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GLOBAL ONCOLOGY: RESEARCH ARTICLE

An evaluation of the disparities affecting the underdiagnosis of pediatric cancer in Western Kenya

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Abstract

Introduction: Western Kenya is home to approximately 24 million people, with 10 million children under the age of 15 years.[1] Based on estimates of cancer incidence in similar populations from around the world, approximately 1500 patients should be diagnosed with pediatric cancer each year. This article describes the international collaboration that investigates potential barriers preventing the effective diagnosis of pediatric patients with cancer.

Methods: Here, we describe a multidisciplinary and sequential approach to better evaluate the complex factors affecting the lack of appropriate diagnosis of pediatric cancer in Western Kenya.

Results: Internal review at a large tertiary hospital noted 200–250 patients were diagnosed annually, suggesting the remaining 75%–80% of patients go undiagnosed and do not receive treatment. Following our screening process at a local referring hospital, 41 malaria slides demonstrated both morphologic and genetic evidence of leukemia. Knowledge assessments of local providers at referring institutions suggested a lack of education and training as the factors that contribute to lower rates of diagnosis.

Discussion: Through a multi-step approach, our teams were better able to isolate potential issues impeding the appropriate and timely diagnosis of pediatric cancer in Kenya.

KEYWORDS

Africa, diagnosis, disparities, global health, pediatric oncology

1 | INTRODUCTION

Over the past decade, efforts have been made to identify health care disparities affecting children in Sub-Saharan Africa. Western Kenya is home to approximately 24 million people, with 10 million children under the age of 15.[1] Based on estimates of cancer incidence in similar populations from around the world, approximately 1500 patients should be diagnosed with pediatric cancer each year in Western Kenya.[2] However, the number of children presenting for cancer treatment is far below what would be anticipated based on population-based epidemiology at large referral centers in lower-middle income countries (LMIC). When patients fail to

Abbreviations: AMPATH, Academic Model Providing Access to Healthcare; ECHO, Extension for Community Health Outcomes; LMIC, low- and middle-income countries; MTRH, Moi Teaching and Referral Hospital; MU, Moi University; SEER, Surveillance, Epidemiology and End Results; SIOP, International Society of Paediatric Oncology; SME, subject matter expert.

receive an appropriate diagnosis and treatment, they do not survive.

The Academic Model Providing Access to Healthcare (AMPATH) represents a partnership in global health connecting North American medical institutions with a regional tertiary care center in Eldoret Kenya, Moi Teaching and Referral Hospital (MTRH), and an academic medical institution, Moi University College of Health Sciences (MU).[3,4] For more than 30 years, Indiana University has been a partner in this collaboration with well-established success in addressing disparities for infectious disease outcomes such as tuberculosis and human immunodeficiency virus in Kenya.[5,6] Given this success, these institutions have gradually broadened their scope to include other specialties and disease types as well as other partners around the world. For the past decade, pediatric cancer has become an even greater focus of care within AMPATH leading to improved awareness, diagnosis, and understanding of pediatric cancer treatment plans.[7–15] These efforts were further bolstered by the complementary twinning collaboration with Princess Máxima Center for Pediatric Oncology in the Netherlands.[16–18] As a result of all of these partnerships, and the efforts of regional pediatricians, MTRH has been established as the primary comprehensive diagnostic and treatment facility for pediatric cancer in Western Kenya.

Additional evidence of the success of this international collaboration was seen in a recent comprehensive evaluation of pediatric cancer services in Africa. Specifically identified areas of impact include continuous availability of chemotherapy, availability of radiotherapy, the presence of pediatric oncologic surgeons, and trained pediatric oncologists.[19] The presence of a national health insurance program further supports pediatric patients with cancer, although this only becomes available when a formal diagnosis is made. Finally, in addition to the comprehensive center in Eldoret (Kenya), there exists a similarly structured hospital in Nairobi which covers the Eastern regions of the country. Despite operating independently, there is collaboration of ideas and expertise with a shared interest in improving pediatric cancer care. When utilizing the SIOP (International Society of Paediatric Oncology) characteristics of infrastructure and levels of service line outlined by Howard et al., the services of MTRH have also shown growth over the past decade.[20] While previously showing capabilities consistent with a level 0 institution, there has been an upward trajectory and MTRH is now consistent with levels 1 and 2 depending on the specific service line.

