Challenges, hurdles and possible approaches to improve cancer care in developing countries – A short breakdown of the status quo and future perspective

Sabine D. Brookman-May1*, Oscar Rodriguez-Faba2, Johan F. Langenhuijsen3, Bulent Akdogan4, Estefania Linares5, Andrea Minervini6, Tobias Klatte7, Alessandro Volpe8, Maurizio Brausi9, Martin Marszalek10

1 Department of Urology, Ludwig-Maximilians University (LMU) Munich, Germany
2 Department of Urology, Fundació Puigvert, Barcelona, Spain
3 Department of Urology, Radboud University Medical Center, Nijmegen, The Netherlands
4 Department of Urology, Hacettepe University, School of Medicine, Ankara, Turkey
5 Department of Urology, Hospital Universitario La Paz, University Madrid, Spain
6 Department of Urology, University of Florence, Careggi Hospital, Florence, Italy
7 Department of Urology, University of Vienna, Vienna, Austria
8 Department of Urology, University of Eastern Piedmont, Maggiore della Carità Hospital, Novara, Italy
9 Department of Urology, A.S.L. Modena, Bernardino Ramazzini Hospital, Carpi, Italy
10 Department of Urology and Andrology, Donauspital, Vienna, Austria

Abstract: It was estimated that in 2012, 57% of the incidence and 65% of cancer deaths have occurred in developing countries, and in the future, the incidence of cancer-related mortality is even expected to rise significantly in these countries. Despite this alarming data, there are still significant disparities in access to cancer care and cancer control between developing nations and higher income countries. There are several hurdles for cancer patients in developing countries which impair adequate treatment, including very little access to programs of cancer prevention and screening measures, early diagnosis and adequate surgical and medical tumor treatment. In this article, we provide a short assessment and breakdown of the main barriers for proper cancer treatment admission and provide a perspective on potential approached and solutions to enhance cancer research and care in developing countries.

Keywords: cancer care; clinical research; oncology; developing countries; hurdles


*Correspondence to: Sabine D. Brookman-May, LMU Munich, Department of Urology, Munich, Germany; sabine.brookman-may@email.de

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Introduction

Based on estimations, in 2012, there was a 57% incidence of cancer. Also, 65% of cancer deaths have occurred in developing countries[1]. Furthermore, the incidence of cancer-related mortality in developing countries all over the world is expected to even rise significantly in the near future, due to lifestyle changes and multiple environmental factors, and it has recently been projected that in 2020 more than 60% of cancer cases will occur in developing countries causing more deaths than AIDS, malaria, and tuberculosis together[2–4]. Despite this data, there is no doubt that there are significant disparities in access to cancer care and cancer control between developing nations and higher income countries. The population of developing countries has very little, to no access whatsoever, to programs of cancer prevention and screening measures, early diagnosis and adequate surgical and medical tumor treatment.
Hurdles for adequate cancer research and care in developing countries

Besides other reasons, poor education and widely spread misconceptions regarding all issues related to cancer, i.e., its cause and biology, potential curability, and effectiveness of scientifically-based or traditional treatment are causative for this disparity.\(^5\) According to a few experts, the gap between the rich and the poor in accessing modern cancer care is projected to be widened due to the liberality of global economy, leading to increasing unemployment and poverty and pressure on national budgets, which impacts resources for health care. In addition, there are increasing costs for modern medical equipment, new drugs, education and employment of health professionals.\(^5\) Many other factors contribute to disparities in cancer care which are effective at various levels, i.e., individual, social group, national or even global. Poorer cancer control occurs in populations living remotely from urban centers, low socioeconomic and some ethnic groups who have lifestyle and belief systems which impact on cancer control. Further potential factors may include the following:

Lifestyle factors

Higher rates of specific lifestyle risk factors such as smoking tobacco, alcohol or drug consumption (including chewing betel quid) have consistently been reported for developing countries.\(^6,7\) Also risk factors such as obesity have severely increased in a number of developing countries, partially due to adoption of Western lifestyle and diet. Lower socioeconomic status (SES) in developing countries in general or in remote areas does furthermore negatively impact lifestyle behaviors.

