Public health oncology: a framework for progress in low- and middle-income countries†

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Background: The problems of cancer are increasing in low- and middle-income countries (LMCs), which now have significant majorities of the global case and mortality burdens. The professional oncology community is being increasingly called upon to define pragmatic and realistic approaches to these problems.

Patients and methods: Focusing on mortality and case burden outcomes defines public health oncology or population-affecting cancer medicine. We use this focus to consider practical approaches.

Results: The greatest cancer burdens are in Asia. A public health oncology perspective mandates: first, addressing the major and social challenges of cancer medicine for populations: human rights, health systems, corruption, and our limited knowledge base for value-conscious interventions. Second, adoption of evolving concepts and models for sustainable development in LMCs. Third, clear and realistic statements of action and inaction affecting populations, grounded in our best cancer science, and attention to these. Finally, framing the goals and challenges for population-affecting cancer medicine requires a change in paradigm from historical top-down models of technology transfer, to one which is community-grounded and local-evidence based.

Conclusion: Public health oncology perspectives define clear focus for much needed research on country-specific practical approaches to cancer control.

Key words: cancer in low-income countries, public health oncology

introduction

With rising global burdens of cancer case numbers, deaths, incidence and mortality, medical science, humanitarian and medical diplomatic agendas and efforts to address these need to be pragmatic and realistic. In this communication, we propose to practitioners addressing this rising global burdens problem as one of public health oncology or population-affecting cancer medicine, and then consider the major functional variables, models of international development efforts and specific areas of interventions likely to combat these mortality and case burdens successfully.

methods

demographic imperatives and the need for public health oncology

Globally, cancer is now the second leading cause of death [1]. Of the cancer global burdens, 50% of all new cases and 66% of all cancer deaths occur in citizens of low- and middle-income countries (LMCs) and these percentages are projected to be 70% and 80%, respectively, by 2020 [2]. Further, a low cancer incidence:mortality ratio for LMCs primarily reflects the circumstance that 80% of cancers diagnosed in LMCs are in advanced stages, for which treatments are marginal to ineffective.

While greater attention to poor outcomes from cancer is needed across all countries, numerically the major burdens are falling on Asian countries. As Table 1 suggests, more than half of the world’s population lives in South and East Asian countries. Thus, the focus of our communication is on countries in this part of the world.

In broad frameworks, in the United States in particular, we have usually seen cancers as isolated events to individuals and have framed the challenges and issues in private sector business terms. This dominant framework is limiting in that the focus is mostly on cancer biology in humans and less on the ecological circumstances so critical in the causation, development and management cycles in our complex societies [3]. (Here focusing on human ecology—the relationships between human beings and their natural, social and constructed environments.) One cancer-related area in which broad societal approaches have been effective has been smoking. Otherwise however, with dominantly private sector, individual patient-focused medical approaches, an underlying assumption (again in the US in particular) about addressing cancer globally has been that our individual approaches and market mechanisms should and will ‘deliver the goods’ to the top, as well as the bottom billions of our populations. In fact, markets at the bottom of our global population pyramid have been ignored [4].
A decade ago, Helen Epstein wrote scathingly that we live in a ‘time of indifference’ with respect to global public health—that we are reluctant to think of specific health problems in population perspectives [5]. With respect to cancer, perhaps in the intervening time things have become even worse. From the Asian and poor people perspectives, the situation in health care is just as the crying Russian pilot says in the documentary about peoples’ livelihoods in central Africa, *Darwin’s Nightmare*: ‘It’s all business’ [6]. Paralysis and neglect best characterize cancer medicine for most citizens in LMCs, where cost issues scare government officials, big business and major pharmaceutical companies control what care is given for everyone, and the majority of any funds for cancer is spent on individual systemic treatments of marginal value.

In summary, for these reasons we propose here that a paradigm of public health oncology-population cancer medicine perspectives may be useful in addressing global cancer burdens more effectively. In the remainder of this communication, we spell out what such perspectives show us and indicate for specific actions interested practitioners can consider.

