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A Strategy for Cancer Prevention in Bangladesh

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Abstract

Better control of communicable diseases has contributed to an epidemiologic transition under which majorities of deaths in low- and middle-income countries are from non-communicable diseases including cancers. The sustainable development goals for 2030 include a target of reducing by one-third premature mortality from non-communicable diseases.

For Bangladesh, in prevention the foci of needed efforts are clear- tobacco abuse, indoor smoke exposure, betel-nut chewing, HPV and HBV vaccination - areas where population-wide interventions can have major impacts. Bottom-up/local interventional research with clear goals, measurement of processes and endpoints, and rigorous evaluation should be emphasized. Multiple major in-country contextual issues however can easily overwhelm, thwart and nullify the impact of targeted programs. In Bangladesh, climate change, poverty, human rights shortcomings, poor governance and limited education are such commanding issues. Globally, the creation of mega biological and social science parameter databases, combined with rapidly growing synthetic and analytic capacity are creating an intelligence explosion. Technical inventions in robotics with drones and in financing additionally are challenging the often prolonged timeframes for defining more powerful cancer prevention interventions.

In reviewing details of current knowledge and these contexts, this communication suggests a strategy for Bangladesh of prioritized, short-term local intervention research projects and think-tank planning.

Keywords: Hepatitis B Virus (HBV); Human Papilloma Virus (HPV); Cancer Epidemiology; Non-Communicable diseases

Introduction

The major goals for cancer prevention in low- and middle-income countries (LMICs) are very similar to those among high-income countries, but the major in-country contexts and therefore potential approaches are significantly different. This communication will first consider prioritized research approaches for Bangladesh based on major causes and then focus on those contexts. Further, with respect to context it will consider, in particular, the accelerating pace of discoveries in cancer biology, social sciences, and technology, and the impacts of these and of break-through findings on research and the practice of public health oncology in this country [1]. Finally it will consider a practical strategy in the face of these challenges.

The goal of cancer prevention, as discussed here, is decreasing premature mortality from malignancies by interventions which decrease incidence rates in middle-aged and young populations. Because malignancies are significantly consequences of aging, some metrics of impact may not change at all with successful cancer prevention efforts. For example, overall numbers of deaths from cancer (from tobacco-induced malignancies specifically) may not decrease while premature cancer deaths may fall. Further here "secondary prevention" or "early detection" will not be discussed because this subject present a radically different series of considerations, and for some scientists, including this author, offers but limited opportunities in public health oncology in LMICs [1].

The Relevant Descriptive and Analytic Epidemiology for Bangladesh

With a population of 160 million, Bangladesh is the 7th most populous country in the world. Unlike circumstances in several fellow Asian

countries, rural urban migration has been limited such that the rural urban population distribution is still 70/30%. There is some temporary urban migration of rural populations for parts of the year, particularly to Dhaka, the capital and major city, which practice makes census data uncertain.

The age pyramid is broad at its base: almost 1/3rd of the population is under age 15 and more than half is under age 25. Thus certain preventive interventions have similarly large fractions of the populations as their targets (http://www.indexmundi.com/bangladesh/age_structure.html).

There is no population-based cancer registry system in Bangladesh. There is a Kolkata (India) registry which populations differ from those of the entirety of Bangladesh principally in that they are more Hindu [2]. Bangladesh is now perhaps 85% Sunni Moslem. The Economist Intelligence Unit used these data in its 2009 report with estimates for Bangladesh [3]. These reports together with a hospital registry report from the National Cancer Research Institute and Hospital covering 2008-2010 suggest the distribution and figures shown in table 1.

Incidence rates are uncertain because the age structures of the Kolkata and Bangladeshi populations differ, but details are lacking - in Bangladesh the last census was in 2011, its methods have been criticized, and the noted two-way rural-urban migration practice confounds attempts at precision.

