

AFRICAN HPV PATHOLOGY AND CONTROL: THE WORK OF THE WAKA NETWORK

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Human Papilloma Virus (HPV)-related disease, such as cervical cancer, is a metaphor for an African healthcare challenge: it stimulates researchers to innovate horizontally, combining existing knowledge into new models. Cervical cancer is disappearing in the western world but is rising in Africa. Key to better access to prevention and vaccination is academic expertise, patients' awareness and education, healthcare providers and political commitment. This is the objective of the WAKA network, the "Wanavyama wa Kudhibiti ya HPV" or "artners in controlling HPV". An overview of current WAKA activities is discussed.

Cervical cancer, the most frequent HPV-associated pathology: A metaphor

Cervical cancer is a metaphor for healthcare access in Africa. Of the yearly 528,000 new cervical cancer diagnoses and 260,000 deaths worldwide in 2012 (Globocan data), 85% of the burden occurs in low- and middle-income countries (LMIC). In 2012, 92,000 new diagnoses were made in Africa alone and 57,000 African women died as a consequence of the disease (1). The prevalence is rising. In South Africa alone, each day eight women die of cervical cancer. This could rise to 12 by 2025, according to the WHO, if access to prevention and vaccination programmes is not improved (2).

Cervical cancer is caused by persistent HPV (human papilloma virus) infection. HPV 16 and 18 genotypes alone account for 70% of all cervical cancers. Visual, cellular and molecular markers for HPV infection, early indicators of potential cancer development over the next 10 years, exist (3). Cervical cancer is therefore preventable through HPV screening and vaccination (4). What makes HPV screening particularly interesting for Africa is that it takes 10 years or more to develop cancer after a positive test (5).

HPV disease is therefore a metaphor for an African healthcare challenge: it stimulates researchers to innovate horizontally in combining existing knowledge into new models. HPV challenges us to think of doing more with less:

less frequent but different screening algorithms, attention to different HPV genome strains, "single step screen and treat" approaches will make a difference in Africa. This calls for attention to truly innovative thinking, research and action on HPV in Africa.

While cervical cancer is slowly disappearing in the western world, it is rising in Africa (6). Even though the overall healthcare challenges in Africa are enormous, this gross healthcare access inequality between western and African geographies cannot be accepted. Cervical cancer in Africa calls on all stakeholders such as patients, healthcare workers, scientists and politicians to act together and to act fast in order to inverse the rising prevalence and give good life back to vulnerable African women in their most productive years of life (7).

Developing HPV screening tools and implementing vaccination strategies that are actionable, affordable and accessible in Africa will lead to better overall medicine and healthcare policies (8). It will improve women's health, which is one of the 17 Sustainable Development Goals of the United Nations (9).

Key to better access to prevention and vaccination programmes is increasing awareness and education with patients and healthcare providers and firm political commitment. The prevention tools are available, it is up to the fine-tuned collaboration of medicine, science and political willingness to reverse the spread of cervical cancer and other

HPV-associated pathologies in Africa.

The WAKA network (“Wanavyama wa Kudhibiti ya HPV” or “Partners in controlling HPV”), a multidisciplinary and multi-site collaborative effort led by the University of Antwerp, Belgium, aims at just this. Driven by six project objectives, WAKA aims at increasing scientific, medical and family care knowledge, and at activating a political will to drive a large-scale HPV screening and prevention programme.

Cervical cancer: Key issues

As cervical cancer is caused by a persistent HPV infection (10), HPV can be screened for and potential pre-cancerous lesions can be treated in time. In Africa, a true “pre-cancer screening” can be developed. This is not systematically happening.

Zooming in on key issues that limit access to and implementation of HPV-related screening and prevention, it is striking that most African women are not aware of screening for precancerous risks. Moreover, the notion of “cancer screening” is not accepted in most African cultures (11). They are aware of HIV however, and live with it, but not of or with HPV. Awareness is a prerequisite to action and is therefore key to HPV prevention programme entry.

