

# IGNORANCE IS NOT STRENGTH: THE NEED FOR A GLOBAL EVIDENCE BASE FOR CANCER CONTROL IN DEVELOPING COUNTRIES



**MARK LODGE**, ASSOCIATE FELLOW, PARTICLE THERAPY RESEARCH INSTITUTE, UNIVERSITY OF OXFORD

**In the Introduction to his pamphlet *Common Sense* published in 1776, Thomas Paine wrote “A long habit of not thinking a thing wrong, gives it a superficial appearance of being right”<sup>1</sup>. This is demonstrably true when it comes to the marshalling of published evidence relevant to cancer control in low- and middle-income countries.**

On the twelfth day of the twelfth month of the twelfth year of this Millennium, representatives from nine African countries along with colleagues from the Netherlands, the UK and the World Health Organization (WHO) signed the Kigali Declaration calling for the widespread establishment of evidence-based health care in Africa. The Declaration recognised that while evidence-based methodology had significantly improved health practice and influenced policy in many countries elsewhere in the world over the past two decades, it had not yet widely penetrated health care systems in Africa and that there is still insufficient health research infrastructure and a lack of research projects and programmes relevant to African needs. The signatories – the majority of whom had travelled to Kigali, Rwanda from universities, health colleges, hospitals, NGOs and research institutions across Africa – called for African Health Ministries to take the lead in supporting evidence-based health care by prioritizing interventions and strategies that have been proven – by proper methodology – to be effective, and for the international scientific community to support and collaborate on primary and secondary research relevant to African health needs and priorities.<sup>2</sup>

Twenty years of research commissioning have established two rules for evidence gathering: 1) All existing sources of evidence, especially systematic reviews, must be considered carefully before undertaking research<sup>3</sup>. 2) Ensuring that literature searches are comprehensive helps minimize selection bias. Relying exclusively on one database will retrieve a set of reports unrepresentative of all reports that would have been identified through a comprehensive search of several sources<sup>4</sup>.

Searches of the research literature relevant to the

management of cancer in developing countries are likely to show that these rules have been largely ignored in favour of minimal searches of the sources that are easiest to access<sup>5-8</sup>. Global databases such as PubMed/Medline are excellent resources but they mainly index studies conducted in the advanced, higher income countries; settings that differ widely from low- or middle-income countries with respect to the types and patterns of cancer, levels of cancer incidence, patient genetics, health care governance, socioeconomic status, literacy rates and behaviour of populations, as well as with respect to the resources (human, physical or financial) that are available.

A large proportion of papers relevant to low- and middle-income countries will not be represented in these databases. A systematic literature review conducted by the International Network for Cancer Treatment and Research (INCTR) of articles relevant to the management of breast cancer in low- and middle-income countries published between 2000 and 2010 identified 4,362 papers (including 210 reports of randomized controlled trials) of which only 53% were indexed in Medline<sup>9</sup>. The disparity between the number of papers that have been published and the number of published papers that are easily accessible presents a false impression of the amount of research conducted in low- and middle-income countries.

A substantial body of reports of scientific research studies relevant to these poorer-resourced countries lies scattered across the international literature in a multitude of databases and non-indexed sources; generally unread and unreferenced. This situation is contrary to the requirements indicated by Resolution WHA58.22 of the World Health Assembly 2005 (Figure 1) which presupposes the existence of an accessible evidence base

Figure 1: World Health Assembly Resolution WHA58.22: Cancer Prevention & Control<sup>10</sup>

**Member States should... collaborate with the Organization in developing and reinforcing comprehensive cancer control programmes tailored to the socioeconomic context, and aimed at reducing cancer incidence and mortality and improving the quality of life of cancer patients and their families, specifically through the systematic, stepwise and equitable implementation of evidence-based strategies for prevention, early detection, diagnosis, treatment, rehabilitation and palliative care and to evaluate the impact of implementing such programmes.**

of relevant research that can be used to guide and inform the drawing up of effective cancer control plans<sup>10</sup>. For the developing countries' no such evidence base currently exists.

This chaos within the international literature can act as a barrier to identifying reports of indigenous research. The unintended consequences of this barrier are that the scientific profiles of the poorer countries are artificially depressed, the development of domestic careers in research is impaired (through reduced opportunities for citation), the identification of strategies that are (or are not) effective is delayed and cases of scientific fraud remain safely hidden.

