

Identifying Best Cancer Management Strategies for Undeveloped Nations: A Literary Review

Submitted by

Anthony Ligeski

Biology

To

The Honors College

Oakland University

In partial fulfillment of the
requirement to graduate from

The Honors College

Mentor: Jonathan Yates, Professor of Biology

Department of Biology

Oakland University

04/01/22

Abstract

Today, cancer research is often done in developed nations in expensive labs thanks to funding from wealthy donors. However, cancer is a global disease and is expected to become much more prevalent in undeveloped nations, due to severe lack of medical infrastructure and properly trained personnel. Given the limited resources available in undeveloped countries, more research is needed to find effective cancer management tools which don't require a hospital or expensive medical equipment. These treatments must also be easy to administer to patients as the medical training in these nations isn't the same as developed countries. By finding more cost-effective treatment options for underdeveloped countries, developed nations can also use them in poorer communities to help alleviate the burden of costly medical treatments. Through the review of literature on global cancer prevalence and the various treatment options available in different countries, I hope to highlight where specific cancers are expected to be most prevalent and guide research towards finding treatments that can be effective in those areas given resource availability. Additionally, as new cancer treatments are developed they should be designed to work in areas where the cancer it is treating will be most common. Together, this information should help guide countries to make smarter decisions in regards to how they can best improve cancer management for their people.

Current Research

Cancer has been on the rise all over the globe as the population continues to age. Currently many developed nations see the highest number of cancer cases, however the expected growth in cases is highest among less-developed countries (Pilleron et al., 2019). This presents a serious issue where research and development focuses on places with the highest number of cases now without taking into account what the future will hold. By the time the scientific community notices the spike in growth, it will be too late to help those underdeveloped nations who are already struggling to diagnose and treat the cancer patients they have today.

Currently, plenty of research has been done to look at global trends of various types of cancers, such as bladder, pancreatic, liver, and prostate (Huang, 2021; Hu, 2021; Teoh, 2019; Wong, 2018). These articles tend to identify certain high risk-groups in terms of age, gender, and location along with explaining some reasons as to why this might be the case. However these articles fail to provide solutions of how these high-risk groups can be helped, and what, if anything, can be done to lower the cancer risk for those individuals. Combining the latest research on how to treat cancers prevalent in certain areas with where it is needed most, can help governments and other policy leaders refine how they should go about developing a cost effective cancer management strategy based on where it will be used the most now and in the future (Gelband et al., 2015).

There are guidelines currently in place for cancer management set forth by international organizations and though some take into account the limited resources of low-income and middle income countries (LMICs), many haven't taken into consideration potentially more cost effective measures. Some research has been done to look into ways of improving these guidelines and

have often suggested taking cost-effectiveness and feasibility into account. For example, in order to better help LMICs, more developed nations should not only share physical resources such as medical equipment, water, drugs, and other supplies, they should share the human resources to help train local healthcare workers how to use the technology.

Aims and Objectives

Introduction

The cancer burden on LMICs is increasing and despite advancements being made in cancer research, more needs to be done to address this growing issue. Current research is looking into advanced treatment and diagnostic tools that are too expensive or too complicated to be used in underdeveloped nations. The scientific community should focus on developing cancer management tools that will help the most people, not just the people with the most money. In-depth research on the limited health care resources available to LMICs is prevalent, however research into what can and should be done to fix it isn't as widespread.

Aims

1. To identify gaps in cancer incidence between developed and underdeveloped nations
2. To determine what treatments and diagnostic tools are available in low income countries
3. To investigate whether or not the current cancer management techniques in LMICs are the most cost-effective
4. To discover what guidelines are currently in place for LMICs to manage cancer

Objectives

1. By discovering what cancer types are disproportionately present in underdeveloped nations, research and humanitarian efforts can be focused on treating those cancers first.
2. Identifying what is currently available to manage cancer in LMICs, future efforts can be made to fill in the gaps either by expanding availability or introducing better tools.
3. Underdeveloped countries have fewer resources available for health care, so finding which cancer management methods are most cost-effective will allow them to help more people.
4. Determining if current guidelines are realistic and beneficial for LMICs can help guide revisions to them as more effective research comes and cheaper treatments become available.

Methodology

In order to gain the most knowledge on this subject a literature review will be conducted. This will provide the widest range of currently available information on what is being done to manage cancer in underdeveloped nations and what attempts if any are being made to improve the overall level of care. Using research databases such as PubMed and search tools like Oakland University Library OneSearch the main keywords used were “cancer”, “cost-effectiveness”, “low income countries”, “LMIC”, and “underdeveloped”. After a thorough review and selection process, about 30 articles were chosen to be analyzed in detail for information regarding current cancer management techniques and what suggestions are being made for future development within LMICs. It was essential to include articles that evaluated cost-effectiveness of various options before making any recommendations to LMICs because cost was by far the biggest barrier they faced in terms of improving their cancer control strategies. By focusing on this within the review, more cost-effective methods have been identified and should be implemented

in more LMICs going forward. Lastly this review has highlighted there are some gaps in research regarding what more can be done to help LMICs with cancer management and emphasizes the need to reevaluate current recommendations to be changed to ones which are more cost effective.