The healthcare system (both doctors and nurses) is not widely educated to screen for HPV or the development of precancerous lesions. Moreover, access to screening tools, vaccines and precancerous lesion treatment is most often not available. The healthcare system does not reach the less privileged women.

Although cervical cancer is a leading cause of death in active women, it is not high on the political agenda because of lack of knowledge of the seriousness and prevalence of the disease.

The WAKA Africa HPV Network

Established in 2014 by the University of Antwerp, in collaboration with the Sefako Makgatho Health Science University in Pretoria (then University of Limpopo – Medunsa campus), the WAKA network concentrates on nine African countries with six objectives that address the main concerns listed above.

The six WAKA objectives are to:

- 1) Share the knowledge amongst the local HPV research communities.
- 2) Strengthen HPV knowledge and action with researchers, healthcare workers and laboratory physicians.
- 3) Contribute to improving capacity-related issues, such as setting up a quality-controlled local laboratory, the HPV and STI Reference Lab and Training Centre for Africa, which opened on 27 May 2015 and is operational at the Sefako Makgatho Health Science University (SMU) in Pretoria. This reference lab organises the referral of samples, analysis and

transitional management of the lab. It ensures training for interested African partners.

- 4) Coordinate HPV-related research and PhD projects in Africa.
- 5) Drive political commitment to action through creating awareness with local policy-makers of the HPV-lab-quality-data paradigm.
- 6) Anchor its work with international bodies such as the WHO.

Delivering on the WAKA objectives:

Sharing knowledge

WAKA is active in nine African countries: South Africa, Malawi, Zambia, Tanzania, Burundi, Kenya, Democratic Republic of Congo, Uganda and Ethiopia. In the years to come, WAKA aims at strengthening its collaboration with French-speaking African countries.

So far, five WAKA symposia (Pretoria 2014, Johannesburg 2015, Kinshasa 2015, a satellite meeting during the SASGO congress in Vereeniging 2016 and during the IPV meeting in Capetown (March 2017)) discussed the progress of the various research projects in each country. Training on quality issues such as GCP was organised. Clinical trial protocols are shared. In future, the collaboration with the ETICCS group in Heidelberg, Germany, may allow central data processing of African trials.

This shared expertise has been discussed with the international HPV community at the yearly world congress on HPV (HPV 2017) held in Cape Town.

WAKA aims at further strengthening the collaborative efforts by improving centralized quality control, sample analysis on HPV presence and genotype.

Strengthening and coordinating knowledge

WAKA will continue to link up interested researchers from different interested and participating academic collaborations and expand the network to the French-speaking part of Africa. Adding to the scientists and physicians who are already involved in the network, WAKA aims at attracting more (informal) healthcare workers, pathologists and gynaecologists to specifically research and act on HPV in cancer.

Improving capacity

A central HPV analysis and genotyping laboratory has been set up with the help of government and industrial partners. Its goal is to analyse samples sent from studies in other African countries. The laboratory is fully equipped and quality controlled. It provides analysis and quality training to interested African research partners. This is an important step in increasing the learning curve and capacity of performing HPV-related analyses.

Coordination of research and PhD projects

Twelve PhD students in six countries work in multidisciplinary collaboration on different topics in HPV research. For example, in fundamental diagnostic-treatment research, a controlled clinical study is set up in DRC: the KINNAV study (NCT02346227), which aims at evaluating the use of a topical antiviral agent, AV2, during colposcopic examination.

In this research, genotyping studies are conducted on cervical samples to investigate the genotype profile of HPV infections in Africa, which may be different from Western genotype profiles. This information is crucial to validate or correct the vaccination approach in Africa. In a recent addition, 400 cases from invasive cervical cancer were included to look at HPV strain prevalence in cancer, facilitating the discussion of which HPV types really cause cancer besides being “just” present in the population.