### results

#### the broad challenges in cancer medicine for populations

The dominant high-income country framework for better cancer care applied globally repeatedly leads to calls for workforce development (or capacity building), national cancer control plans and guidelines, drug pricing system creation, innovative financing and infusions of large volumes of capital [7, 8]. The challenge is seen to be a ‘technology transfer’ one. It is hard to not compare these approaches with those advocated for economic development generally for the last half century, and found by many to have been so wanting [9, 10]. We believe that in fact, the major issues are broader than these, and that in any event, these current dominant framework foci can hardly be successfully addressed without attention to bigger ecological issues and themes such as:

- Weak, dysfunctional and underfinanced health systems, overall
- Governance, corruption and transparency
- Human rights shortcomings
- Incomplete knowledge about diseases, patient/host factors and cost-effective interventions.

With respect to these major areas: The discussions about weak health systems have been a dominant theme in WHO reports; and attention to social determinants of health and the ‘pathologies of power’ have, appropriately in our view, characterized academic discussions of how to improve health [3, 11–13]. A particular challenge, now greater in LMCs than high-income countries, is rural to urban migration (initially transiently) with creation of ‘arrival cities’ within or on the borders of major established cities. Such transient communities or communities in development present particular challenges to struggling health systems. One cannot work in the most populous Asian countries without being repeatedly challenged by cultures of corruption and poor governance [14].

Discussions, however, for cancer medicine ‘verticalize’ the major considerations, with disease-focused proposals, and rarely mention these major and action-controlling circumstances and the important roles of horizontal or more broad-based approaches.

The critical importance of human rights issues in health has received far less attention than these deserve. The strongest and most rigorous statement has been made by Farmer in his book *Pathologies of Power* [13]. The important intersection with human rights and health for women in particular is being increasingly recognized [http://www.un.org/womenwatch/daw/beijing/platform/declar.htm](http://www.un.org/womenwatch/daw/beijing/platform/declar.htm) and [15].

Finally, with respect to our Western high-income country ‘solutions’ and interventions in cancer: For LMCs, ‘technology transfer’ of current approaches have some specific contributions (e.g. with immunization interventions for hepatitis, or antibiotic treatment for *Helicobacter pylori*), but additionally yet-undefined biological, ecological and social issues are critical in defining successful implementation programs for these technologic ‘solutions’ in different communities. For example, with respect to host factors and current drug therapies, there are clear emerging pharmacogenomic differences among genetic/ethnic groups associated with differences in toxic effects and efficacy of these treatments [16]. For a second example, with respect to absence of cost effective interventions, to be discussed in detail below, it is common to emphasize early detection, including screening mammography, as a strategy for addressing the problem of the high frequency of locally advanced breast cancer in LMCs, when basic epidemiologic (‘population cancer medicine’) considerations, available outcomes data and cost-effectiveness analysis shows this to be unrealistic [17].

In summary, the most important issues governing cancer ‘health’ and poor outcomes from cancer in LMCs are broad and often-suggested technical ‘fixes’ are highly unlikely to be useful in addressing important population-affecting goals.

#### an emerging ‘new’ model for international development in LMCs

Increasingly, responsibility for social development and problem solving in LMCs, particularly in South Asia, has fallen on non-governmental organizations. In the development field, there has been a shift in focus, toward local community and small-scale enterprise (e.g. ‘social business’) solutions to poverty through job creation [18]. This reflects a gradual 50-year trend to community empowerment and an increasingly active citizenship, with local ownership of developmental processes. There is a growing understanding that the active involvement

### Table 1. Population estimates (in billions = B) for eight largest countries in 2005 [29]

<table>
<thead>
<tr>
<th>Country</th>
<th>Population (B)</th>
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<tbody>
<tr>
<td>1. China</td>
<td>1.31</td>
</tr>
<tr>
<td>2. India</td>
<td>1.03</td>
</tr>
<tr>
<td>3. USA</td>
<td>0.29</td>
</tr>
<tr>
<td>4. Indonesia</td>
<td>0.23</td>
</tr>
<tr>
<td>5. Brazil</td>
<td>0.186</td>
</tr>
<tr>
<td>6. Pakistan</td>
<td>0.157</td>
</tr>
<tr>
<td>7. Russia</td>
<td>0.143</td>
</tr>
<tr>
<td>8. Bangladesh</td>
<td>0.141</td>
</tr>
</tbody>
</table>
of communities, within which members promote self-reliance, is critical to the long-term sustainability of development activities [19, 20]. While there appears to be no consensus on an ideal model for international development, this new emphasis on community assets—of individuals, associations and institutions—and of local successes, is an essential starting point [19]. Intracommunity relationship building and active citizen participation can then ‘discover,’ ‘dream’ and deliver appropriate outside-assisted development programs.

