

Review article

## Improving quality of care and timely access to radiation therapy for patients with invasive cervical cancer at the National Cancer Institute Paraguay



Geraldine Jacobson<sup>a,\*</sup>, Linus Chuang<sup>b</sup>, Maximilian Pankow<sup>c</sup>

<sup>a</sup> Department of Radiation Oncology, West Virginia University, 1 Medical Center Drive, Morgantown, WV 26506, United States

<sup>b</sup> Department of Obstetrics and Gynecology, Western Connecticut Health Network, 24 Hospital Avenue, Danbury, CT 06810, United States

<sup>c</sup> Department of Radiation Oncology, National Cancer Institute Paraguay, Teniente Jara Mendez 477 e/Pitiantuta, Asunción, Paraguay

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### ABSTRACT

The purpose of this report is to describe the interventions implemented between 2012 and 2017 at the National Cancer Institute Paraguay (NCI Paraguay) to improve treatment quality and efficiency for patients with cervical cancer, with an emphasis on radiation quality and access. The NCI Paraguay requested collaboration with Health Volunteers Overseas (HVO), an international volunteer organization, to improve the care of patients with cervical cancer. This report is based on site visits to NCI Paraguay by HVO volunteers in 2012, 2013, and 2016, with a follow-up report from the site in 2017. During the study period, increased access to external beam radiation and brachytherapy led to a decrease in wait time to start radiation from 2 to 3 months to 4–6 weeks. The center transitioned from 2-dimensional (2D) to 3-D planning and was able to offer concurrent chemotherapy and radiation, including brachytherapy, to patients with locally advanced cervical cancer. Based on the American Society of Clinical Oncology's resource-stratified clinical guidelines, from 2012 to 2017, the practice transitioned from a "basic setting" to an "enhanced setting".

### 1. Introduction

Access to cancer care in low- and middle-income countries (LMIC) is a global problem; effective solutions are likely to be local and institutional. This report describes a collaborative effort to improve the quality of cervical cancer treatment and access to timely radiation therapy at the National Cancer Institute Paraguay (NCI Paraguay). While some of the details focus on changes in radiotherapy access and practice, the overall approach was comprehensive and included changes in availability of diagnostic and imaging services as well as implementation of multidisciplinary collaboration.

There is a global imbalance in access to information and resources. Information is easily transmitted, but resources are unevenly distributed. Healthcare personnel in many LMIC can obtain developed-world recommendations for cancer treatment but do not have access to modern facilities, radiation therapy, chemotherapy, and targeted therapy. European and North American treatment guidelines may not be practical in resource-limited areas. The American Society of Clinical Oncology (ASCO) and other groups have created clinical guidelines for optimal cancer care in resource-limited settings (Chuang et al., 2016), yet each locale has unique constraints and opportunities.

Two-thirds of cancer cases in the next decade are expected to occur in LMIC. In Latin America and the Caribbean region, an estimated 1.7 million cases will be diagnosed in 2030 (Goss et al., 2013). While overall cancer incidence is lower in Latin America than in North America and Europe, the cancer burden is greater because of advanced stage at diagnosis and lack of access to treatment. Access to medical care varies between countries and regions in Latin America, with worse access and health outcomes in rural areas.

Paraguay is a landlocked country in the heart of South America with a population approaching 7 million people. Paraguay's per capita gross national income is the 2nd lowest on the continent after Bolivia. Over the past decade, the Paraguayan economy grew at an average rate of 5% (The World Bank, 2017). The economy has grown in recent years because of increased agricultural exports and production of hydroelectric power, and Paraguay is currently considered a middle-income country (The World Bank [2017]).

The Paraguayan government initiated healthcare reform in 2008 and implemented a cancer control policy that year. To date, there is no national cancer registry (Globcan, 2012).

Seven percent of Paraguay's population of 6.1 million currently has private health coverage, 20% are covered by the health services of the

\* Corresponding author at: Department of Radiation Oncology, West Virginia University, 1 Medical Center Drive HSS B848B, PO Box 9234, Morgantown, WV 26506-9234, United States.

E-mail addresses: [gjacobsen@hsc.wvu.edu](mailto:gjacobsen@hsc.wvu.edu) (G. Jacobson), [linus.chuang@wchn.org](mailto:linus.chuang@wchn.org) (L. Chuang).

social security institute (the Instituto de Previsión Social), and the rest depend on the public health system.