Introduction

Cancer is one of the fastest growing health challenges all over the world and its impact is far from fair. Currently more developed regions have higher cancer incidence rates, however this will not be true moving forward, due to the lack of accurate patient data coming from undeveloped countries, many of which do not have a cancer registry. As it stands, current projections see less developed regions such as the Middle East and Africa have a 144% increase in new cancer cases by 2035 while developed regions will only see a 54% increase (Pilleron et al., 2018). This growth rate is almost three times higher than what developed nations are expecting, and these less developed areas don't even have the health infrastructure to deal with current case loads. Given this knowledge, it is critical that work be done to improve cancer management in these regions. Current attempts are far from comprehensive and often misguided due to misinformation and lack of cultural awareness

Cancer management is a complex issue and there are many vital steps each with their own set of challenges for LMICs to overcome. However, this is no excuse for more developed nations to not step in and offer assistance, especially considering the resources available to them. It isn't just about the money for these nations, they also need guidance as to what they should do with the funding they receive. Oftentimes donors will come in with one specific idea in mind and in order to please them, these countries will do exactly as they say, even though the money could be more helpful elsewhere. To combat this, leaders in the medical community from developed

countries should assist fellow leaders within LMICs to help identify where the area of greatest need is based on the population. It is also vital to ensure whatever measures are put into place, they should be cost-effective, accurate, and sustainable to maintain or else the investment will have been worthless. Beyond this, given the limited resources of the LMICs it is important to prioritize which step of cancer management is funded first with relation to what type of cancer is prevalent in the area.

Overall, this review will bring together a wide array of information with the goal of identifying how LMICs can properly implement the key aspects of cancer management; namely prevention and screening, early diagnosis, and treatment. By analyzing each area individually, potential cost-saving measures can be identified and priorities set on what steps should be taken next in order to have the greatest impact both in the short and long-term for these countries.

Prevention

The first step in cancer management is prevention and it offers the best opportunities for reducing cancer mortality and incidence rates while also limiting the financial impact they have on a country's economy. This is particularly important in LMICs where they have the highest cancer-related mortality rates among people under the age of 65; in other words, those who are primarily responsible for economic output and those years of lost productivity hurt these nations who are trying to develop economically (Shah, Kayamba, Peek, & Heimbürger, 2019).

Preventative strategies are broken down into two different types, primary prevention, which includes any measure that can reduce the chance of initial cancer formation, while secondary prevention involves measures that attempt to contain a cancerous growth before it becomes invasive or harmful. The biggest benefit of preventive measures is the ability to reduce cancer

rates entirely and not have to deal with the financial impact that treating a cancer patient would require.

By far the most effective primary preventative measure are vaccines against infection-related cancers. Currently a successful rollout of the Hepatitis B Virus (HBV) vaccine in LMICs among children has over 80% global coverage and as such has resulted in a significant reduction in HBV associated liver cancer (Dare et al., 2021). This success has led to the implementation of other types of vaccines, specifically the Human Papillomavirus (HPV) vaccine which protects against the development of cervical cancer, which is the second most prevalent cancer among women in LMICs (Brisson et al., 2020). It has been shown in multiple studies (Brisson et al., 2020; Drolet et al., 2021; Ralaidovy et al., 2018) that HPV vaccinations are the most effective tool available in preventing cervical cancer. This is possible due to the fact that about 90% of cervical cancer cases are caused by one of the 14 currently known oncogenic HPV strains (“Global strategy”, 2020). It has been determined that the most cost-effective vaccine implementation is when more than 70% of girls between the ages of 9 and 12 receive the full vaccine regimen (Dare et al., 2021). This process of vaccine rollout has been slow since the vaccine requires multiple doses and needs to be kept at fairly cold temperatures, which can be quite challenging in LMICs where medical facilities are far apart and lack the infrastructure to keep large quantities of vaccine doses cold in their warmer climates.

For lung cancer, smoking cessation for at least seven years has shown an incredible ability to drastically reduce lung cancer mortality rates and is as effective as starting a new screening program (Saul et al., 2020). In fact, for every year a person doesn’t smoke, the chance they die from lung cancer decreases by 6% (Saul et al., 2020). This is crucial for people living in LMICs because they contain over 80% of the 1.3 billion smokers globally and account for 70%

of smoking-related deaths (Saul et al., 2020). Educating these areas about the harms of smoking or encouraging governments to tax and decentivize the practice would help in bringing the number of smokers down in these countries and thus reduce lung cancer incidence rates. This will also make screening cheaper since there will be fewer smokers to screen in the first place, allowing more money to be spent on other cancer management tools. Additionally, the money raised from taxing the purchase of tobacco products can be reinvested into lung cancer screening or any other health care related expense that a nation deems important. In fact, the WHO considers smoking control the most cost-effective cancer prevention tool available, costing roughly 11 cents per capita among everyone living in an LMIC (Saul et al., 2020).