In similar circumstances it is often argued that a priority should be creation of a cancer registry, if only one covering a fraction of the country's population. At present because of the dysfunctional and underfunded state of the health system, combined with the absence of a health insurance system such that patients have to pay out of pocket for most medical services, the majority of patients with malignancy in Bangladesh do not

have a pathological diagnosis. Again two-way rural-urban migration further confounds accurate measurements of both numbers of cases and the population from which the cases are drawn. As for any new registry it is difficult to imagine that with creation of even a limited population-based registry, reasonably representative data might be forthcoming in under a decade. Other contextual issues considered below further suggest that creation of a cancer registry is unlikely to be a genuinely successful and more importantly useful exercise. Research cohort studies may offer opportunities to refine estimates provided in table 1.

The listing of malignancies in table 1 suggests likely potentially alterable risk factors such as tobacco abuse, hepatitis B virus (HBV) and human papilloma virus (HPV) and these data, combined with certain cultural practices like betel nut chewing and indoor smoke exposure, suggest others. These five then are the focus of the interventions discussion here.

Other factors important in common malignancies deserve comments here. In Bangladesh age at first full term pregnancy is increasing and parity is decreasing, both of which trends might be expected to increase population incidence rates for breast cancer. From a societal perspective the benefits of these trends outweigh these costs. Over-nutrition and obesity are emerging and important problems and contributors to the development of malignancies worldwide and likely are contributing modestly in Bangladesh. The major nutritional issue in the country however is under nutrition of young children—fully one quarter of this population is so affected with major adverse consequences for nervous system development. (UNICEF estimates even higher rates: http://www.unicef.org/nutrition/bangladesh_68757.html) These circumstances challenge addressing the nutritional issues associated with malignancies at a population level. Limited exercise has been identified as an important co-factor in cancer development, but application of this information must be limited in a country where a majority of citizens engage in manual labor on a daily basis. Finally alcohol abuse is important as a major factor or co-factor in malignancies; consumption is very limited in dominantly Moslem Bangladesh.

A Prioritized Interventional Research Agenda in Cancer Prevention for Bangladesh

Tobacco

The prevalence of smoking among the 2/3rds of Bangladeshi men over age 15 approaches 50%, while this is less than 2% among women [4,5]. One quarter of deaths among Bangladeshi men are attributed to cigarette smoking [4]. Bangladesh has signed the Framework Convention on Tobacco Control and then passed a Smoking and Tobacco Product Usage (Control) Act in 2004 prohibiting advertising and requiring a warning label on packets, and proposed revisions in 2013 [6,7]. There are graded excise taxes, which are high (60%) and highest for commercial cigarettes.

Men(% of 90,000)	Women (% of 80,000)
Lung 25%	Breast 20%
Head and neck 20% Mouth 5% Pharynx 5% Larynx 5% Esophagus 4%	Uterine cervix 18%
	Lung 5%
	Head and neck 5%
Lymphoma 5%	
Stomach 4%	
Liver 4%	

Table 1 [2,3]: Distribution of annual cancer case burdens in Bangladesh (total estimated to be 170,000 cases)

Globally, a WHO-endorsed package of evidence-based interventions called MPOWER has shown the potential of environmental changes to change behaviors [8]. The obvious categories of intervention for tobacco are three: policy, public education, and personal (medical) intervention.

In Bangladesh, regarding policy, the status of enforcement of the 2004 Act and the implementation of the 2013 revisions (if finally approved), are uncertain. The tobacco lobby is powerful in Bangladesh (which in some areas produces a large tobacco crop), and the leeway for encouraging enforcement and a “Truth campaign” with anti-tobacco messages to promote a better social environment and health literacy is unclear. Based on the contents of such campaigns in other settings some themes are suggested in table 2. Similarly the ability of local communities to launch “tobacco-free” campaigns is uncertain. The Bangladesh Center for Communication Programs which has collaborated with The Johns Hopkins University Bloomberg School of Public Health on tobacco control research would seem ideally suited to further lead in this area. In the area of personal/medical intervention with patient smokers, there has been but very limited activity, and given the contextual issues (see below) it is difficult to anticipate within the foreseeable future this area of intervention as a major contributor to better tobacco control.

In summary, despite the most significant numerically, large and growing adverse impact of tobacco abuse on development of mostly incurable malignancies in Bangladesh, it is difficult to be optimistic that the suggested strategies, proven effective in other settings, are likely to be adopted comprehensively any time soon.