Socioeconomic status

A lower SES of a population may correlate with poorer cancer outcomes and people of lower SES are over-represented in more remote areas.\(^8\) However, the impact of SES on cancer incidence and outcomes has been more difficult to differentiate from other factors. For example, some studies have shown a low SES to be a significant determinant of stage and survival of oral cancer or impacting colorectal cancer survival; on the other hand, the overall evidence concerning SES and cancer control has delivered conflicting data.\(^9,10\) The complexity of assessing the impact of socioeconomic factors was also highlighted in a qualitative study using the Welsh database of low SES individuals and found a poor awareness of non-specific symptoms in this group with an often fatalistic view on cancer. Poverty also often meant that essentials like daily food had priority over seeking medical advice.\(^11\)

Poor health literacy

In developing nations, limited access to complete and accurate information continues to pose a challenge for cancer patients and family caregivers. Poor health literacy is associated with reduced quality of health decision-making and health outcomes especially in patients facing a cancer diagnosis.

Remoteness

Many of the studies focusing on the disparities between rural and urban patients come from high-income countries, but may provide a guide to factors which can be applied to developing countries. Data from Australia have provided further evidence showing that cancer deaths were higher in inner regional areas than major cities.\(^13,14\) A correlation was also seen with lower SES, demonstrating that 39% of patients with poorer cancer outcomes were living in remote areas, compared to 24% in rural areas and only 17% in major cities. Moreover, those living in rural and remote areas, particularly men, were less likely to have considered cancer prevention messages and more likely to engage in lifestyle behaviors associated with a greater cancer risk, such as e.g. tobacco smoking and harmful levels of alcohol intake over time.\(^13,14\) Also risk factors such as obesity and overweight were 10% higher in absolute terms in regional and rural areas, while sedentary behavior applied to 60% compared to 54% in major cities.\(^8,13,14\) Furthermore, an impact of living in rural locations was found in long-term cancer survivors when health-related quality of life was assessed.\(^15\) Rurality may also impact social function and financial difficulty. Also reluctance to travel away from communities in rural and remote locations may compromise cancer care.\(^16\)

Ethnicity

Different cultures may have lifestyle and traditional belief systems that impact cancer control. At times, family and community responsibilities in some cultures may also outweigh the individual requirement for treatment, which
can impact treatment schedules. On the other hand, diets such as the Mediterranean diet or vegetarian diets dictated by cultural prohibitions against meat may have a favorable impact on cancer risk compared to an energy dense Western diet. In addition, there may be genetic differences impacting cancer risk based on ethnicity. For example, Maori and Pacific Islander women have been found to have poorer survival from breast cancer, less triple negative breast cancer, and more HER2-positive cancers. When adjusting for other known risk factors (e.g., location, grade, nodal stage), Maori women still had a higher risk to die from cancer\textsuperscript{[17]}. Another example is the high risk of prostate cancer in African men, even more raising under Western lifestyle and diet in African American men who finally have the highest risk of developing prostate cancer worldwide.

**Limited access to screening and prevention measures**

Access to preventive vaccines or to screening for cancer is limited; in addition, there is also often poor availability of centers with appropriate diagnostic and treatment facilities\textsuperscript{[19]}. Furthermore, cancer control outcomes can vary between ethnic groups where the uptake of cancer services will be dependent on cultural appropriateness\textsuperscript{[19]}.

**Access to treatment**

One of the major causes of disparate outcomes in cancer control is variable access to the treatment modalities of surgery, radiotherapy, and systemic therapies. Surgery is often the primary treatment for solid tumors, but surgeons in LMIC are partially not perfectly trained or resources to treat curable cancers at an early stage are limited\textsuperscript{[20]}. A great challenge is to be able to afford increasingly high-cost cancer drugs. In Southeast Asia for example, in a high-income country, Singapore, 55% of patients had access to a range of drugs and targeted therapies in common usage; in contrast, only 15% of patients in LMICs had the same access\textsuperscript{[21]}.

**Childhood cancer**

One special aspect includes also the awareness of childhood cancer. Although 90% of children worldwide live in developing countries, childhood cancer is given very low priority by governments’ funding the in these countries, not only due to its complexity\textsuperscript{[21,22]}. The weak health systems, poor and late access to diagnosis and care, fewer numbers of trained health care professionals, and lack of cancer drugs are amongst the many challenges faced. Furthermore, children health care lacks protective and supportive lobbyist activities. A major challenge for the future is extending the work to reach as many children as possible in developing countries, who die without access to cancer treatment.