Utilizing the current Kenya healthcare infrastructure and the multiple partnerships with MTRH, MU, IU, and Princess Maxima Center for Pediatric Oncology, we have developed a multidisciplinary and sequential approach to better evaluate the complex factors affecting the lack of appropriate diagnosis of pediatric cancer in Western Kenya with a particular emphasis on childhood leukemia, the most common malignancy affecting children.[2] First, we developed a database to better track all pediatric cancer diagnoses, geographic distribution, and patient outcomes. Second, we utilized a retrospective review of lab values and malaria slides at a district hospital to identify patients with pediatric leukemia to determine which patients may have presented to health care facilities with underlying leukemia but had not received a proper diagnosis. Finally, we surveyed pediatric healthcare providers in Western Kenya utilizing a general oncology knowledge assessment to test basic knowledge of pediatric oncology epidemiology, presentation, and diagnosis. The results of these comprehensive, decade-long initiatives are reported here. In addition, we discuss the findings how these insights can direct continued improvement in pediatric cancer diagnosis and treatment throughout the region.

2 | METHODS

2.1 | Part 1

The pediatric oncology team at Indiana University, the Dutch team from Princess Máxima Center, and the oncologists working with AMPATH together with the local pediatricians taking care of the children with cancer established a formalized database in January 2010 for all pediatric cancer patients seen at MTRH. The registry collects information regarding disease type, patient age, location, and treatment outcome. For the purposes of this database, pediatric patients were considered to be any child 14 years of age or younger. Diagnosis for leukemia and lymphoma was typically made based on morphology, flow cytometry, or immunochemistry, while the diagnosis of solid tumors was often based on tissue immunohistochemistry or pathology. Results have been continuously collected over the past decade, maintained by a local coordinator who can review medical records, communicate with clinicians and nursing team members, and connect with primary health care providers for established patients. Patient information has been collected at multiple time points including at diagnosis and end of treatment at a minimum. For patients who experienced relapsed disease, this was also captured by the registry once confirmed with tissue diagnosis.

After each calendar year, the total number of pediatric cancer diagnoses and each individual cancer type are compared to the anticipated diagnoses based on epidemiologic estimates relative to the regional population. These epidemiologic estimates are derived from extrapolated data from various databases including the Surveillance, Epidemiology and End Results Program (SEER) and the Union for International Cancer Control.[2,21,22]

2.2 | Part 2

Following the review of the initial data in Part 1, our groups sought to better understand the mechanisms leading to poor referral and diagnosis rates at the local level. As district and county hospitals act as the first triage point for many patients referred to MTRH, this served as a natural site of the subsequent investigation. One of these district hospitals was identified as a focus center to investigate potential patients who could not be appropriately diagnosed or referred.

Due to the similar clinical presentation between leukemia and malaria, as well as the ready availability of slides, we chose to review peripheral blood smears made for malaria detection to retrospectively screen for leukemia. Over 30,000 malaria slides were reviewed over 17 months from September 2012 through February 2014. Through a series of checkpoints including cell counts and pathology review, slides that were highly consistent with acute leukemia were identified. These slides were then processed, and cells were evaluated for leukemia via polymerase chain reaction analysis after manually scraping individual them off the slide. Although this review included both pediatric and adult patients and the clinical data at the lab facility was incomplete, the majority of these slides were from children 14 years of age or younger. We then compared the data to the registry to determine if the patients were being referred or evaluated at MTRH (T. Vik, personal communication, November 16, 2020).