Indoor smoke

While it is difficult to get numerical data to support an assertion that air pollution from general urban sources, industrial sources such as brick making, deforestation (one-third attributable to tobacco cultivation), and importantly wood and dung burning for cooking in homes, is an attributable cause of lung cancer, the combination of low rates of tobacco abuse in women and the (increasing) presence of female patients with lung cancer (table 1) with no personal tobacco exposure history (author’s experience), makes this assertion credible. Consistent with this suggestion are data that second hand smoke exposure is said to occur in 42% of children under age 16 [4]. In the home for cooking, inexpensive electric stoves have been promoted as a feasible approach to this problem, but rural electrification is limited in Bangladesh.

Betel-nut chewing

Betel-nut (Areca catechu) chewing is a powerful risk factor for oral and esophageal cancer [9]. Data are limited, but suggest that approaching one-third of Bangladeshi women use oral tobacco with or without betel-nuts [5,10]. Investigators describe a true dependency/addiction syndrome associated with Areca use [11]. The significant cultural, religious and economic components of this habit and the completely uncontrolled marketing of paan (Betel-nut quid) products, pose major challenges to addressing this important risk factor for malignancy [12]. The apparent greater use of paan by women offers an avenue of approach through the broad area of women’s health.

*Contents of cigarettes
*Addiction from cigarettes
*Suffering from cigarettes: Blackened lungs, big neck tumor, facial deformity with tumor, bone with metastasis.
*Vignettes of people suffering; social leaders speaking out against tobacco

Table 2: A suggested Truth campaign of anti-tobacco messages

HPV

In a recent study, HPV prevalence in women was found to be 7.7% [13]. A small randomized pilot study of the bivalent HPV 16/18 vaccine found 97.5% sero conversion after 7 months [14]. These data are found in a background wherein there has been on paper a National Cervical Cancer screening program for a decade, reportedly covering 2/3rds of districts. A formal review after 6 years found that population coverage was poor and there was limited follow up and treatment of visual inspection-positive cases [15]. It is unclear what the status of this program is currently; it is certain that it has had very limited, if any presence, in one of the 7 divisions of the country, the Khulna division.

At the federal level in Bangladesh there is a strong immunization program which has implemented very successful population-coverage programs (example for DPT3-93%, and a more recent (2014) measles-rubella campaign reaching close to 100% of the target population). A two year GAVI-supported HPV demonstration project is planned to begin in early 2016, using the bivalent vaccine, targeting over two years all 10 year old girls in the Gazipur district (90% of whom are in school)—a total of 66,000 girls. Various considerations contribute to defining a project goal of achieving 75% population coverage. The operating budget for this project is approximately \$360,000 or \$5.5/target subject.

A review of the GAVI decision letter from March 2015 regarding this project elicits mixed responses. It is important that there is a federal effort for HPV vaccination, but the extent of the apparent leadership, expertise, objectives, evaluation and funding leave a reviewer feeling that far less will be achieved than is possible and the ability to scale-up to a national coverage program from this modest effort is likely to be poor.

HBV

The population prevalence of HB sero-positivity is reported to be as high as 5.4% (<http://hepatmon.com/631.fulltext>). Bangladesh is reported to have instituted childhood HBV vaccination (3 doses) a decade ago, but the extent of current HBV children's coverage is uncertain and while targeting children is optimal, the possibility of adult coverage deserves attention.

A prioritized agenda

The quality of evidence suggesting foci on tobacco, indoor smoke, betel nut chewing/pan use, and HPV and HBV vaccination for cancer prevention is adequate, if limited specifically in Bangladesh. Strong cases can be made for major attention to each of these five areas. The major challenge is that across these areas, defining well-justified scalable interventions is essentially impossible absent considerable interventional research. Bangladesh is rich in non-governmental organizations which have been useful laboratories for social entrepreneurship, and this author has advocated such bottom-up local community research as the most promising approach to better cancer control in LMICs (1). Given the weak research traditions in Bangladesh, research partnerships with high-income country universities offer a mechanism for such work [16]. The success with Millennium Development Goals (MDGs) suggests that Sustainable Development Goal (SDG) efforts should be precisely targeted and publicized [17].