These concepts are reviewed in http://www.mystfx.ca/institutes/coady/text/about_publications_new_situating.html and a series of case studies from Bangladesh that emphasize this issue of community ‘acceptability’ are reviewed in the new volume, From One to Many [20]. [This emphasis on local communities and intracommunity relationships should not detract from the major importance of (often pre-existing) inter (global) community professional and other relationships that so facilitate addressing emergencies and building successful in-country cancer programs.]

Applied to public health oncology, these ideas emphasize the major and important roles of local communities in successfully addressing health issues like cancer. Under such approaches, ecological considerations and cultural anthropological realities play important roles in defining actions.

Considering such a model then more specifically, the common approach defines:

- ‘needs’ (funding, funding mechanisms);
- ‘deficiencies’ (National ‘plans’ and facilities); and
- ‘problems’ (drug pricing, workforce inadequacies).

This common approach de facto often leads to outsider-defined, unsustainable solutions, making citizens dependent consumers of services and products (drugs), all with unintended consequences [19, 20].

The ‘new’ model: a community-building approach first defines the capacities, assets (of individuals, associations and institutions) and skills of communities, and connects these. This approach is based on the compelling historic evidence that significant and sustainable development takes place when local people in communities define ‘their’ problems and solutions, and invest themselves and their resources [9, 19 and web citation above]. The application of this model to public health oncology calls for multiple small scale experiments—Easterly’s ‘search and research’ approach—trial and error searches for what works on the ground, one step at a time, measuring success wherever it comes—and not the usually outsider-defined large-scale demonstrations for which we often seem poorly prepared. Indeed as summarized in the case studies from Bangladesh, community involvement is critically necessary to scaling up apparently successful health interventions, a continuing challenge overall anyway [20].

specific mandates for action and inaction across disease and disciplinary spectra

action area: prevention

There are considerable data that should encourage much greater efforts to prevent cancer in populations: activities directed at limiting tobacco use, immunization against or treatment for oncogenic infectious agents—hepatitis B virus (HBV), human papilloma virus (HPV), Helicobacter pylori and reducing exposure to indoor smoke [21–23]. These efforts however are all ones directed at populations and ones for which, in specific countries optimal implementation strategies have yet to be defined. Additionally, nutritional change is strongly suggested to be beneficial, but exactly what nutritional change and how any change is to be achieved in populations are research matters for gastric, esophageal, colorectal and for aflatoxin-induced liver malignancies [24, 25]. The Bloomberg funding opportunities for tobacco control projects in LMCs have attracted far fewer proposals than the problems warrant (http://tobaccocontrolgrants.org/Pages/44/About-the-Bloomberg-Initiative).

inaction areas: early detection and ‘awareness-raising’

There has been only limited attention to the severe limitations of early detection strategies for populations with low incidences of disease. First, we need to be clear about the early ‘detection’ myth. As a general observation in LMCs, cancers are diagnosed in advanced stages. A critical distinction here must be made between diagnosed and detected; most cancers are detected or suspected by patients themselves, but not acted upon because of complex human rights issues which give victims in LMCs no viable choices to act. This reality is not going to change significantly without interventions directed at or changes in the major human rights situations. Concern that we need ‘early detection’ efforts for cancers in most LMCs is really knocking a straw man—education—‘awareness’ because patients already are ‘aware.’ Current screening technologies are very unlikely to be truly effective or applicable in LMCs circumstances, with low incidences of specific malignancies and major human rights challenges. For breast cancer, a recent analysis lays out the numerical considerations in detail [12]. In sum, as a general premise, we suggest that there are no specific rigorous scientific grounds as yet for major demonstration or other efforts in early detection of cancers in LMC.

Investigation of specific strategies in individual countries is appropriate, and in particular, ongoing research into cost effective strategies for detection of uterine cervical and oral cancers in LMCs deserve strong and substantial international support. As is recognized by people in LMCs but often underestimated is the sense of futility for ‘early detection’ when it is obvious that treatment is not available or accessible.