2.3 | Part 3

Beginning in 2010, we host an annual 2-day pediatric oncology conference at MTRH located in Eldoret, Kenya, for clinicians and nurses in the referral region who care for pediatric patients who may have cancer. These providers typically practice at the level of the county hospital or mission hospital where patients receive complete blood counts and basic imaging including X-ray and ultrasound services. The conference consists of didactic lectures given by pediatric oncologists and other specialists as well as interactive small group instruction. This instruction targeted previously determined areas of need from prior years as well as content that was expected of a general provider. At the onset of the conference, all participants were given a general oncology knowledge assessment prepared by subject matter experts (SMEs). This is a 25-question test featuring clinical vignettes and relevant pediatric oncology factual information. At the conclusion of the conference, the participants were asked to complete the assessment for a second time. The test was made by a compilation of SMEs each contributing two to four questions for their disease-specific area and was verified by colleagues in the AMPATH network and the Dutch group. All knowledge evaluated in the assessment was covered during the conference teaching. The assessments are not anonymous and pre- and posttests were matched to each participant to determine the level of improvement. For participants who completed only a pretest or only a posttest, their results were excluded from the analysis. After collecting all the results, a paired *t*-test was used to assess for significant change as a result of the delivered educational conference curriculum.

Moreover, after the conclusion of the conference, each participant was given an opportunity to make additional recommendations for future education and outreach to better address the noted gap in pediatric cancer cases. These answers were reviewed by the hosting pediatric oncologists. This was supplemented with the results from the 2016 and 2018 conference attendees, which were also available and reviewed. Results from the conference in 2017 were not available. Questions and comments that were endorsed by multiple attendees were kept for review by the pediatric oncology team at MTRH.

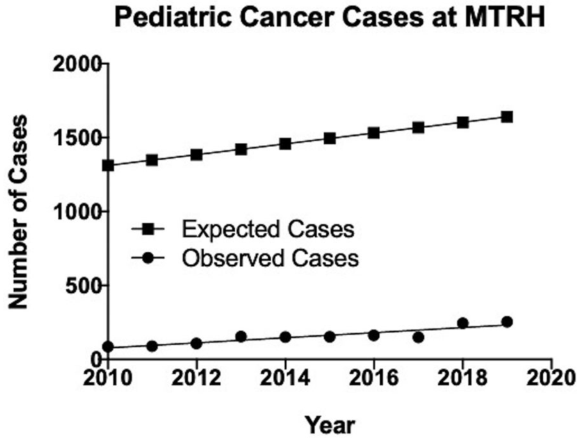

FIGURE 1 The number of diagnosed cases of pediatric cancer at Moi Teaching and Referral Hospital (MTRH) since 2010 compared to the number of expected cases based on the population of the referral region

3 | RESULTS

3.1 | Part 1

The pediatric cancer database was established in 2010 and has been maintained and continuously updated since its launch. The overall trends in pediatric cancer cases have been compared to the estimated incidence, which is shown in Figure 1. Although 10 years of data were included in this registry, recent trends reveal that only 200–250 patients were diagnosed annually in the last several years. Despite the increasing number of diagnosed cases shown in Figure 1, this suggests that the remaining 75%–80% of patients go undiagnosed and do not receive treatment. Figure 2 shows the distribution of pediatric cancer in 2019 confirming that pediatric acute lymphoblastic leukemia is the most common type of pediatric cancer in this region. Although this should represent about 30%–40% of all pediatric cancer diagnoses, only 49 cases (20%) were diagnosed in 2019 with slightly lower numbers in previous years.[2,21,22]

3.2 | Part 2

Our internal review of the malaria slides from the district hospital was completed over a 17-month period during which more than 31,000 slides were collected. Following our screening process, 41 malaria slides demonstrated both morphologic and genetic evidence of leukemia. In comparison with the pediatric cancer database at our referral hospital, none of the patients with peripheral evidence of leukemia were referred for either diagnosis or treatment at MRTH. As the age of the patient was not actively and reliably recorded by the outlying facility, the exact number of pediatric samples remained unclear. However, multiple verbal discussions with lab personnel confirmed that the majority of samples were from pediatric patients.