Since the majority of patients do not have private insurance and have uneven access to cancer screening, they often present with advanced stage disease requiring multimodal care.

The obstacles to cancer treatment are numerous and include inadequate screening, distance from medical facilities, lack of facilities, and logistic and cultural barriers to treatment. Paraguay's transportation system ranges from adequate to poor, largely depending on the region of the country. The country has a network of roads, railroads, rivers, and airports, but significant infrastructure and regulation improvements are needed. The highway is comprised of single lane roads, which makes it difficult and time consuming to commute between cities. NCI Paraguay, where the government radiation facility is housed, is approximately 1 h outside of the capital city, Asuncion, which makes access to radiation treatment challenging for many people. Radiotherapy units are 1 per 2–3 million people in Paraguay, compared with 1 per 500,000 people in Uruguay (<http://nigatom.org.ng/wp-content/uploads/2017/12/Radiotherapy-in-Cancer-Care-Facing-the-Global-Challenge.pdf>, nd). There are 4 radiotherapy centers in the country. Based on estimates by the International Atomic Energy Agency (IAEA), only 44.2% of patients in Paraguay who need radiotherapy have access to this modality (Pan American Health Organization, 2013). In Paraguay, breast cancer is the most common cancer in women, followed by cervical cancer. Clinical breast examination and mammography are available but not free, and mammography facilities are not abundant. Mammography units are 0.42 per 100,000 people in Paraguay, compared with 12.97 per 100,000 people in St. Vincent and the Grenadines (Pan American Health Organization, 2013). Lack of screening partly explains the high incidence of advanced-stage breast cancer in Paraguay.

According to a Pan American Health Organization (PAHO) report, there is a national cervical cancer prevention and control plan in place (Pan American Health Organization, 2013). Clinical practice guidelines are available for cancer treatment, and there is a referral system established for which NCI Paraguay is the major public referral center. Pap is the screening test included in the program. Despite the availability of these programs, the country is experiencing difficulties dealing with the challenges posed by prevention programs based exclusively on cytology. In a resource-limited environment like Paraguay, with low coverage, difficulties in providing follow-up, and deficient or incomplete quality control systems, PAHO recommends that alternative cervical cancer screening technologies are needed.

While breast cancer is the most common cancer in women in Paraguay, cervical cancer is the number one of cause of death. The mortality rate from cervical cancer in Paraguay is among the highest in Latin America. The incidence is 34.2/100,000, and the mortality is 15.7/100,000 (Globcan, 2012).

NCI Paraguay initiated a collaboration with Health Volunteers Overseas (HVO), an international volunteer organization, in 2012 to improve the process of care for patients with cervical and breast cancer. HVO is a volunteer-based organization dedicated to improving the availability and quality of healthcare in resource scarce countries through education, training, and professional development. Healthcare providers join HVO on a volunteer basis to provide teaching and service rather than direct clinical care.

## 2. Methods

This report describes interventions initiated by NCI Paraguay, in collaboration with HVO, to improve the process of care for patients with cervical cancer and some outcomes of this intervention. The project addressed the diagnosis, evaluation, and treatment of patients with cervical cancer with a focus on improvement in access to radiation therapy and improved quality of radiation therapy. The interventions were implemented by NCI Paraguay between 2012 and 2017. The

report is based on site visits by HVO volunteers to NCI Paraguay in 2012, 2013, and 2016, with a follow-up report from the site in 2017. During each site visit, HVO volunteers served as educators and consultants. The visits lasted approximately 1 week and included attendance in clinics and surgery; interviews with staff, leadership, and residents; and participation in seminars and presentations. Interventions to improve patient care were initiated and implemented by the physicians and leaders of NCI Paraguay.

### 2.1. NCI Paraguay

NCI Paraguay, Instituto Nacional del Cancer de Paraguay, is the only cancer center in Paraguay and the primary site for training in cancer medicine specialties. It is 1 of 3 centers for medical oncology training, the single site for surgical and radiation oncology training in Paraguay, and provides training in gynecology.