**Perspective – Possible approaches to enhance clinical research and cancer care in developing countries**

From the before mentioned aspects as potential reasons for poorer cancer outcome and as hurdles for improving cancer care in developing countries, specific approaches may be derived, including the following:

**Lifestyle and associated risk factors**

Effective strategies to reduce obesity and alcohol consumption in developing countries need to be implemented. Cultural practices around food and alcohol consumption can be strongly entrenched in both low- and high-income countries. Food and alcohol industry and advertising industries can form strong lobby groups preventing governments from acting in the public good. However, lobbyism should not apply to governments’ protecting a nation’s population. Furthermore, each country must implement programs to meet the UN cancer prevention targets in order to improve global cancer control. The risk factor with the most widely accepted framework for its control is reducing tobacco use with the Framework Convention on Tobacco Control of the World Health Organization. Countries can learn strategies for implementation from other countries in which such were already successfully implemented (E.g., programs against tobacco use in several countries worldwide).

**Poor health literacy**

Another important hurdle to tackle in developing countries is poor health literacy, which is associated with reduced quality of health decision-making and health outcomes especially in patients facing a cancer diagnosis\textsuperscript{[12]}. Broad access of the entire population in developing countries to general education represents a first generic step in this regard. Specifically, access to complete and accurate health information needs to be provided by local and
international health organization and health authorities. In addition, pharmaceutical companies should focus on their responsibility to provide access to objective and reliable intelligence to family and caregivers.

**Remoteness**

One possible solution to better delivering healthcare to rural and remote communities, harnesses technologies which enhance connectivity. Telemedicine can be used to export multidisciplinary opinions from large urban centers to isolated practitioners or to deliver personal care. In both cases, the need for costly and time-consuming travel by either patients or medical staff may be reduced.[23]. Web-based support resources and information tailored to patients’ needs could be easily accessed by rural and remote communities.[24]

**Cancer registries**

Population-based cancer registries aim to capture new cases of cancer in geographically defined populations. To improve cancer control, it is essential to have an accurate record of cancer incidence, prevalence and survival and their changes over time. Unfortunately, about 85% of the world lacks quality cancer registries to record incidence, mortality and prevalence and many countries are reliant on Globocan estimates of their cancer burden.[25,26]. The initial step in most countries will be to establish a cancer registry to define the incidence of cancer and measure the mortality from different cancer types in order to enable the assessment of the disease burden and to evaluate the success of cancer control strategies. This determines the extent of the cancer problem and where resources are most needed and allows monitoring of the impact of screening programs and new treatment regimes. Cancer registries may also help identify disparities which span the spectrum of cancer prevention, early detection and treatment. There are initiatives supporting countries in establishing cancer registries by providing suitable software, such as e.g. CanReg 5, and guidelines on how to manage a registry, and minimum data sets have been defined along with networks and regional hubs.[27]. Finally, such support strategies are helpful initiatives, but ongoing resource implications and follow-up needs to be considered and may be problematic.