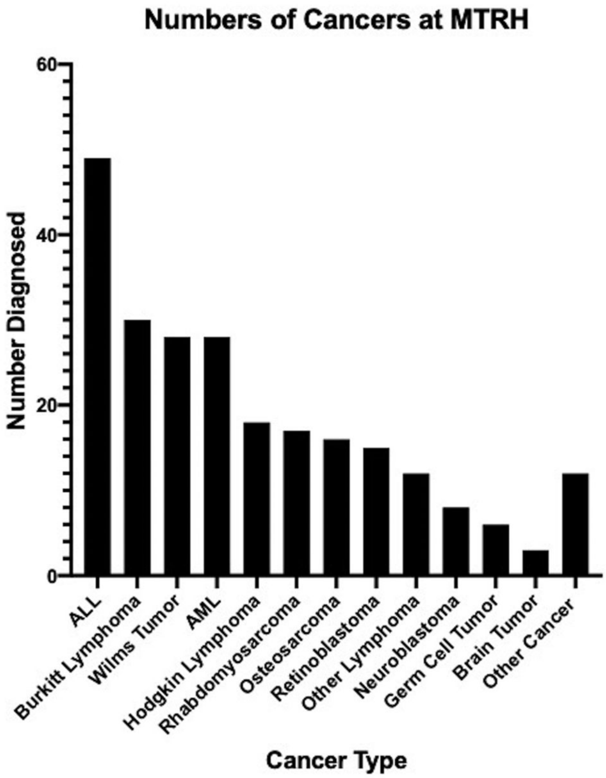

FIGURE 2 Frequency of each pediatric cancer diagnosis at Moi Teaching and Referral Hospital (MTRH) in 2019

3.3 | Part 3

At the 2020 annual pediatric oncology conference at MTRH, there were a total of 45 attendees from various regions throughout Western Kenya. Among these participants, 39 completed the pretest and 43 completed the posttest. There were 37 individuals who completed both tests. For data analysis, only participants who completed both the pretest and posttest were included. The average pretest score was 13.9 and the average posttest score was 17.8 yielding an average increase of 3.9 ($p = <0.001$). These results were supplemented with attendance from prior years, dating back to 2016. In total, 124 participants completed both a pretest and a posttest. The mean increase was 4.52 questions and the p-value was <0.001.

In addition to the quantitative scoring assessments, the qualitative answers from attendees at the 2020 conference were reviewed. The suggestions for future interventions found that over half of all attendees were seeking additional educational opportunities moving forward. This was consistent with the findings from previous conferences as well.

4 | DISCUSSION

The goal of this study was to better understand the scope and subsequently the mechanisms associated with the underdiagnosis of pediatric cancer in Western Kenya. By first defining the magnitude of the problem, and then examining it at the local patient and provider level, our teams could better identify the next steps needed to help address these disparities.

The first step was to better understand the rate of pediatric cancer diagnosis in our hospital relative to population estimates. By building a comprehensive pediatric cancer database, the local rates of diagnosis could be followed in real time. This also better helped to highlight the gaps between what our teams were seeing at MTRH in comparison to the expected rates via epidemiologic estimates. Further, although the extrapolation of SEER data for populations such as those in Kenya is limited, this database represents the best available anticipated baseline for the purposes of this work.

The next step was to help elucidate the presumably large population of pediatric patients who likely do have cancer but have not received a formal diagnosis and subsequent medical referral and treatment. In its current state, the majority of referrals come from county hospitals where initial workups including blood cell counts and imaging can occur. Our team elected to focus on the local level to better evaluate barriers to a proper diagnosis. Malaria has many overlapping signs and symptoms with pediatric leukemia and typically requires a fingerstick blood test to evaluate, which is readily available at district hospitals. These coinciding diseases offered an opportunity to potentially find patients with leukemia who were not referred for further workup and thus not receiving appropriate diagnosis and treatment.

Based on the analysis of malarial slides which isolated dozens of cases of undiagnosed pediatric leukemia from a single district hospital, it is reasonable to speculate that these patients are presenting to local providers for evaluation. However, based on various system failures, the right tests and therefore the right diagnoses are not found. As the district hospital sends the majority of patients to MTRH for further care, it is suspected that these patients ultimately did not receive an appropriate diagnosis and therefore did not survive. Although this evaluation is based on the overlapping signs of malaria and acute leukemia, it supports the idea that a lack of education and awareness by primary healthcare providers could be a leading issue. This lack of knowledge was one of the driving mechanisms for assessing the potential impact that educational interventions could have at the site of initial patient contact.

The results of the knowledge assessments from the annual pediatric oncology conference are also important to emphasize. As a result of the improvement in posttest scores, it is noted that primary healthcare providers do not yet have the general knowledge foundation to appropriately evaluate pediatric patients who may have cancer. As a result, it becomes less likely that the appropriate diagnostic workups are completed. The brief academic intervention at the conference showed significant improvement following dedicated didactic learning. This would suggest that the relevant practitioners in the region have a willingness and aptitude to learn more about pediatric oncology if given the opportunity. Additionally, results of qualitative responses following the conference suggest that additional academic opportunities would be welcome.