The last form of primary prevention is applicable to many types of cancer, but is most applicable to colorectal cancer (CRC) given its growing prevalence in LMICs and its asymptomatic early stage prognosis. The reason for its recent rise in LMICs is because they have picked up more “Western” habits such as a sedentary lifestyle, poor diet, and alcohol consumption, all of which are risk factors associated with an increased likelihood of developing CRC (Xi and Xu, 2021). In order to combat this, experts suggest the promotion of a more healthy lifestyle including regular exercise, nutritious diet, and reduced alcohol intake. These changes have been promoted in HICs in an attempt to reduce cases, which means they should be strongly encouraged within LMICs to ensure they don’t experience the same level of CRC cases.

Screening

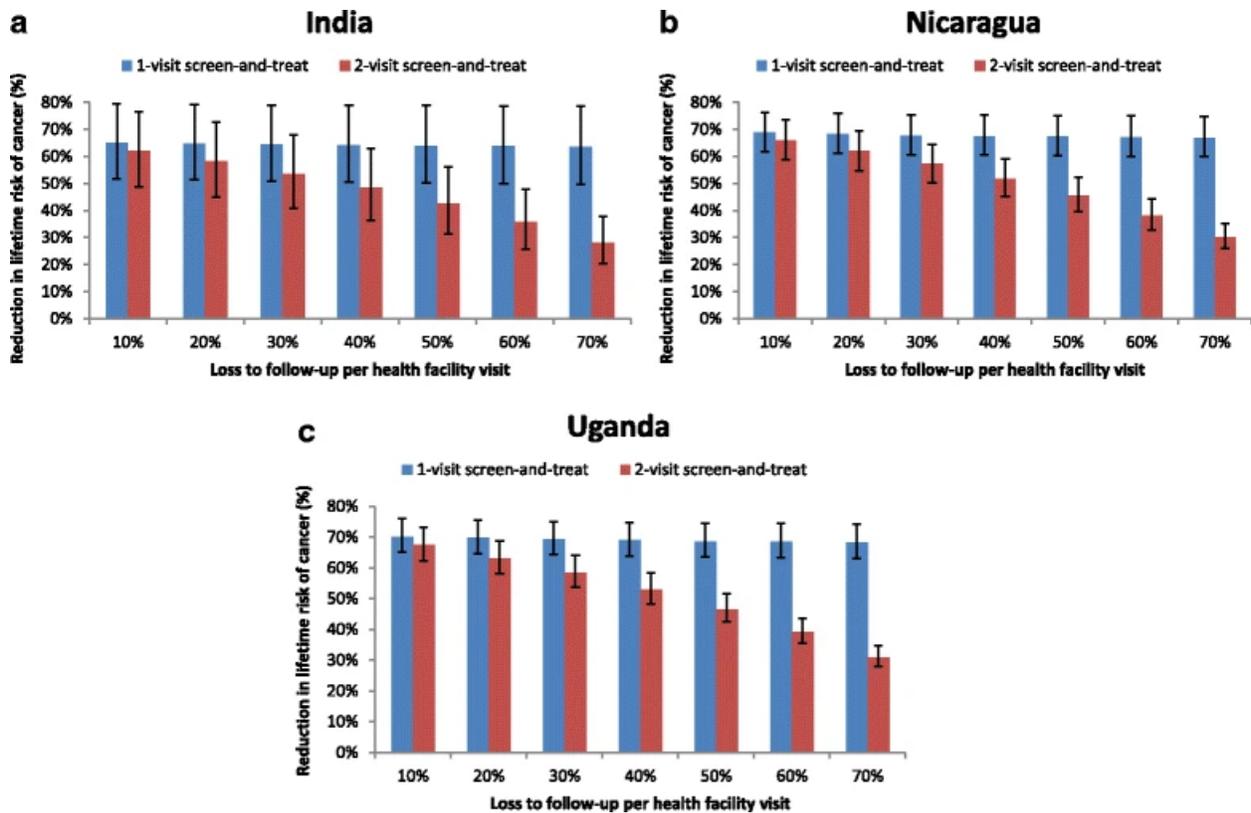
Screening is a secondary preventative measure that has been extremely successful in high income countries (HICs) but its impact hasn’t been well researched within LMICs (Shah et al., 2019). The research that has been conducted highlights that in some cases, it can be beneficial, but if set up incorrectly, can cause more harm than good. The WHO Cancer Report (2020) says

they should be implemented with caution due to the fact that the healthcare systems need to be able to handle additional patients who are in early stages in order for screening to be truly effective. Despite these concerns, there are some cancers where screening can be done efficiently and provide a great deal of benefits. The key to effective screening is to focus on certain subsets of the population to prevent the program from becoming overwhelmed.

