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Guidelines for sub-Saharan Africa: a call for evidence

Matthew Painschab, **Satish Gopal**

Lineberger Comprehensive Cancer Center, Chapel Hill, NC 27599, USA; and University of North Carolina Project-Malawi, Lilongwe, Malawi

To address the increasing cancer burden in sub-Saharan Africa, in November, 2017, at the African Organization for Research and Training in Cancer conference in Rwanda, the National Comprehensive Cancer Network (NCCN) and African Cancer Coalition released the first Harmonized Guidelines for sub-Saharan Africa. Although the guidelines provide an excellent opportunity to improve cancer care in this region, they also require region-specific evidence to inform them.

In high-income countries, NCCN guidelines have been widely used to improve and standardise cancer care. Guidelines are used frequently by 77% of medical oncologists in the USA,[1] and NCCN reports that approximately half of registered guideline users reside outside the USA. Concordance of cancer care with guideline recommendations has been associated with improved outcomes.[2] Use of NCCN guidelines and their effectiveness in improving outcomes depend on a strong evidence base. As of 2011, 89% of NCCN guideline recommendations were based on category 1 evidence (high level of evidence, such as randomised controlled trials with uniform consensus) or category 2A evidence (lower level of evidence with uniform consensus).[3]

However, cancer care in sub-Saharan Africa is radically different enough to cancer care in resource-rich settings to warrant caution when applying clinical trial data. One key difference is the high prevalence of HIV among patients with cancer in sub-Saharan Africa, which ranges from 30 to 80% across the region.[4] Inclusion of patients with HIV in clinical trials in the USA and Europe historically has been low, and epidemiological studies of patients with cancer and HIV have often identifed worse outcomes compared with patients with cancer who are not infected with HIV.[5] Conversely, prospective trials have shown similar outcomes in patients with or without HIV,[6] although data are scarce or absent for many specific tumour types and treatments. Clarifying the effects of HIV on cancer outcomes remains an important priority for cancer research, even for patients with a cancer type that has no increased risk conferred by HIV—eg, breast cancer.

HIV care in sub-Saharan Africa also provides a valuable illustration of the need for region-specific data. HIV treatment guidelines developed for resource-rich settings recommend stopping co-trimoxazole *Pneumocystis* prophylaxis when a patient's CD4 count is greater than 200 cells per mm^3 for 3 months. However, trials from sub-Saharan Africa showed

matthew.painschab@unchealth.unc.edu .

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an increase in mortality if co-trimoxazole treatment was stopped, largely due to increased malaria and bacterial infections.[7,8] These unanticipated findings led WHO to recommend continuous co-trimoxazole for all patients living with HIV in sub-Saharan Africa regardless of CD4 count—a perfect instance where clinical evidence from different parts of the world led to opposite guideline recommendations.

Another caveat to extrapolating guidelines from resource-rich settings to sub-Saharan Africa is the general absence of cancer care infrastructure. For example, Burkitt's lymphoma is one of the most common paediatric cancers in sub-Saharan Africa. In resource-rich settings, intensive, multiagent chemotherapy has led to lifelong cure rates of over 90%.[9] However, when modified regimens have been used in sub-Saharan Africa, survival has ranged from 30–60%.[10] These differences are influenced by late presentation and underlying biology, but weak supportive care also contributes to low survival rates. High-dose methotrexate is an integral component of treatment for Burkitt's lymphoma in resource-rich settings, but it can lead to severe bone marrow and liver toxicity if not administered safely. If a health system cannot complete the necessary steps to deliver methotrexate safely (urinary alkalinzation, folinic acid administration, methotrexate level monitoring), as many health systems cannot in sub-Saharan Africa, other protocols should be prospectively tested. Alternatively, methotrexate-free regimens might be preferred. However, trial data that are specific to sub-Saharan Africa are urgently needed to prevent deaths from this highly curable cancer in young Africans.

Guidelines drawing on robust clinical trial data from sub-Saharan Africa will give providers confidence to provide the best care possible, even in resource-limited settings. The WHO consolidated guidelines for HIV are an excellent, established model that provide regularly updated, evidence-based recommendations that can be adapted to formulate country-specific guidelines based on high-quality data from sub-Saharan Africa. The NCCN and African Cancer Coalition Harmonized Guidelines can be a similar resource for cancer control in this region. However, to take optimal advantage of the opportunity presented by these guidelines, the cancer community in sub-Saharan Africa must recommit itself to generating the level of high-grade evidence needed. We echo the view from the last line of each page of each of the NCCN guidelines to encourages patients from sub-Saharan Africa to participate in clinical trials, especially at a time when this extremely welcome initiative is launched.

References

1. Dillmon M, Goldberg JM, Ramalingam SS, Mayer RJ, Loehrer P, Van Poznak C. Clinical practice guidelines for cancer care: utilization and expectations of the practicing oncologist. J Oncol Practice 2012; 8: 350–53.
2. Boland GM, Chang GJ, Haynes AB, et al. Association between adherence to National Comprehensive Cancer Network treatment guidelines and improved survival in patients with colon cancer. Cancer 2013; 119: 1593–1601. [PubMed: 23280510]
3. Poonacha TK, Go RS. Level of scientific evidence underlying recommendations arising from the National Comprehensive Cancer Network clinical practice guidelines. J Clin Oncol 2011; 29: 186–91. [PubMed: 21149653]
4. Dryden-Peterson S, Medhin H, Kebabonye-Pusoentsi M, et al. Cancer incidence following expansion of HIV treatment in Botswana. PLOS One 2015; 10: e0138742. [PubMed: 26376079]

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5. Coghill AE, Shiels MS, Suneja G, Engels EA. Elevated cancer-specific mortality among HIV-infected patients in the United States. J Clin Oncol 2015; 33: 2376–83. [PubMed: 26077242]

6. Oriol A, Ribera JM, Bergua J, et al. High-dose chemotherapy and immunotherapy in adult Burkitt lymphoma: comparison of results in human immunodeficiency virus-infected and noninfected patients. Cancer 2008; 113: 117–25. [PubMed: 18457327]

7. Bwakura-Dangarembizi M, Kendall L, Bakeera-Kitaka S, et al. A randomized trial of prolonged co-trimoxazole in HIV-infected children in Africa. N Engl J Med 2014; 370: 41–53. [PubMed: 24382064]

8. Suthar AB, Vitoria MA, Nagata JM, et al. Co-trimoxazole prophylaxis in adults, including pregnant women, with HIV: a systematic review and meta-analysis. Lancet HIV 2015; 2: e137–50. [PubMed: 26424674]

9. Patte C, Auperin A, Michon J, et al. The Societe Francaise d'Oncologie Pediatrique LMB89 protocol: highly effective multiagent chemotherapy tailored to the tumor burder and initial response in 561 unselected children with B-cell lymphomas and L3 leukemia. Blood 2001; 97: 3370–79. [PubMed: 11369626]

10. Harif M, Barsaoui S, Benchekroun S, et al. Treatment of B-cell lymphoma with LMB modified protocols in Africa—report of the French-African Pediatric Oncology Group (GFAOP). Pediatr Blood Cancer 2008; 50: 1138–42. [PubMed: 18213709]