The Major In-Country Contextual Issues for Bangladesh

Broad contextual issues easily overwhelm, thwart and nullify the impact of scientific investigations and service improvements, and general service itself in health [18]. In this author's experience, in developing and operating a breast care center over the last several years, in multiple individual women reasonable and possible medical interventions have

Relative secularity and religiosity
Climate change
Poverty
Human rights
Governance
Limited education
Limited electrification
"Floating" populations
Dependence of global health funding
Very limited research capacity
Terrorism

Table 3: Major in-country contextual issues for Bangladesh

been impossible because of issues in each of these areas [19]. The major issues for Bangladesh are suggested in table 3 and brief consideration of these follows here.

Relative secularity and religiosity

In recent years Bangladesh has become more Sunni Moslem and less Hindu. Attacks on Hindus generally, and then more recently on Hindu shrines, Buddhist temples, Shia Moslem gatherings and foreigners have elicited commentaries on the loss of secularity in the country generally. Beards and burkas, thought to reflect more Moslem piousness, are more widely seen. In particular these turns in Bangladeshi society are likely to be reflected in greater sense of determinism in life events and illness often associated with religiosity.

Climate change

In southern Bangladesh where three of 8 divisions of the country are located 18% of current mostly arable land in Bangladesh is predicted to be lost to rising water levels in next 15 years. The population density in Bangladesh is the greatest of any country in the world excluding Singapore. The raw figures suggest that as many as 30 million people will be displaced by loss of land. Heretofore international assistance has been very limited and the focus has been on adaptation strategies. This subject dominates federal planning, budget, and foreign aid discussions.

Poverty

Bangladesh is one of the poorest countries in the world with a GDP that first rose past \$1000 in 2010, and is comparable to that of Haiti, South Sudan and Zimbabwe, and behind that of India and even Myanmar. While average incomes are rising, a huge proportion of the population has very low incomes. In southern Khulna division from which this communication comes, 90% of families are living on less than \$1 per person per day [20].

Human rights

While extensive poverty is the most important human right shortcoming, other major issues powerfully impacting health include women's rights, absence of federal support in many ways for health, food-under nutrition, water safety, and social, cultural, racial, and minority discrimination (<http://www.ohchr.org/EN/Issues/Pages/ListOfIssues.aspx>)

Governance

Bangladesh is a highly politicized country in which the party in federal power patronizes its supporters with government employment during its tenure, and corruption is institutionalized. This pattern extends to medical

institutions and practice generally where making money is the dominant ethos. The government has made enormous progress however in public health in decreasing the fertility rate, infant mortality and childhood deaths from diarrheal disease. A federal plan for addressing Non-communicable diseases exists but translation into action has been lacking.

Education

Bangladesh has made major progress in education especially of girls, but literacy among adults is remarkably low, particularly in women.

Limited electrification

Only 60% of the population has access to electricity.

“Floating” populations

Large populations migrate temporarily in connection with employment opportunities, in particular in the garment industry.

Dependence on global health funding

Bangladesh is heavily dependent on international funding for health. Internationally the epidemiologic transition to greater non-communicable disease (NCD) burdens in countries like Bangladesh is getting more attention, but NCDs are still way underfunded. Disease burdens (in DALYs) and international funding are not in synch: non-communicable diseases, with half the DALYS burden, currently get less than 2% of global health funding [21].

Research capacity

The country has minimal research capacity which is most concentrated at the post graduate institution of BSMMU in Dhaka. This and other less academic institutions are overwhelmed with their patient-care missions.

Terrorism

A last unlisted, but much talked about contextual issue is terrorism. There have been lethal attacks on various populations in recent times; the motivations behind these have been unclear, but may be credibly simply extensions of the country's extreme politicization, and not (yet) reflections of international terrorist presence. Bangladeshis have been part of European and Southern Asian migrations and have been among recruits to extremist Islamic organizations.

In the bigger global context of MDGs and SDGs Murray suggest there have been four key lessons important in attention to major activities such as those suggested for cancer prevention [17].

1. Make strongly the connection of health and development
2. Focus attention on outcomes that resonate with the public
3. Assure attention in the media to progress toward goals
4. Donors prioritized support to MDGs

In summary, regarding domestic and global contexts for cancer prevention in Bangladesh, these are of major importance-any targeted efforts are likely to have minimal impact without thoughtful attention and sensitivity to these contexts, and further these dictate that local research initiatives are likely to be the most successful approach to defining strategies that can be scaled up for population impact.