One example of this is the secondary prevention of cervical cancer among patients who did not receive the vaccine at the target age either because they chose not to get it, or were unable to due to a lack of easy access. This demographic of people are still quite numerous within LMICs and deserve equal access to treatment. In order to limit the spread of cervical cancer, there has to be a system in place that can screen and treat precancerous lesions caused by HPV. In terms of screening, the two most common tests are visual inspection with acetic acid (VIA) and HPV (Denny et al., 2017). The VIA test is much easier to perform as you apply a solution to the suspected region and wait for a reaction to indicate the results. However since it is a visual test, it requires a healthcare provider to accurately interpret the results, which can be difficult given the minute differences between a positive and negative result. On the other hand, the HPV test is objective and much more accurate than the VIA test, however it is more expensive and elaborate to run. However after running an analysis of the two tests and taking into account variables such as test accuracy, test frequency, and overall costs, it was determined that HPV testing is the most cost effective (Denny et al., 2017). In an attempt to reduce the cost of doing an HPV test, a company has developed a tool that makes HPV testing significantly cheaper and faster. This point-of-care (POC) PCR test is called GeneXpert, and it has revolutionized the way cervical cancer can be managed in LMICs. This machine can detect 16 high risk HPV strains that are known to cause cancer in about one hour, which enables the ability

for providers to screen, diagnose and treat patients, all in one visit (Einstein et al., 2014). This is important because most people in LMICs have to travel far and take off work in order to visit a medical facility. It can be extremely difficult for them to return multiple times if screening tests take too long and treatment has to be delayed. In some cases, even with a positive test result, patients won't follow-up for treatment, meaning the test was a waste of resources (Campos et al., 2017). Figure 1 from the same article shows the drop off in potential cancer reduction among various LMICs if a second visit is needed. The GeneXpert avoids this issue by being a relatively quick test that can give results back early enough so that anyone who needs treatment can receive it on the same day as their test.

Figure 1: Risk of cancer associated with the two visit verses one visit screen and treat strategy



Another cancer where screening can be beneficial is with CRC, a type that has been on the rise in recent years within LMICs. In fact, while CRC incidence has stabilized in high income countries, it has increased rapidly among LMICs due to exposure to various environmental

factors along with shifts to more unhealthy, Western lifestyles (Xi and Xu, 2021). Screening for CRC is vital to its management because it can't be diagnosed easily in early stages, in part due to the lack of initial symptoms present during that time (Xi and Xu, 2021). This means that currently many patients in LMICs present with late-stage disease, which is extremely difficult and expensive to treat, and is often not very effective in leading to a complete recovery (Xi and Xu, 2021). This ultimately means that CRC has an extremely high mortality rate, and the discrepancy in mortality rate is very high between HICs and LMICs. Now the proper diagnostic test for CRC is a colonoscopy, a procedure that requires trained medical professionals, complicated equipment, and proper medical infrastructure to conduct. This is why many experts believe a shift needs to be made to put more focus on developing CRC screening programs in LMICs. Currently, stool-based tests such as the fecal immunochemical test (FIT) and the guaiac faecal occult blood test (gFOBT), are considered to be the best screening tests since both are non-invasive and inexpensive (Schliemann et al., 2020). These tests both look for small amounts of blood in the stool, which is often a symptom found in early stages of CRC, but it often goes unnoticed by people who are otherwise asymptomatic. However, of the two FIT has been shown to be more sensitive while also being easier to use (Lauby-Secretan et al., 2018). Additionally, it can be given as a take home test which makes it more approachable for skeptical patients in LMICs and generally results in a better patient adherence rate (Tze, Fitzgerald, Qureshi, Tan, & Low, 2016). These combinations of factors make the FIT the best screening option for most LMICs once they start rolling out programs.

As beneficial as screening programs are for some cancer types, there are others where it is not cost effective, or helpful for LMICs to implement at this time. Part of this comes from the WHO recommendations, stating screening programs should only be implemented if proper

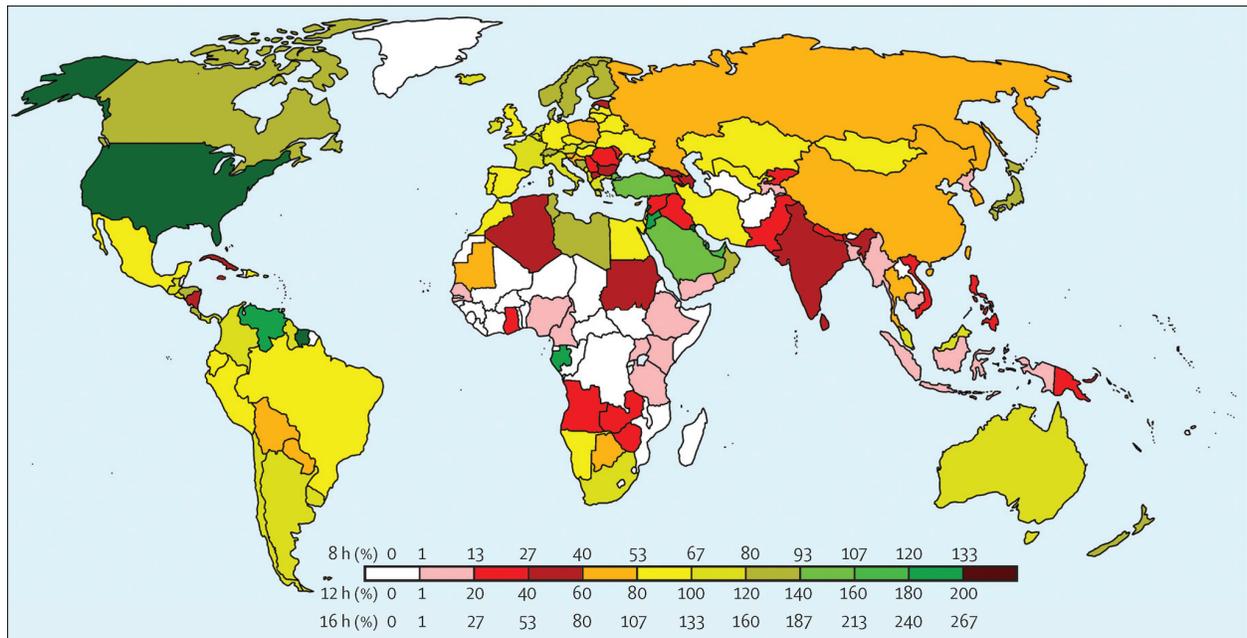
follow-up treatment services can be provided (“WHO Cancer Report”, 2020). Mammography is currently the best screening tool available for breast cancer but it is far too expensive, requires lots of infrastructure, and needs trained radiologists to operate. There are some LMICs who have a limited number of mammography machines available but they aren’t following the WHO guidelines of who to screen, especially considering that with the aging populations in LMICs, they are more prone to false-positive results (Denny et al., 2016). In addition, the WHO Cancer Report from 2020 states that the benefits of a screening program can take up to 10 years to materialize whereas early diagnosis has an immediate impact. Even in HICs, like the United Kingdom who have a national screening program, they discovered 90% of cancers were detected outside of their national screening programs (Whitaker, 2020). Regardless of how cost effective a screening program is for an LMIC, it is only beneficial if proper treatment can be provided to patients who need it.