The growing awareness of the importance of providing reliable information in a timely fashion to clinical practitioners, researchers and policy makers serving developing country populations has accelerated the drive to improve access to knowledge across many areas of health care. In this context, "accessible" has to mean affordable. Transnational collaborations such as the Collaboration for Evidence Based Health Care in Africa<sup>11</sup> act as portals to multiple points of affordable access. Recognizing the "considerable amount of important and valuable medical and health documentation from countries outside the major industrialized areas" that is not included on databases such as Medline/PubMed or Embase (and that consequently "receive less global visibility in spite of its higher relevance for other developing countries") the World Health Organization has developed its own network of regional databases of articles published in local journals<sup>12</sup>. Access to published research has been greatly enhanced by multi-sectoral initiatives such as the HINARI Access to Research in Health Programme<sup>13</sup>. Independent online regional initiatives such as African Journals Online<sup>14</sup> and INDMED<sup>15</sup> have also added to the fund of knowledge.

Collecting up the raw evidence is not enough. Systematic reviews of the relevant papers are needed to draw attention to the outcomes, and methodological quality, of research conducted on the ground in low- and middle-income countries and to encourage the spirit of scientific enquiry. But gathering together even a modest amount of evidence for a review, or in order to develop a national cancer prevention or treatment plan, still requires months of work; a situation that should no longer be professionally acceptable in the twenty-first century. Given where the majority of new cases of cancer and

of cancer deaths are now occurring, there is a job of work to be done: the collection and collation of all scientific research evidence relevant to the control of cancer in low- and middle- income countries, and its uploading to an accessible platform for general reference.

INCTR established its Evidence Base Programme in 2007 with the objective of working collaboratively with others to build a "Global Evidence Base for Cancer Control in Developing Countries" with four functions:

- to provide a comprehensive source of evidence to policy makers and to donors funding research, capacity building and health systems strengthening projects in low- or middle-income countries;
- to provide the evidence base for systematic reviews of the quality and outcomes of reported research and the development of contextually-relevant evidence-based guidelines and national cancer control plans;
- to facilitate the identification of areas where more or better research is needed;
- to provide examples of good and bad research for postgraduate training curricula in modern research skills.

So far INCTR has established two databases: an Egyptian pilot database in collaboration with the National Cancer Institute, Cairo and Cairo University<sup>16</sup> and a database of breast cancer studies in collaboration with the Breast Health Global Initiative<sup>9</sup>. Supported by a two year grant from the Elsevier Foundation, the Egyptian pilot database is now being extended to cover all of Egyptian cancer research published from 2000 onwards. Ten biomedical databases have been searched for published reports of cancer control research relevant to, or conducted upon, the Egyptian population. 10,036 reports published between 2000 and 2010 have been identified of which 8,245 met the programme's inclusion criteria; reduced to 4,031 reports after de-duplication. Discussions are underway with the Centre for Agricultural Bioscience International (CABI) to include these within a hosted online database site and INCTR is discussing with institutional partners in Africa the establishment of a larger regional evidence base that will become the African "chapter" of the Global Database.

It is important that all pools of knowledge in the field of cancer control be identified and joined up in order to get a full picture of the research that has previously been conducted. In the development of its Global Database, INCTR will be drawing on all these sources, as well as the "grey literature" which includes conference proceedings, industrial surveys, technical

assessment reports and ministerial policy documents.

In the meantime, more attention needs to be paid to the double standard that has developed in the editorial review processes of some journals. The same expectation of comprehensive literature searches to support articles relevant to cancer management in advanced high-income countries should be applied to those articles relating to low- or middle-income countries. Journal editors should require authors to submit evidence of searches of multiple databases, and especially of local databases that might contain reported data relevant to the subject of their paper. They should be particularly vigilant for the type of prejudice evidenced in the following passage:

“In 2008, there were 12 publications about cervical cancer from Nigeria indexed in PubMed. There may be other publications in local journals that are not indexed by PubMed but these are not likely to be of greater quality than the ones indexed.”<sup>6</sup>

If indexed journals are popularly supposed to publish better quality research than local non-indexed journals, to demand greater research quality from the local journals than from indexed journals is to stand reason on its head.

Quality is a serious issue and authors are right to be careful about the reliability of the research data they cite in their writings. But the low level of cited searches of local journals and databases suggests that many authors have fallen into the error of leaving unread much of the evidence from studies conducted on the ground in low- and middle-income countries. This may be due to concerns about the methodological quality of the studies, or due to the time, expense and labour involved in properly searching the literature. For whatever reason, when writing about cancer in poorer-resourced countries, searches of a minimum number of sources have become “sufficient” for publication. We have developed, in Paine’s words the ‘long habit

of not thinking a thing wrong”.