**Access to cancer prevention and screening**

Prevention and early detection should ideally be the mainstays of cancer control. Population screening of asymptomatic individuals allows early detection at localized stages where cure is possible, or detection of precancerous lesions which can be prevented from becoming invasive cancer. There is evidence of the efficacy of this approach in screening for cancer of the cervix, breast and bowel, but benefits must be weighed against the potential of over-diagnosis and overtreatment. Generally, people from lower SES groups and various ethnic groups have lower rates of participation in screening programs.[28]. Most LMICs have no screening programs, but partially sporadic programs which, however, lack population-wide impact.[29]. The greatest advances in cancer prevention has been shown by the development of the human papilloma virus (HPV) vaccine which can prevent at least 70% of cervix cancers, and vaccination programs against hepatitis B against the incidence of hepatocellular cancer.[29,30]. The HPV vaccine represents a breakthrough in the prevention of cancer of the cervix, which is only limited by the ability to disseminate the vaccine. Within eight years after the introduction of the HPV vaccine, 64 countries have it available nationally, four countries regionally and 13 overseas territories have developed vaccination programs, which targets around 118 million women. However, only 1% of women were from LMIC, where the death rates from cervix cancer are highest, with the GAVI initiative improving access to this vaccine in eligible low-income countries.[30,31]. Despite subsidies, some developing countries were not able or unwilling to allocate resources to fund the vaccine and lack the infrastructure to administer it, which leads to disturbing disparities. As an example, Papua New Guinea (PNG) is just four km from the closest island off Australia. While Australia has a very low incidence of mortality from cervix cancer because of decades of screening and vaccination programs now for both and girls with the real possibility of eliminating the disease, still the greatest cause of cancer deaths in women in PNG where there is neither screening nor HPV vaccination programs is cervix cancer. Solving such disparities requires international collaborative action. Concerning the hepatitis B vaccination programs, these have been more effective with 184 member states of the WHO vaccinating up to 82% of their infants.[21].
Access to drugs and treatment

Global co-operation will be needed to reduce the cancer burden in LMICs. Incentives to make cancer drugs available may depend on whether other priorities such as food security or countering resistant infectious diseases need to take precedence in developing countries. Defining specific tumor treatment options as essential on a national level might be a first step as it is done already in some developing countries (as well as in developed countries). Concerning indispensable medicines on a global level, the WHO has attempted to construct an essential medicines list as a guide and in 2014 had UICC (Union for International Cancer Control) convened groups of oncologists to update the list. They looked at the potential for long-term remissions, the contribution of the drugs over other treatment modalities, and whether the therapies required advanced pathology testing such as for instance genomic analysis. The 2015 WHO list includes 46 medicines for 26 different cancers. However, such efforts will not be effective without making essential drugs also available and affordable for the population, which finally needs a clear dedication on the local level as well as international collaboration and support. There is a range of measures suggested where LMICs may be able to access these medicines for more of their population. The creation of some form of universal healthcare may help, but more taxes in a low-resourced population is a challenge. Also the use of generics and biosimilars for drugs off patent may eventually increase availability, but any compulsory licensing of essential medicines may contravene trade agreements. One relevant option to improve access to effective drugs is the participation in clinical research. Although having improved over recent years, clinical research infrastructure in developing countries still needs to be enhanced. There may be also industry-led access schemes funding drugs or schemes where governments partner additionally with private industry or organizations to make drugs available. Finally, concerning treatment in general and partially lacking adequate training for medical doctors and surgeons, one solution is that surgical societies and individual surgeons can provide training programs and fellowships for their colleagues in LMICs. Teaching can be enhanced by using electronic communication and mobile health technology solutions.

Building local capacity

What is needed to improve cancer care in developing countries is building local capacity for cancer and genomics research in these nations. By now, the poor genomics research capacity in developing countries has prevented maximal benefit from the applications of genomics in the practice of medicine and research. Adedokun et al. have recently published results of a study in which they examined author affiliations of genomic epidemiology publications in order to make recommendations for building local research capacity in sub-saharan African (SSA) countries. The most commonly studied population was South Africa, accounting for 31.1%, followed by Ghana (10.6%) and Kenya (7.5%). Fewer than half of the first authors (46.9%) were affiliated with an African institution. The authors concluded that significant disparities currently exist among SSA countries in genomics research capacity. South Africa has the highest genomics research output, which is reflected in the investments made in its genomics and biotechnology sector. These findings underscore the need to focus on developing local capacity, especially among those affiliated with SSA universities where there are more opportunities for teaching and research.

Independent cancer research

During the previous decades, understanding of cancer biology, diagnostics, and treatment has changed dramatically and it is virtually impossible to find a cancer for which the optimal treatment has not changed. Either cure or prolonged survival is a realistic expectation for the majority of cancer patients. The basis for this significant progress is clinical research including modern diagnostic procedures, enhanced pathological analysis and imaging techniques to monitor disease extent and response to treatment. However, most newly developed cancer drugs are finally not affordable and available for all nations and disparities in cancer care worldwide are a reality. Current clinical research is dominated by pharmaceutical companies and researchers from the developed world. Problems specific to cancer care in developing countries are not ignored by industry, but finally underrepresented. While industry dependent clinical research also offers the possibility to access new drugs within the framework of clinical trials, also independent clinical research is needed, which can offer new valuable knowledge and identify...
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affordable and cost-effective treatments. As such, research not depending on commercial sponsors should become one of the important avenues to alleviate the problem of cancer disparities. Academically driven studies focusing on treatment modalities which are not commercially interesting might have a strong value, e.g. innovative combinations of drugs for which the patent protection has expired. Promotion of independent clinical research focused on particular problems of specific populations is needed. Clinical research without (strong) financial support is feasible and can lead to valuable new knowledge.