Formative social research is held to investigate Knowledge/Attitude and Practice (KAP study) of community-based healthcare providers and patients to understand the social barriers to screening for HPV.

Other projects investigate new screening models for Africa that are scientifically solid as well as actionable in the African context. One project will research a Southern Africa-specific model for a single step cervical cancer screening that will be tested on affordability, accessibility and feasibility with community-based healthcare workers.

These studies will be scalable. They aim at being shared between countries – such as the KINNAV study. This builds on the collaborative nature of all current African research projects, adds to data value and overall quality concern and education.

The PhD promoters are associated with both the local university and to a European WAKA partner. This strengthens the common approach and standardization of the research approach and relevance. Two PhD projects have been completed and successfully defended over the last three years, more will follow in the next few years. One of these PhD graduates is now responsible for the reference and training laboratory.

Political commitment

Africa has an important number of fundamental healthcare problems, such as HIV, tuberculosis and maternal health. In this context, inadequate attention is given to HPV-associated disease – especially cervical cancer. The local researchers will publish their findings and their African context in peer-reviewed journals. This will be leveraged to create more contacts with and between political stakeholders from different countries, sharing facts and findings that challenge the current HPV prioritization. WAKA will defend prioritization of HPV-related

pathology, especially cervical cancer.

International healthcare organisations

WAKA has twice presented its achievements, plans and approach to the World Health Assembly of the WHO in Geneva.

WAKA is setting up collaboration agreements with ETiCCS (Emerging Technologies in Cervical Cancer Screening) in Heidelberg, Germany, and with INCTR, the International Network for Cancer Treatment and Research. ETiCCS works with SAP on a cutting-edge cloud-based data capture and data transfer technology. This technology allows for reliable data handling in an internet unstable environment such as Africa. WAKA and ETiCCS aim at bringing self-sampling technology closer to the communities and the homes of people in Africa. As Professor Magnus von Knebel-Doeberitz, the head of ETiCCS stated: “Through the ETiCCS programme, we were able to complement applied medical research around biomarkers with the power of cutting-edge cloud technology to bring co-innovation to Africa in a way which really helps to improve people’s lives.” This is in full agreement with the WAKA research vision for Africa.

INCTR is a WHO-recognized not-for-profit organization dedicated to helping build capacity for cancer research and treatment in developing countries.

The future for WAKA

The future challenges will be the internal organisation and its collaboration with external partners in order to better the lives of people with HPV-related disease.

Internally, the focus will be to strengthen local research and action in more African countries, with a strong African oversight and with help from European universities. Local researchers and laboratory facilities will be empowered, educated and included in a programme that aims at understanding culture, HPV-specific research, and action (local studies, an African HPV Registry). Researchers will be guided into performing better and more structured research protocols to increase the chance for high-impact publication, the potential for external funding and, in the long run, sustainability.

The researchers will be trained in both quantitative and qualitative methods as well as general research methodology and writing. They will be guided in their contacts with local key stakeholders.

Setting up training, awareness and structures for external quality control will increase the general quality of the central, accredited laboratory.

Externally, the expansion of the WAKA network to collaborate intensely with partners in HPV research and

action will be paramount. Geographically, expansion to French-speaking Africa, and the organisations that operate in those countries, is scheduled. Finally, the recognition by the WHO, the World Bank and other international healthcare organisations may help the WAKA network to achieve an independent status.

Conclusions

The HPV pathology in Africa, with its far-reaching healthcare and social impact, calls on all healthcare workers and research organisations to think in a different way. More has to be done with less in order to save the lives of more women and to reverse the rising trend of HPV-related disease in Africa.

The only structural way to move HPV research to reach its goal in a reasonable time is to collaborate. With each other in a multidisciplinary setting in which stakeholders and organisations aim at the one, single goal that Africa needs: a down to earth innovative approach that brings health to women's homes.