The hospital has 200 beds and a large outpatient clinic capacity. The gynecology department sees around 8000 patients a year. In 2017, the NCI had 603 new cervical cancer cases. The NCI clinics uses paper records.

The center was established in 1986 by the government in Capiata, a rural area approximately 18 miles outside the capital city of Asuncion. Patients are referred to NCI Paraguay from all over the country, usually with a confirmed cancer diagnosis or high suspicion of cancer. The cancer center does not provide transportation. Free lodging is located on the hospital grounds, and off-site lodging is available. Treatment is covered by the government under the universal healthcare system.

Cervical cancer is the leading cancer diagnosis at NCI Paraguay, with 4212 cases seen from 2000 to 2010 (range, 345–479 cases per year); breast cancer numbers were 2245 for the same period (range, 182–334 cases per year). Ovarian cancer is the 2nd most common gynecologic malignancy, with 300 cases seen in 10 years (range, 11–49 cases per year). Data are not available for stage distribution, treatment outcomes, or survival.

The physicians at NCI Paraguay (surgical, medical, and radiation oncologists) are well trained and have access to international treatment guidelines. Oncology specialists complete additional training after medical school. Radiation oncologists complete a 4-year residency. Gynecologic and surgical oncologists have additional specialty training after surgical residency. Many specialists obtain additional training in the United States and other Latin American and European countries.

Most physicians at NCI Paraguay work part time. They have a private practice to support their income and work at the cancer center 2–5 days a week.

NCI Paraguay collaborated with HVO to improve the delivery of care to patients with cervical cancer. The stated goals of the project included: assisting in developing diagnostic and treatment pathways for cervical cancer, including triaging patients for immediate access to radiation and brachytherapy, and reinforcing a multidisciplinary approach to the diagnosis and treatment of cervical cancer.

During the site visits, the volunteers, staff, and center leadership discussed interventions to improve the existing system and make it more efficient without the need for major spending. The team focused on developing diagnostic and treatment pathways and reinforcing a multidisciplinary approach.

### 2.2. Initial visit and assessment

An initial site visit to NCI Paraguay was made in 2012. At that time, radiation oncology was staffed by 3 part-time radiation oncologists and 1 resident. A single linear accelerator at the facility operated from 7 am to 7 pm. Radiation planning was clinical, based on external anatomic landmarks, or based on 2-dimensional (D) imaging (i.e., X-rays). Time from radiation oncology referral to consultation was 3–4 weeks. Waiting time for a diagnostic computed tomography (CT) scan and biopsy results took an additional 3–4 weeks. Pathology reports took up

to 2 months, as the pathology department was understaffed. There were 2 part-time staff pathologists (2 days a week, 6 h a day) and 1 resident. This resulted in significant treatment delays, since patients did not begin treatment until a pathology report was available. The average time to begin radiation and chemotherapy for a patient diagnosed with cervical cancer was 8–12 weeks or longer after presenting to the center. Because of delays in initiating radiation, some patients were treated with neoadjuvant chemotherapy followed by surgery, consistent with ASCO guidelines for a basic resource setting (Chuang et al., 2016). Brachytherapy was available only as a low-dose-rate (LDR) treatment and was limited to 2 patients per week. This limitation was due to the hospital having a single set of applicators as well as a single set of Cs137 sources for LDR treatment. One treatment would last approximately 48–36 h, and treatment days were Monday through Friday. High-dose-rate (HDR) treatment was not available at the time. The ideal standard of care at NCI for patients with locally advanced cervical cancer was chemoradiation followed by brachytherapy. Because of the limitations to brachytherapy access, this policy was not always feasible and external beam radiation was commonly followed by hysterectomy, consistent with ASCO guidelines for limited settings (Chuang et al., 2016).

Both external beam radiation and brachytherapy were available, but because of the mismatch of large patient volume and limited radiation facilities, strategies more appropriate to a basic and limited setting were employed to treat patients in a timely manner.

Six gynecologic oncologists performed all surgeries for gynecologic malignancies. There is no formal gynecologic oncology training in Paraguay. Residents gain their experience managing patients with gynecologic cancers during their residency. Minimally invasive surgery is not performed.

The medical oncologists had a large outpatient clinic serving approximately 100 patients per day and had access to many common cancer drugs, including cisplatin and paclitaxel. Fifteen part-time medical oncologists practice at the center.