What then should be done? It would seem that the central issues involve identifying men and women with serious problems likely to be cancer (case finding, not screening) at local levels and facilitating their entry into and through available tertiary care systems.

major area focus for action: health systems

All countries need much more attention to centralization and coordination of efficient, guideline-based cancer treatment and the roles of innovation—particularly with information technology (IT)—and horizontal health system strengthening, dominantly for outpatient systems [13, 26]. These are collectively individual practitioner, but really public health oncology issues.
As has been noted above, in high-income countries, we behave as though we have much better evidence and interventions than we in fact have in truth, we are prisoners of half-way technologies. For systemic therapies, which account for large fractions of the expenditures for cancer care in high-income countries, for one comprehensive and leading set of guidelines, a recent review found limited high-quality evidence [27].

The WHO Report 2010 found that 20%–40% of health spending is wasted on [14]:

- Unnecessary or not-used and nongeneric drugs (especially growth factors and sequential therapies in incurable patients). Here, a complex of health system, corruption and unethical behavioral issues demand greater attention [16, 26].
- Unnecessary tests
- Hospitalization inefficiencies
- Poor use of skilled professional time

There is a significant need to demonstrate for cancer, bundled-care packages which give good value for expenditure [26].

The American Board of Internal Medicine (ABIM) and the American Society of Clinical Oncology (ASCO) have highlighted five top specific activities of concern in their ‘Choosing wisely’ campaign: (i) limit cancer-directed therapies in patients unlikely to benefit (patients with low performance status, e.g. frequently represented in LMCs patient populations); (ii) and (iii) Omit high-cost staging studies in patients with low-stage breast and prostate cancer; (iv) omit surveillance testing in breast cancer patients without evidence of disease; and (v) omit use of white-cell-stimulating growth factors in patients with limited risk for neutropenia.

Table 2. Major specific cancer burdens in low- and middle-income countries (with 70% of global citizens), shortcomings of available cancer control strategies, and mandates for progress

<table>
<thead>
<tr>
<th></th>
<th>Annual* of new cases (in thousands)</th>
<th>Shortcomings of current strategiesb</th>
<th>Mandates for progress</th>
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<tbody>
<tr>
<td><strong>Female</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td>700</td>
<td>Manipulable causes limited</td>
<td>Human rights and health systems interventions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Early detection impractical</td>
<td>Access to essential therapies: drugs and radiation therapy</td>
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<td></td>
<td></td>
<td>Optimal treatments not defined</td>
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<td></td>
<td></td>
<td>Treatment toxic and expensive</td>
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<td></td>
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<td>Full evaluated screening strategies unavailable</td>
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<td></td>
<td></td>
<td>Treatment efficacy limited</td>
<td>Vaccination at value</td>
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<td></td>
<td></td>
<td>Treatment costly</td>
<td>Access to effective therapies</td>
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<tr>
<td><strong>Male</strong></td>
<td></td>
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<tr>
<td>Lung</td>
<td>800</td>
<td>Treatment ineffective</td>
<td>Comprehensive strategies for limiting tobacco abuse and indoor smoke pollution</td>
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<tr>
<td><strong>Genders combined</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stomach</td>
<td>700</td>
<td>Treatment efficacy very limited</td>
<td>Nutritional change</td>
</tr>
<tr>
<td>Liver</td>
<td>700</td>
<td>Treatment ineffective</td>
<td>Hepatitis B vaccination at value</td>
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<td></td>
<td></td>
<td></td>
<td>Hepatitis C vaccine</td>
</tr>
<tr>
<td>Esophagus</td>
<td>500</td>
<td>Treatment ineffective</td>
<td>Aflatoxin exposure reduction strategies</td>
</tr>
<tr>
<td>Head and neck</td>
<td>450</td>
<td>Treatment efficacy limited</td>
<td>Strategies for limiting tobacco and areca (betel) nut chewing abuse</td>
</tr>
<tr>
<td>Colorectal</td>
<td>400</td>
<td>Early detection impractical.</td>
<td>HPV vaccination at value?</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Adjuvant treatment has limited evaluation in LMC settings and is expensive</td>
<td>Nutritional change</td>
</tr>
<tr>
<td><strong>All types</strong></td>
<td>~4750 (70%)</td>
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bIn low- and middle-income countries, as patients with these cancers usually present for medical care.
Further in cancer, as in health generally in LMCs, we need to demonstrate IT sustainable efficiency tools: for example Telemedicine Case Conferences, reinforcing locally defined guidelines from testing to treatment; use of cell-phone platforms and electronic medical records by all health care workers and electronic web-based test reporting.