Ignorance is not strength. Not to look for all the potential relevant evidence is wrong; it is anti-science. By not accessing and critically appraising their literature we are neither protecting vulnerable populations in these poorer countries from the ravages of malignant disease nor helping colleagues in the clinical and research communities raise their game.

The need for an authoritative and accessible Global Evidence Base for Cancer Control in Developing Countries that can cut the time spent identifying contextually relevant studies from months to minutes grows as the number of new cases of cancer and of preventable and premature deaths from cancer rises in developing countries. By now, systematic reviews based on the pool of evidence collected from the equivalent of 12 databases<sup>16</sup> (as opposed to one or two databases) should have become the norm. Reports of innovative low cost or low tech interventions that have been shown to be effective in the management of cancer should be being shared with other health care systems (North and South) where they might help reduce costs and accelerate the delivery of care. Systematic reviews of methodological quality should be identifying the necessary improvements in the conduct or reportage of research practice so that they can be properly addressed in training curricula. And instances of fraudulent or unethical research or egregious wastefulness should be exposed rather than ignored. ●

*Mark Lodge worked for the Cochrane Collaboration in many roles before joining the International Network for Cancer Treatment and Research as its Director for Programme Development. Mark is also Director of INCTR’s UK Office with special responsibility for the development of the Network’s Evidence Base Programme. Mark Lodge is an Associate Fellow, Particle Therapy Research Institute, University of Oxford.*

References

<sup>1</sup> ‘Doctors pledge to spread evidence based healthcare in Africa *BMJ* 2013;346:f356’

<sup>2</sup> Paine T, *Common Sense* publ. 1776 text available at <http://www.let.rug.nl/usa/documents/1776-1785/thomas-paine-common-sense/introduction.php>

<sup>3</sup> Research Governance Framework for Health and Social Care (RGFHSC) UK Department of Health 2005 Section 2.3.1)

<sup>4</sup> Cochrane Handbook for Systematic Reviews of Interventions 4.2.6 Updated September 2006

<sup>5</sup> Pilszczek F. Helminthic infections mimicking malignancy: a review of published case reports. *Journal of Infection in Developing Countries*, North America, 4, apr. 2010

<sup>6</sup> Dalal S, Beunza JJ, Volmink J, Adebamowo C, Bajunirwe F, Njelekela M, Mozaffarian D, Fawzi W, Willett W, Olov dami H, Holmes MD. Non-communicable diseases in sub-Saharan Africa: what we know now. *Int. J. Epidemiol.* (2011) 40 (4): 885-901.

<sup>7</sup> Akinwande O, OgunDIRAN T, Akarolo SA, Mamadu I, Dakum P, Blattner W, Adebamowo C. Challenges in Treating Malignancies in HIV in Nigeria. *Curr Opin Oncol.* 2009 21(5): 455-461.

<sup>8</sup> Moore MA, Kunimoto T, Tsuda H. Cancer Screening Literature in the Period 2000-2002 : Pointers to Future Research Avenues. *Asian Pacific Journal of Cancer Prevention*

2003 4(1): 57-60

<sup>9</sup> Lodge M, Corbex M. Establishing an evidence-base for breast cancer control in developing countries. *Breast.* 2011 Apr;20 Suppl 2:S65-9.

<sup>10</sup> Resolution WHA58.22: Cancer Prevention and Control 58th World Health Assembly 2005

<sup>11</sup> <http://www.cebha.org/>

<sup>12</sup> <http://www.who.int/library/databases/en/>

<sup>13</sup> <http://www.who.int/hinari/en/>

<sup>14</sup> <http://www.ajol.info/>

<sup>15</sup> <http://indmed.nic.in/indmed.html>

<sup>16</sup> Lodge M The Database of Cancer Control for Developing Countries 2nd ASCO-SEMCO Workshop. 26-28 March 2008, Cairo, Egypt

<sup>17</sup> Chamot E, Kristensen S, Stringer JS, Mwanahamuntu MH. Are treatments for cervical precancerous lesions in less-developed countries safe enough to promote scaling-up of cervical screening programs? A systematic review. *BMC Womens Health.* 2010 Apr 1;10:11.