Clinical research of pharma research and development

While independent academic research should play a major role in clinical research, pharma research & development (R&D) will and should have a strong role in improving cancer worldwide including developing countries. The system of R&D at least partially relies on patents, market monopolies, and high prices of drugs to recoup costs, which also results in the fact that there is a limited presence of pharma R&D activities in some areas of actual need in developing as well as wealthy countries, including increasing antibiotic resistance in many parts of the world. Besides, there is not only unavailability of drugs for medical needs, but also unaffordability when drugs are priced out of the reach of most people, even considering that pharmaceutical companies have clearly recognized that patients often need support for life saving drugs and have established accordant patient assistant programs. While it is undoubtedly true that high drug prices need to cover the costs to develop these drugs and pharma also has the intellectual property rights and patents on new medicines, this approach doesn’t entirely work to deliver public health benefits. One future vision for R&D could involve an overhaul of the current system including the development of drugs according to actual medical needs in a system that does not exclusively rely on patents and high prices to recoup costs. However, there need to be alternative ways to pay for R&D and alternative business models that can be used instead and accordant structures need to be developed to make drugs affordable worldwide on the one hand, but drug development still effective and commercially attractive on the other hand. It is essential to ensure that innovators are sufficiently and transparently rewarded for developing useful products and develop drugs for neglected diseases and diseases that affect the developing world. In this regard, a strong cooperation of the academic community with commercial sponsors is invaluable in exploring new approaches in cancer management. Furthermore, also governments need to take their responsibility for making effective drugs available and affordable in their countries, which also includes a close cooperation with pharmaceutical industry to build the infrastructure and basis for an adequate health management.

Childhood cancer

As outlined above, beside the general disparity in cancer care worldwide, children in developing countries have the least access to cancer treatment. Given the inequalities in the survival rates of children with cancer, there is an urgent need to close the gap between developed and developing countries. Strategies at individual, institutional, country, regional and global levels must be implemented by improving care and research, increase awareness and coordinate training of medical doctors to improve cancer survival in children, which have finally the weakest position in the systems.

Global collaboration

International partnerships offer the opportunity to provide expertise, advice, support, and transfer of technology to build local capacity for cancer treatment and research with a vision of developing functioning local networks. Furthermore, local teams in developing countries must drive projects and volunteers; funding organizations can help to achieve progress. This will overall require a tremendous effort of both wealthy and developing countries.

Conclusion

Finally, it is encouraging that the worldwide burden from non-communicable diseases such as cancer has been recognized by the United Nations who have created targets for member countries to achieve to improving cancer prevention and control. This has been a first step in the right direction, but actually several initiatives need to be implemented focusing on different aspects of current cancer disparity. Improving cancer control is a multifaceted exercise and defining achievable international targets for reducing the burden of cancer is a required first step. There are several approaches how to improve cancer care in
developing countries and how to reduce global disparities, however, we need to be aware that any single and isolated interventions may only bring limited benefit; finally, a combination of relevant interventions and an effective interaction between relevant stakeholders (academia, medical community, pharmaceutical industry, health organizations, governments) will be necessary. Eventually also political efforts need to be undertaken considering the presence of partially corrupt governmental regimes in some developing countries which impairs fair medical supply and infrastructure implementation. Ultimately, in order to introduce effective solutions in the long term, first a thorough understanding of developing countries’ current capabilities is an essential step to develop a realistic plan to reduce cancer burden worldwide.

Conflict of interest
The authors declare no potential conflict of interest with respect to the research, authorship, and/or publication of this article.

References
5. The Garvan Research Foundation, 2015