There was limited dialogue between the surgeons, medical oncologists, and radiation oncologists. The main barriers to optimal treatment delivery were identified as a lack of resources and lack of coordination of care between the different medical specialties. These were identified by the HVO volunteers on site through observation of the hospital dynamic for this subset of patients (cervical cancer) as well as meetings with hospital staff and administration. Inadequate communication between the specialties prevented optimal use of the limited resources in pathology/laboratory, medical oncology/chemotherapy, and radiation oncology. There were no institutional diagnosis-specific guidelines for work-up and treatment. Long delays at each step, from diagnosis to completion of treatment, were identified as an opportunity to improve the use of existing resources and promote the acquisition of needed resources.

Additional issues included the change of cancer center leadership following each national election and the staffing model of part-time physicians, since most physicians had an additional private practice. Paraguay has national elections every 5 years. When there is a change in party leadership, a new cancer director is appointed.

In summary, the cancer center physicians and HVO identified multiple barriers to timely treatment of patients with invasive cervical cancer. These included delays in pathologic confirmation of diagnosis, delays in obtaining CT scans, lack of care coordination between oncology specialists, and lack of access to timely radiation treatment because of a limited number of treatment machines and the constraints of LDR brachytherapy.

Suggested approaches by the visiting HVO team included the development of a weekly multidisciplinary clinic for patients with cervical cancer, the development of treatment guidelines for patients with cervical cancer using published models but modifying them based on available resources, utilizing visiting specialists for updates on treatments and technology, and using teleconferencing for lectures and case conferences.

ASCO guidelines for the management of invasive cervical cancer in resource-limited settings are based on surgical skill levels, availability of recommended chemotherapy, radiation equipment, pathology services, and palliative care availability. Clinical settings are defined as basic, limited, enhanced, and maximal (Chuang et al., 2016). Treatment guidelines are based on medical resources: physician skills and technology. They do not address other practical barriers to treatment, such as limited availability of medical resources in relation to the population served, the logistics of an underserved population travelling to a treatment facility, and payment for treatment.

While published guidelines can serve as a template for improvement, the actual process of changing practice is accomplished by assessing the practice environment, optimally using the resources and expertise at hand, and obtaining additional critical resources if possible.

### 2.3. Practice improvements: 2012–2017

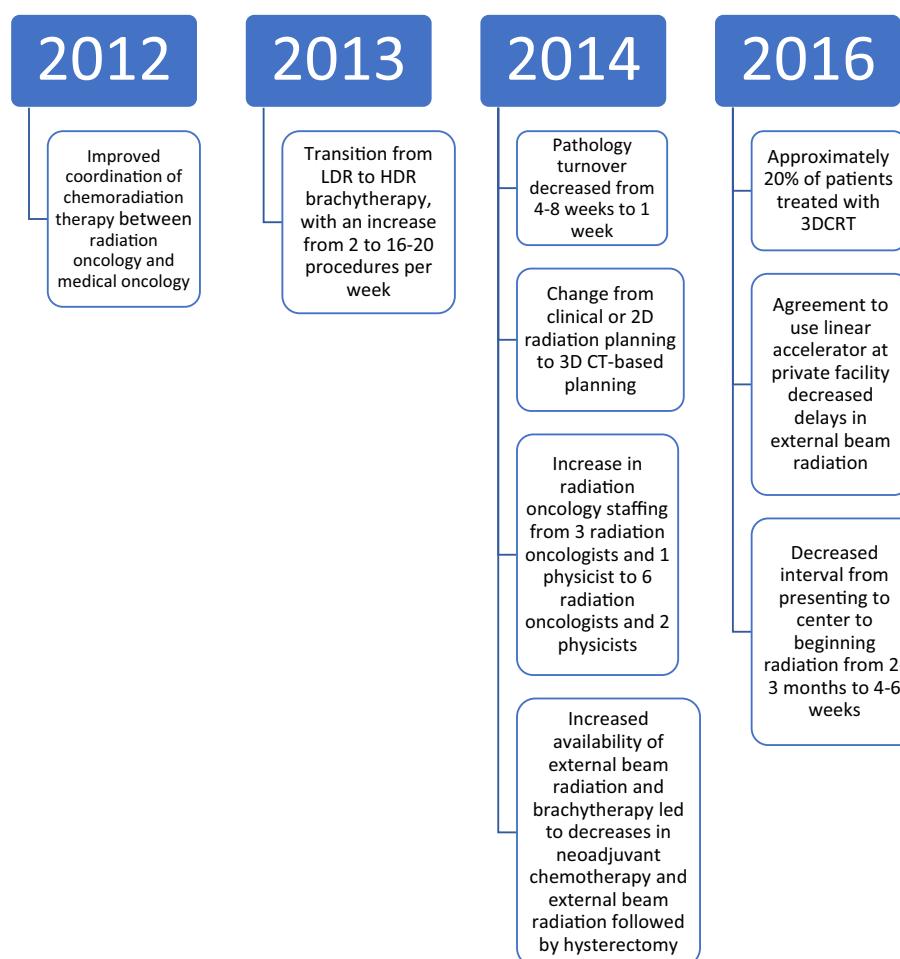
Despite changes in cancer center leadership, the center and physicians were committed to improving patient care and able to implement improvements in workflow and treatment. The leadership and administrators purchased additional equipment, hired personnel, and collaborated with non-governmental organizations and private facilities to improve quality of care.