Finally in treatment, we all need coordinated palliative care to provide everyone in need greater comfort at lower costs [26]. Again, IT solutions need development and testing.

We need far more attention to assessing the value of interventions and to the absolute necessity of using such information: the benefits, harms and costs, including the downstream costs; and the incremental cost-effectiveness ratios [26, 28]. The most obvious opportunities for such attention are in (international) scientific meetings where LMC health professionals are present, and when high-income country health professional participate in LMC in-country meetings, and can learn first-hand about local circumstances.

Health systems are significantly country-specific and ‘solutions’ must therefore of necessity be country-specific.

We believe that considerable attention in LMCs to these health system issues is desperately needed before, in fact, tight insurance systems or government payments for cancer care can be compellingly argued for.

specific mandates for action and inaction by major LMC cancer sites
A more complete and, perhaps for cancer specialists, a more specific picture of where more rational efforts for cancer control in LMCs may lie can come from consideration of information for the most common specific malignancies (Table 2).

Practitioners in high-income countries or settings are very aware of the marginal efficacies of their systemic interventions for solid tumors, and of the expensive infrastructure necessary to provide likely benefit for systemic or radiotherapeutic interventions. Such credible practitioners need to lead in calling attention to and pursuing the mandates for progress listed in this table. The aforementioned ABIM and ASCO ‘choose wisely’ campaign is an example.

strategies for populations: public health oncology in real LMCs worlds
In another communication, we have stressed policy priorities in cancer, which appear appropriate for governments in LMC, and the need for more broad-spectrum research in cancer [21]. LMCs governments are significantly resourced-challenged at present however, and the major need for better data and on-site, country-specific solutions bring us again to the critical roles of local communities in public health oncology [19, 20]. Broadly in economic development, Easterly has called for ‘search and research’ approaches [9]. As we have suggested above, responding to such a mandate for efforts in cancer with local exploratory projects makes sense to us.

The more common roles of universities and cancer-specific foundations, in our view, should be to partner sustainably with local LMC communities to define rigorous potentially scalable community grown cancer control solutions, which can also inform national and international policies [20]. There is a need for a sustainable effort that can only come about if this work is valued as a bona fide part of physicians’ careers. This should be considered an integral part of medical practice and academic promotion but is indeed implementation science (http://www.fic.nih.gov/researchtopics/pages/implementationscience.aspx).

conclusions
There are many well-intentioned and generous efforts to improve cancer outcomes in LMCs. Recent increased concern in addressing the challenges with cancer in LMCs is laudable and a positive sign. We have argued that efforts for better cancer control in LMCs would benefit from horizontal public health oncology perspectives. Practitioners should champion efforts addressing the broad challenges of defining better health systems, addressing governance, corruption and human rights and defining cost-effective practical interventions. Bottom-up activities with local communities are the time-tested most successful framework. While treatment interventions are what high-income country practitioners do, they more than any other professionals realize the limitations of current approaches, and can therefore most credibly lead in encouraging public health-mandated efforts.

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references
Clinical benefit in patients with metastatic bone disease: results of a phase 3 study of denosumab versus zoledronic acid†


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Background: Patients with metastatic bone disease are living longer in the metastatic stage due to improvements in cancer therapy, making strategies to prevent the aggravation of bone disease and its complications, such as skeletal-related events (SREs) and pain, increasingly important.

Patients and results: In this phase 3 trial in patients with advanced cancer (excluding breast and prostate cancer) or multiple myeloma, denosumab reduced the risk of radiation to bone by 22% relative to zoledronic acid (P = 0.026), prevented worsening of pain and pain interference (2-point increase in Brief Pain Inventory score; P < 0.05 versus zoledronic acid), and reduced the frequency of a shift from no/weak opioid analgesic use to strong opioids (P < 0.05

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