Treatments

Radiotherapy

Radiotherapy is an extremely versatile cancer management tool that is unfortunately unavailable to many people who live in LMICs. Figure 2 below from Atun et al. (2015), shows the current coverage of radiotherapy available within each country. Unsurprisingly poorer nations have the lowest coverage currently, and these same places are expected to see the greatest increase in cancer cases moving forward. In fact, it is estimated that by 2035, nearly 12 million cancer patients will need some form of radiotherapy treatment (Atun et al., 2015).

Figure 2: Coverage of radiotherapy services according to country



Implementing radiotherapy is crucial given its wide range of uses and cancers it can effectively treat. It is especially important for LMICs because some of the most common cancers in these areas are ones that can benefit most from radiotherapy. According to Atun et al. (2015), breast and cervical cancer have the highest incidence and mortality rates in LMICs. These two also have the highest radiotherapy utilization rate given it is the preferred method of treatment recommended by most medical guidelines. However, given all of the apparent benefits of radiotherapy, it is quite puzzling that it is typically overlooked when it comes to investment within LMICs. This is due to a number of factors, but perhaps the biggest is the cost. Radiotherapy requires substantial upfront investment for construction and equipment while also needing further funding in order to cover the operational and maintenance costs of such services (Atun et al., 2015). In addition, the operation of radiotherapy devices relies on a large team of highly trained medical professionals that are often difficult and expensive to find, train, and retain within many LMICs (Atun et al., 2015). It is these barriers, among others, that has led to

the extreme lack of access many patients in LMICs are currently facing today, which is only expected to worsen moving forward. Thankfully, there are some ways of better managing these costs in order for LMICs to gain access to this vital treatment tool. The first of which involves the implementation of cobalt devices instead of linear accelerators as a first step in developing radiotherapy services. The cobalt system is recommended by the medical community for LMICs because it is cheaper to set up and can treat many of the cancers common in these areas (Atun et al., 2015). Though linear accelerators can treat a wider range of cancers they require much more up front investment such as building a bunker for it to be housed in, something that is extremely difficult to do in low-resource settings. Once built, there are cost-saving measures which can be used during operation in order to get a better return on investment. These measures include bulk equipment purchase, longer operating hours, and an increase in the number of patients treated per hour, which if done in combination can lead to relative cost savings of up to 50% in LMICs (Atun et al., 2015).

Overall an investment of around \$50 billion over the next 20 years is needed to scale up radiotherapy services in LMICs if some of the efficiency measures mentioned above are put into place (Atun et al., 2015). Despite these costs, it is currently estimated that if implemented, nearly 26.9 million life-years could be saved among LMIC patients who receive radiotherapy during the scale up period, which would result in a net monetary benefit of close to \$40 billion in those areas (Atun et al., 2015). This goes to show that even if it is expensive to start up, the potential to save lives and gain more economic output is far too great to ignore, and more LMICs need to start looking at building up access to radiotherapy treatment for their citizens. Now, as helpful as radiotherapy is, the implementation and eventual benefits will take some time to be fully

realized, which is why other treatment tools, such as chemotherapy, have seen extensive interest recently among many LMICs.