To this extent, our team intends to implement Project ECHO (Extension for Community Health Outcomes) as a mechanism to continue to offer additional educational opportunities to these providers. In this way, we can utilize both case-based learning as well as previously effective didactic educational sessions to help sustain the progress made at this annual conference. As Project ECHO is a validated and sustainable teleclinic tool adhering to the hub and spokes model,[23–26] it is intended that additional progress can still be made in the rate of pediatric cancer detection and appropriate referral. Further, as this is a validated distance education platform, it is well suited for virtual learning during a global pandemic, such as the coronavirus disease of 2019 or Ebola, when travel and close contact are restricted. As the only tertiary referral hospital in the region, MTRH is uniquely positioned to offer both the specialty expertise to function as a hub team as well as the resources to offer further diagnostic and therapeutic interventions.

Although there are not recently published articles detailing the implementation of Project ECHO and improvement of pediatric oncology outcomes, there are other instances of education achieving success in LMIC. Cervical cancer represents a disease where multiple points along the cancer continuum can effectuate care including prevention with vaccination, early and effective screening, and ultimately timely referral and treatment. There are several instances of telehealth education being implemented to successfully address healthcare disparities using the Project ECHO model in LMIC.[24,27,28]

Additionally, previous work from international organizations such as SIOP helps to better outline anticipated issues as the referral infrastructure continues to grow. As more patients are referred and appropriately diagnosed, new issues such as treatment abandonment, funding, and access to standard chemotherapy are likely to arise. A strong regional network of connected and educated personnel will be better equipped to not only identify but also address these concerns.

5 | CONCLUSION

Through a multi-step approach, our teams were better able to isolate potential issues impeding the appropriate and timely diagnosis of pediatric cancer in Kenya. First, epidemiological data and treatment records at a large regional tertiary care center suggested at least 75% of patients with pediatric cancer were undiagnosed. A review of malaria slides at a district hospital found several dozen cases of leukemia which were not referred for diagnosis or treatment. This suggests that these patients are presenting for care; however, the correct labs and workup are not pursued leading to a lack of appropriate diagnosis. Lack of general oncology knowledge played a critical role, based on a pediatric oncology assessment of healthcare providers in the region. The pre- and posttest results suggest significant learning potential for clinicians in medically underserved regions of Kenya. Given the suggestions for continued improvement, our teams will plan to use continuous virtual education platforms such as Project ECHO to further address these disparities.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES

1. 2019 Kenya Population and Housing Census, Volume I: Population by County and Sub-County. Kenya National Bureau of Statistics; 2019.
2. Howlader NNA, Krapcho M, Miller D, et al. *SEER Cancer Statistics Review, 1975–2017*. National Cancer Institute; 2020.
3. Mercer T, Gardner A, Andama B, et al. Leveraging the power of partnerships: spreading the vision for a population health care delivery model in Western Kenya. *Global Health*. 2018;14(1):44.
4. Quigley F. *Walking Together, Walking Far: How a U.S. and African Medical School Partnership is Winning the Fight against HIV/AIDS*. Indiana University Press; 2009.
5. Inui TS, Nyandiko WM, Kimaiyo SN, et al. AMPATH: living proof that no one has to die from HIV. *J Gen Intern Med*. 2007;22(12):1745-1750.
6. Njuguna B, Vorkoper S, Patel P, et al. Models of integration of HIV and noncommunicable disease care in sub-Saharan Africa: lessons learned and evidence gaps. *AIDS*. 2018;32(1):S33-S42.
7. Martijn HA, Njuguna F, Olbara G, et al. Influence of health insurance status on paediatric non-Hodgkin's lymphoma treatment in Kenya. *BMJ Paediatr Open*. 2017;1(1):e000149.
8. Njuguna F, Martijn H, Langat S, et al. Factors influencing time to diagnosis and treatment among pediatric oncology patients in Kenya. *Pediatr Hematol Oncol*. 2016;33(3):186-199.
9. Olbara G, Martijn HA, Njuguna F, et al. Influence of health insurance status on childhood cancer treatment outcomes in Kenya. *Support Care Cancer*. 2020;28(2):917-924.
10. Njuguna F, Mostert S, Slot A, et al. Abandonment of childhood cancer treatment in Western Kenya. *Arch Dis Child*. 2014;99(7):609-614.
11. Mostert S, Njuguna F, Kemps L, et al. Epidemiology of diagnosed childhood cancer in Western Kenya. *Arch Dis Child*. 2012;97(6):508-512.
12. Olbara G, Parigger J, Njuguna F, et al. Health-care providers' perspectives on traditional and complementary alternative medicine of childhood cancer in Kenya. *Pediatr Blood Cancer*. 2018;65(12):e27309.
13. Langat S, Njuguna F, Kaspers G, Mostert S. Health insurance coverage for vulnerable children: two HIV orphans with Burkitt lymphoma and their quest for health insurance coverage in Kenya. *BMJ Case Rep*. 2020; 13(8). https://doi.org/10.1136/bcr-2019-230508
14. Njuguna F, Martijn HA, Kuremu RT, et al. Wilms tumor treatment outcomes: perspectives from a low-income setting. *J Glob Oncol*. 2017;3(5):555-562.
15. Cocanour CS. Informed consent—it's more than a signature on a piece of paper. *Am J Surg*. 2017;214(6):993-997.
16. Njuguna F, Mostert S, Seijffert A, et al. Parental experiences of childhood cancer treatment in Kenya. *Support Care Cancer*. 2015;23(5):1251-1259.
17. Mostert S, Njuguna F, Langat SC, et al. Two overlooked contributors to abandonment of childhood cancer treatment in Kenya: parents' social network and experiences with hospital retention policies. *Psychooncology*. 2014;23(6):700-707.
18. Mostert S, Njuguna F, van de Ven PM, et al. Influence of health-insurance access and hospital retention policies on childhood cancer treatment in Kenya. *Pediatr Blood Cancer*. 2014;61(5):913-918.

19. Geel JA, Challinor J, Ranasinghe N, et al. Pediatric cancer care in Africa: sIOP Global Mapping Program report on economic and population indicators. *Pediatr Blood Cancer*. 2021;68(11):e29345.
20. Howard SC, Davidson A, Luna-Fineman S, et al. A framework to develop adapted treatment regimens to manage pediatric cancer in low- and middle-income countries: the Pediatric Oncology in Developing Countries (PODC) Committee of the International Pediatric Oncology Society (SIOP). *Pediatr Blood Cancer*. 2017;64:5.
21. Mackay J, Society AC. *The Cancer Atlas*. American Cancer Society; 2006.
22. Steliarova-Foucher E, Colombet M, Ries LAG, et al. International incidence of childhood cancer, 2001–10: a population-based registry study. *Lancet Oncol*. 2017;18(6):719-731.
23. Arora S, Kalishman S, Dion D, et al. Partnering urban academic medical centers and rural primary care clinicians to provide complex chronic disease care. *Health Aff (Millwood)*. 2011;30(6):1176-1184.
24. Hariprasad R, Arora S, Babu R, et al. Retention of knowledge levels of health care providers in cancer screening through telementoring. *J Glob Oncol*. 2018;4:1-7.
25. Yennurajalingam S, Amos CE Jr, Weru J, et al. Extension for community healthcare outcomes—palliative care in Africa program: improving access to quality palliative care. *J Glob Oncol*. 2019;5:1-8.
26. Zhou C, Crawford A, Serhal E, Kurdyak P, Sockalingam S. The impact of Project ECHO on participant and patient outcomes: a systematic review. *Acad Med*. 2016;91(10):1439-1461.
27. Rossman AH, Reid HW, Pieters MM, et al. Digital health strategies for cervical cancer control in low- and middle-income countries: systematic review of current implementations and gaps in research. *J Med Internet Res*. 2021;23(5):e23350.
28. Varon ML, Baker E, Estrada EE, Schmeler KM, Pareja R. Advancing gynecologic oncology in Latin America through Project ECHO. *Int J Gynecol Cancer*. 2020;30(11):1840-1841.

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