Global Scientific Contextual and Futuristic Perspectives

There are also global contextual issues in scientific development to consider in rationally defining a strategy for cancer prevention in Bangladesh. Specifically the pace and breadth of scientific discoveries are increasing so rapidly that these can dwarf and make obsolete activities of the kinds suggested above as current priorities. For examples broadly there are these kinds of critical developments:

1. Development of huge biological social scientific international and local databases
2. Increased synthetic and analytic capacity → artificial intelligence
3. Increased technical capacity in robotics, drones, communication
4. Increased creative financing capacity

With the following consequences:

1. Increased predictive capacity
2. Increased modeling capacity
3. Breathtaking progress, breakthroughs, sudden leaps forward, unanticipated developments
4. Timetables for activities markedly compressed
5. Obsolescence of ongoing activities with long timelines

In Bangladesh there has been, over the last decade, a major increase in cell phone penetration. Additionally however, in this context, there has been absence of a research culture.

Applying these to thinking about planning cancer prevention activities prompts the following considerations and suggestions:

First, it is true that the future for Bangladesh, governed by the multiple contextual issues presented above, is indeterminate, but this does not deny that rigorous probabilistic thinking can increase chances of successes in particular areas [22]. Thus there is a need to organize specifically to prepare for these developments and consequences. I suggest that this is best done by creating some group or groups to focus on cancer prevention because:

1. Groups do better thinking through and forecasting than individuals.
2. Diverse expertise is essential among group members (include journalists for example besides scientists)
3. Challenging all assumptions continually is critical
4. The need for endless focus on essential questions and breaking these down into component and potentially answerable questions.
5. The need to update predictions and forecasts regularly.

To bring home the relevance of such considerations and suggestions, let us posit some critical “what if” questions for cancer prevention:

#1. What if we rapidly attain the ability to identify high risk population's very precisely.

What if attributable-risk-significant host genetic markers for tobacco caused malignancies (lung, oral-pharynx-larynx) or betel nut chewing cancers are identified and can be inexpensively applied to populations?

What if population data-bases and demographic data quality become so comprehensive and accurate that the level of efficiency in targeting of populations for vaccination for HPV and HBV (and possibly for treatment for helicobacter pylori) goes way up? For example from data such as our Rampal project [23].

#2. What if we rapidly attain the ability to use social and other media behavioral change tools more specifically targeted to at-risk populations and with greater efficacy?

Tools are rapidly becoming available for just such activities: (<http://fortune.com/2015/10/26/ibm-watson-apple-watch-health/>)

Thus for Bangladesh, much targeted anti-tobacco/anti-betel nut chewing behavioral interventions might soon be possible.

#3. What if we rapidly attain the ability to “treat” more precisely identified high risk populations with presumed pre-cancers because

of nanotechnology employing serological testing identifying malignant clones or DNA adducts? (<http://www.ncbi.nlm.nih.gov/pubmed/16140979>).

Possible consequences are that an entirely new approach to cancer prevention might be possible.

Conclusion

The major thrust of this communication is an argument that the major challenge for cancer prevention in an LMIC like Bangladesh is how to think about the problem. Current high-income country “cancer control science” parochial, often large-scale “top-down” approaches (policy, health institution-led, medical practice guideline-defined) are not transferrable to LMIC contexts particularly in the face of rapid scientific developments. To this author Bangladesh will be most benefitted by:

1. Increased local research efforts under experienced in- and out-of country leaders, with tight-short timelines, defined by epidemiologic priorities. The international health funding community needs to rebalance its allocation of yes scarcer monies, to NCDs like cancer and consider longer time lines and more research instead of demonstration activities. There may be imaginative ways that internal Bangladeshi financial resources can be brought to bear on such research efforts also Bangladeshi successes in vaccination and in decreasing maternal and child mortality provide critical models [24].
2. Creation of think tank capacity in an academy or within the federal ministries to address cancer prevention and define and guide the research agenda in Bangladesh’s rapidly evolving society and a scientifically exploding world. Experience with American, European, Japanese and Brazilian models should be looked to.

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