Chemotherapy

Treatments such as radiotherapy and surgery are both vital to proper cancer management, but they have a lot of upfront and recurring costs associated with them, making them difficult to build and maintain in LMICs. Fortunately for LMICs there is chemotherapy, which has the potential to be much more cost effective while also treating the more patients overall. In addition, chemotherapy is quite versatile and is utilized in the treatment of many different kinds of cancer, while also being much easier to administer to patients. For example, late-stage CRC is often associated with metastasis and as such requires additional treatment besides surgery such as chemotherapy. However, many of the current chemotherapy drugs are prohibitively expensive for many MICs to obtain and even fewer patients can afford them. In a study of Nigerian CRC patients, researchers found that about 32% of patients wouldn't receive chemotherapy because of financial restraints (Sharma et al., 2020). This isn't a surprise considering a round of chemotherapy in Nigeria costs around \$140 and most Nigerians only make around \$60 a month (Sharma et al., 2020). Research has shown there are a couple of ways to make chemotherapy more cost-effective. First, chemotherapy is often given in the adjuvant period, which is the time after surgery has been done to remove some of the cancer tissue. Adjuvant chemotherapy in stage 3 colon cancer has been found to be equally effective at 3 months when compared to 6 months when using fluorouracil and capecitabine (CAPOX) (André et al., 2020). This means LMICs should prioritize obtaining CAPOX as opposed to other chemotherapy drugs because they can shorten treatment times which will reduce costs and increase capacity. Another way to increase the cost-effectiveness of chemotherapy is through exercise. In a study by May et al.

(2017), they discovered that having CRC patients undergo an 18-week exercise course while receiving treatment resulted in less health care visits and fewer days of missed work.

Chemotherapy has shown to be an extremely cost-effective tool for breast cancer treatment in underdeveloped nations. The WHO has recently made breast cancer a priority health condition, and in doing so they added multiple drugs to the WHO essential medicines list (Mutebi et al., 2020). This list includes doxorubicin, cyclophosphamide, paclitaxel, docetaxel, tamoxifen, and trastuzumab. Some of these drugs, such as cyclophosphamide, have generic forms available which are generally cheaper and still very effective for patients following a successful mastectomy (Gelband et al., 2015). On the other hand newer drugs such as trastuzumab are still prohibitively expensive for LMICs and aren't cost effective (Gelband et al., 2015; Pace & Shulman, 2016). This is why LMICs must be diligent in what drugs they invest in obtaining and also demonstrates the need for outside regulation of drug prices being offered to LMICs. Under many of the current healthcare systems in LMICs, the budgets for purchasing drugs is quite small so the limited supply would only be given to patients who could pay for it out-of-pocket ("WHO Cancer Report", 2020). This greatly reduced overall access to these medications and came at the cost of not being able to offer cheaper generic or biosimilar medications to a greater number of people. Other developed nations need to step in and ensure pharmaceutical companies are selling to LMICs at fair prices and potentially even subsidize those costs to ensure everyone can have access to these life-saving medications. Though this would be far from a permanent fix, it would provide the temporary help needed while more solid plans are put into place that would allow LMICs to obtain or even manufacture these drugs on their own for much cheaper.

Conclusion

This review only cracked the surface of the challenges and possible solutions to effective cancer management in LMICs. Being able to tackle cancer management from every possible avenue, whether that be prevention, screening, or treatment, is vital to improving the outcome of cancer patients in LMICs. Looking at the bigger picture there are a few additional things that should be put in motion based on the discoveries within this review. First, it is vital more research is done to investigate all cancer types, especially those not covered here in order to discover any worrying trends and what can be done now to solve those issues, particularly if there are any cost-effective prevention strategies available. Next, proper referral networks within LMICs should be developed to help reduce patient confusion as to where to get proper treatment and encourage them to make follow-up visits if needed. Almost every article analyzed that discussed cost in some way indicated the need for universal health care systems to be set up in LMICs in order to help provide proper healthcare to all for a reasonable cost. Investment not only needs to be made into the infrastructure but also to the development of training facilities in order for these countries to properly staff the new medical facilities being built. Many experts believe this is where developed nations could step in to send trained medical professionals to LMICs to help set-up and initially run these institutions until they can be taken over by those living in LMICs. By taking steps like these moving forward, hopefully cancer patients within LMICs will not see their diagnosis as a death sentence, but rather as an obstacle that can be overcome. This future can be achieved if researchers, policy makers, and medical professionals from developed nations work together with their counterparts in LMICs, so that they can grow to be self-sufficient and one day have the cancer management tools necessary to treat their citizens and help make their nation prosperous for years to come.

