of a national cancer control programme. There are a number of international cancer organisations that can provide support for such activities in low- and middle-income countries, as well as ongoing mentoring and sharing of information, and collaboration in research. A major challenge is finding ways to retain skilled staff who might be tempted by the promise of better lives and working conditions elsewhere.

* *Greatly increased funding for cancer.* Only 5% of global resources for cancer are spent in the developing world *(43).* Affected countries, donor governments international organizations and foundations must improve on the relatively small expenditures currently being made to address this health crisis. Far greater efforts are also needed to reduce the prices of cancer drugs and diagnostics in low- and middle-income countries, and increase access to affordable prevention and care services.

* *Political will*. Leadership is an essential, and often missing, component of a successful response to cancer in developing countries. At the national level, governments set the health agenda, and must be both aware of the impact of cancer in their countries, and committed to addressing it. One reason why developing countries may hesitate to commit to cancer control efforts is a lack of knowledge of what will be required, in terms of both financial and human resources. More pilot programmes must be developed and implemented to cost different types of cancer care at different levels of the health system. For the necessary funds to flow to support country-level activities, the international community also needs to be aware and to give cancer the priority it deserves.

Lessons from various other public health initiatives around the world – notably those concerned with HIV/AIDS – suggest that lobbying by health activists, patients' groups and other interested parties plays an important role in stimulating political will, both at the national and international levels. Key to the success of these efforts is the ability of experts and advocates to agree on clear and effective measures to be taken. Developing and moving forward an agreed agenda to improve cancer diagnosis and treatment will be vital to increasing global action in this area.

The challenges of providing quality cancer diagnosis and care are great in developing regions – where caseloads are large, budgets tight and health services stretched – but they are not insurmountable. Governments and health ministries, donors, the international health community, advocates healthcare professional and ordinary citizens all have vital roles to play in addressing the silent crisis of cancer in the developing world. Above all, it is past time for public health leaders, at the local, national and international levels, to exercise the courage, vision and determination needed to make this large and growing killer a global health priority.

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