For WAKA, it is a challenge and privilege to be instrumental in that. For which WAKA thanks all those who are involved as funders, collaborators and advocates. Please feel free to join us. ■

Dr Jo Lissens is Founder and Director of FACTS Healthcare in South Africa. He is a physician with a business administration formation. He served as an international medical director for 32 years and published on fundamental and clinical research, health economic assessment and guideline development review. Since moving to South Africa he works on medical affairs activities, clinical research and medical education with emphasis on HPV and cervical cancer, He is PhD applicant on "Developing a model for secondary cervical cancer screening in a single round in South Africa" with the University of Antwerp, Belgium and Pretoria, South Africa.

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Dr Jean Pierre Van Geertruyden is Professor in Global Health and Coordinates the Global Health Institute at the University of Antwerp, Belgium. As a physician and PhD on HIV & malaria interactions, he designs and implements epidemiological research in resource poor settings. He lectures on different tropical disease, epidemiology modules and clinical trials. He is grant holder of HPV fellowship programs. He supervised over 20 PhD, now mostly professor and collaborator in Africa. He is extensively involved in African research on cervical cancer control in a context of development health. He is co-founder of the WAKA research network.

Dr John-Paul Bogers is Professor of Histology and Cell Biology at the University of Antwerp and medical director of the Algemeen Medisch Laboratorium in Antwerp. As a physician specialized in Anatomic Pathology, a PhD and a master in Public Health, he started an independent research group on HPV related diseases. As guest professor at the International Centre for Reproductive Health of the University of Ghent and of the Sefako Makgatho Health Science University in South Africa, he leads the Flemish government initiatives on HPV related diseases in Limpopo (South-Africa). He is promotor of national and African PhD students working on HPV related diseases and has set-up collaborative efforts with 8 African countries. He is co-founder of the WAKA research network.

References

- Mena M, Cosano R, Muñoz J, Bosch FX, Sanjosé SD. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Journal of Cancer*. 2010
- Viviano M, DeBeaudrap P, Tebeu PM, Fouogue JT, Vassilakos P, Petignat P. A review of screening strategies for cervical cancer in human immunodeficiency virus-positive women in sub-Saharan Africa. *Int J Womens Health*. 2017;9:69-79.
- Dijkstra MG, Snijders PJ, Arbyn M, Rijkaart DC, Berkhof J, Meijer CJ. Cervical cancer screening: on the way to a shift from cytology to full molecular screening. *Ann Oncol*. 2014;25:927-935.
- Aggarwal P. Cervical cancer: Can it be prevented. *World J Clin Oncol*. 2014;5:775-780.
- Bosch FX, Lorincz A, Muñoz N, Meijer CJ, Shah KV. The causal relation between human papillomavirus and cervical cancer. *J Clin Pathol*. 2002;55:244-265.
- Williamson AL. The Interaction between Human Immunodeficiency Virus and Human Papillomaviruses in Heterosexuals in Africa. *J Clin Med*. 2015;4:579-592.
- De Vuyst H, Alemany L, Lacey C et al. The burden of human papillomavirus infections and related diseases in sub-saharan Africa. *Vaccine*. 2013;31 Suppl 5:F32-46.
- Armaroli P, Villain P, Suonio E et al. European Code against Cancer, 4th Edition: Cancer screening. *Cancer Epidemiol*. 2015;39 Suppl 1:S139-52.
- Callister LC, Edwards JE. Sustainable Development Goals and the Ongoing Process of Reducing Maternal Mortality. *J Obstet Gynecol Neonatal Nurs*. 2017
- Sankaranarayanan R, Qiao YL, Keita N. The next steps in cervical screening. *Women's Health (Lond)*. 2015;11:201-212.
- Chan DN, So WK. A Systematic Review of the Factors Influencing Ethnic Minority Women's Cervical Cancer Screening Behavior: From Intrapersonal to Policy Level. *Cancer Nurs*. 2017