References

- André, T., Meyerhardt, J., Iveson, T., Sobrero, A., Yoshino, T., Souglakos, I., Grothey, A., Niedzwiecki, D., Saunders, M., Labianca, R., Yamanaka, T., Boukovinas, I., Vernerey, D., Meyers, J., Harkin, A., Torri, V., Oki, E., Georgoulas, V., Taieb, J., . . . Shi, Q. (2020). Effect of duration of adjuvant chemotherapy for patients with stage III colon cancer (IDEA collaboration): final results from a prospective, pooled analysis of six randomised, phase 3 trials. *The Lancet.Oncology*, *21*(12), 1620-1629. 10.1016/S1470-2045(20)30527-1
- Atun, R., Jaffray, D. A., Barton, M. B., Bray, F., Baumann, M., Vikram, B., Hanna, T. P., Knaul, F. M., Lievens, Y., Lui, T. Y. M., Milosevic, M., O'Sullivan, B., Rodin, D. L., Rosenblatt, E., Van Dyk, J., Yap, M. L., Zubizarreta, E., & Gospodarowicz, M. (2015). Expanding global access to radiotherapy. *The Lancet Oncology*, *16*(10), 1153-1186. [https://doi.org/10.1016/S1470-2045\(15\)00222-3](https://doi.org/10.1016/S1470-2045(15)00222-3)
- Brisson, M., Kim, J. J., Canfell, K., Drolet, M., Gingras, G., Burger, E. A., Martin, D., Simms, K. T., Bénard, É, Boily, M., Sy, S., Regan, C., Keane, A., Caruana, M., Nguyen, D. T. N., Smith, M. A., Laprise, J., Jit, M., Alary, M., . . . Hutubessy, R. (2020). Impact of HPV vaccination and cervical screening on cervical cancer elimination: a comparative modelling analysis in 78 low-income and lower-middle-income countries. *The Lancet (British Edition)*; *Lancet*, *395*(10224), 575-590. 10.1016/S0140-6736(20)30068-4
- Campos, N. G., Tsu, V., Jeronimo, J., Mvundura, M., & Kim, J. J. (2017). Estimating the value of point-of-care HPV testing in three low- and middle-income countries: A modeling study. *BMC Cancer*; *BMC Cancer*, *17*(1), 791. 10.1186/s12885-017-3786-3

- Dare, A. J., Knapp, G. C., Romanoff, A., Olasehinde, O., Famurewa, O. C., Komolafe, A. O., Olatoke, S., Katung, A., Alatise, O. I., & Kingham, T. P. (2021). High-burden Cancers in Middle-income Countries: A Review of Prevention and Early Detection Strategies Targeting At-risk Populations. *Cancer Prevention Research, 14*(12), 1061-1074. 10.1158/1940-6207.CAPR-20-0571
- Denny, L., de Sanjose, S., Mutebi, M., Anderson, B. O., Kim, J., Jeronimo, J., Herrero, R., Yeates, K., Ginsburg, O., & Sankaranarayanan, R. (2017). Interventions to close the divide for women with breast and cervical cancer between low-income and middle-income countries and high-income countries. *The Lancet, 389*(10071), 861-870. 10.1016/S0140-6736(16)31795-0
- Drolet, M., Laprise, J., Martin, D., Jit, M., Bénard, É, Gingras, G., Boily, M., Alary, M., Baussano, I., Hutubessy, R., & Brisson, M. (2021). Optimal human papillomavirus vaccination strategies to prevent cervical cancer in low-income and middle-income countries in the context of limited resources: a mathematical modelling analysis. *The Lancet Infectious Diseases*, [https://doi.org/10.1016/S1473-3099\(20\)30860-4](https://doi.org/10.1016/S1473-3099(20)30860-4)
- Edelman Saul, E., Guerra, R. B., Edelman Saul, M., Lopes da Silva, L., Aleixo, G. F. P., Matuda, R. M. K., & Lopes, G. (2020). The challenges of implementing low-dose computed tomography for lung cancer screening in low- and middle-income countries. *Nature Cancer, 1*(12), 1140-1152. 10.1038/s43018-020-00142-z
- Einstein, M. H., Smith, K. M., Davis, T. E., Schmeler, K. M., Ferris, D. G., Savage, A. H., Gray, J. E., Stoler, M. H., Wright Jr, T., C., Ferenczy, A., & Castle, P. E. (2014). Clinical evaluation of the cartridge-based GeneXpert human papillomavirus assay in women

referred for colposcopy. *Journal of Clinical Microbiology; J Clin Microbiol*, 52(6), 2089-2095. 10.1128/JCM.00176-14

Gelband, H., M.H.S., Sankaranarayanan, R., M.D., Gauvreau, C. L., PhD., Horton, S., Prof, Anderson, B. O., M.D., Bray, F., D.Phil, Cleary, J., M.D., Dare, A. J., PhD., Denny, L., M.D., Gospodarowicz, M. K., M.D., Gupta, S., M.D., Howard, S. C., Prof, Jaffray, D. A., PhD., Knaul, F., PhD., Levin, C., PhD., Rabeneck, L., M.D., Rajaraman, P., PhD., Sullivan, T., PhD., Trimble, E. L., M.D., & Jha, P., Prof. (2015). Costs, affordability, and feasibility of an essential package of cancer control interventions in low-income and middle-income countries: key messages from Disease Control Priorities , 3rd edition. *The Lancet (British Edition); Lancet*, 387(10033), 2133-2144. 10.1016/S0140-6736(15)00755-2

Global strategy to accelerate the elimination of cervical cancer as a public health problem.

Geneva: World Health Organization; 2020. License: CC BY-NC-SA 3.0 IGO.

Hu, J., Zhao, C., Chen, W., Liu, Q., Li, Q., Lin, Y., & Gao, F. (2021). Pancreatic cancer: A review of epidemiology, trend, and risk factors. *World Journal of Gastroenterology*, 27(27), 4298-4321. 10.3748/wjg.v27.i27.4298

Huang, J., Chan, P. S., Lok, V., Chen, X., Ding, H., Jin, Y., Yuan, J., Lao, X., Zheng, Z., & Wong, M. C. (2021). Global incidence and mortality of breast cancer: a trend analysis. *Aging*, 13(4), 5748-5803. 10.18632/aging.202502

Lauby-Secretan, B., Vilahur, N., Bianchini, F., Guha, N., & Straif, K. (2018). The IARC Perspective on Colorectal Cancer Screening. *The New England Journal of Medicine; N Engl J Med*, 378(18), 1734-1740. 10.1056/NEJMSr1714643

- Mutebi, M., Anderson, B. O., Duggan, C., Adebamowo, C., Agarwal, G., Ali, Z., Bird, P., Bourque, J., DeBoer, R., Gebrim, L. H., Masetti, R., Masood, S., Menon, M., Nakigudde, G., Ng'ang'a, A., Niyonzima, N., Rositch, A. F., Unger-Saldaña, K., Villarreal-Garza, C., . . . Eniu, A. (2020). Breast cancer treatment: A phased approach to implementation. *Cancer*, *126*, 2365-2378. 10.1002/cncr.32910
- Pace, L. E., & Shulman, L. N. (2016). Breast Cancer in Sub-Saharan Africa: Challenges and Opportunities to Reduce Mortality. *The Oncologist*, *21*(6), 739-744. 10.1634/theoncologist.2015-0429
- Pilleron, S., Sarfati, D., Janssen-Heijnen, M., Vignat, J., Ferlay, J., Bray, F., & Soerjomataram, I. (2019). Global cancer incidence in older adults, 2012 and 2035: A population-based study: Global cancer incidence in older adults. *International Journal of Cancer*, *144*(1), 49-58. 10.1002/ijc.31664
- Ralaidovy, A. H., Gopalappa, C., Ilbawi, A., Pretorius, C., & Lauer, J. A. (2018). Cost-effective interventions for breast cancer, cervical cancer, and colorectal cancer: new results from WHO-CHOICE. *Cost Effectiveness and Resource Allocation; Cost Eff Resour Alloc*, *16*(1), 38. 10.1186/s12962-018-0157-0
- Schliemann, D., Matovu, N., Ramanathan, K., Muñoz-Aguirre, P., O'Neill, C., Kee, F., Su, T. T., & Donnelly, M. (2020). Implementation of colorectal cancer screening interventions in low-income and middle-income countries: a scoping review protocol. *BMJ Open*, *10*(6), e037520. 10.1136/bmjopen-2020-037520

- Shah, S. C., Kayamba, V., Peek, R. M., Jr, & Heimbürger, D. (2019). Cancer Control in Low- and Middle-Income Countries: Is It Time to Consider Screening? *Journal of Global Oncology*, 5, 1-8. 10.1200/JGO.18.00200 [doi]
- Sharma, A., Alatisé, O. I., Adisa, A. O., Arowolo, O. A., Olasehinde, O., Famurewa, O. C., Omisore, A. D., Komolafe, A. O., Olaofe, O., Katung, A. I., Ibikunle, A. D., Egberongbe, A. A., Olatoke, S. A., Agodirin, S. O., Adesiyun, A. O., Adeyeye, A., Ibrahim, K., Kolawole, O. A., Idris, O. L., . . . Kingham, T. P. (2020). Treatment of colorectal cancer in Sub-Saharan Africa: Results from a prospective Nigerian hospital registry. *Journal of Surgical Oncology; J Surg Oncol*, 121(2), 342-349. 10.1002/jso.25768
- Teoh, J. Y. C., Hirai, H. W., Ho, J. M. W., Chan, F. C. H., Tsoi, K. K. F., & Ng, C. F. (2019). Global incidence of prostate cancer in developing and developed countries with changing age structures. *PLoS ONE*, 14(10)10.1371/journal.pone.0221775
- Tze, C. N. V., Fitzgerald, H., Qureshi, A., Tan, H. J., & Low, M. L. (2016). Pioneering Annual Colorectal Cancer Screening and Treatment Targeting Low Income Communities in Malaysia (2010-2015). *Asian Pacific Journal of Cancer Prevention : APJCP; Asian Pacific Journal of Cancer Prevention : APJCP*, 17(7), 3179-3183.
- Whitaker, K. (2020). Earlier diagnosis: the importance of cancer symptoms. *The Lancet Oncology; Lancet Oncol*, 21(1), 6-8. 10.1016/S1470-2045(19)30658-8
- Wong, M. C. S., Goggins, W. B., Wang, H. H. X., Fung, F. D. H., Leung, C., Wong, S. Y. S., Ng, C. F., & Sung, J. J. Y. (2016). Global Incidence and Mortality for Prostate Cancer: Analysis of Temporal Patterns and Trends in 36 Countries. *European Urology*, 70(5), 862-874. 10.1016/j.eururo.2016.05.043

World, H. O. (2020). *WHO report on cancer: setting priorities, investing wisely and providing care for all*. World Health Organization.

Xi, Y., & Xu, P. (2021). Global colorectal cancer burden in 2020 and projections to 2040. *Translational Oncology*, *14*(10), 101174. [10.1016/j.tranon.2021.101174](https://doi.org/10.1016/j.tranon.2021.101174)