Based on HVO recommendations, a multidisciplinary cervical cancer clinic was established, including a designated staff of gynecologic oncology surgeons (3), medical oncologists (2), radiation oncologists (2), and residents from all 3 areas. The clinic occurs once a week and evaluates all cervical cancer patients seen in that week. Physicians not part of the clinic can refer their cervical cancer patients to the clinic (which became a habit for most). The clinic evaluates the patient to make sure all diagnostic studies are in order (e.g., biopsy, imaging, labs), completes them as necessary, and sends the patient for appropriate treatment (surgery versus chemo radiation).

Between 2012 and 2016, there was significant improvement in the time from surgery to reporting of pathology results, from an average of 4 weeks to 1 week. This was accomplished by hiring additional part-time pathologists, increasing from 2 to 4 pathologists, with each working half a day. By 2017, a biopsy result was available in 5 days. This allowed patients to progress more quickly from biopsy to definitive treatment.

Cisplatin-based chemotherapy is available through NCI Paraguay; concurrent chemotherapy is well coordinated between the radiation oncology and medical oncology departments. The usual regimen is 45 Gy external beam pelvic radiation with concurrent weekly cisplatin chemotherapy at 40 mg/m<sup>2</sup>. Approximately 80% of patients receive chemoradiation therapy. The remaining 20% of patients are not able to receive chemoradiation due to financial or other medical conditions.

During the follow-up site visit in 2016, a notable difference in the radiation process was the transition to 3-D CT-based planning. A staff radiation oncologist obtained additional training regionally, then developed a workflow using the hospital CT scan for volume-based radiation planning. IAEA donated immobilization devices for reproducible patient positioning. An HDR brachytherapy device was purchased by the government, and the vendor provided training. This allowed 16–20 brachytherapy treatments per week. The availability of timely brachytherapy decreased the practice of preoperative external beam radiation followed by hysterectomy. A new linear accelerator was purchased by the government but was not yet installed due to lack of a vault, so access to external beam radiation was still a bottleneck. The Ministry of Health addressed this issue by creating an agreement with a private clinic to treat patients from NCI Paraguay who were funded by the state. This made a significant impact on reducing treatment delays. The number of radiation oncologists increased from 3 to 6. NCI Paraguay is currently considering a plan to employ physicians full time, which should add to the efficiency of medical services. With improvements in work-up, care coordination, and access to radiation treatment,



**Fig. 1.** Timeline of improvements implemented by NCI Paraguay between 2012 and 2017.

the delays between presentation to the center and beginning radiation were reduced from 2 to 3 months to 4–6 weeks.

The current model for patients with invasive cervical cancer stage IB2 or above at NCI Paraguay is external beam pelvic radiation with concurrent cisplatin chemotherapy and brachytherapy. This meets the “maximal” setting guideline from ASCO’s resource-stratified clinical practice guideline (Chuang et al., 2016). The faster turnaround of pathology reports, improved availability of brachytherapy, and additional use of a private facility have decreased the time from diagnosis to treatment and increased the availability of standard of care treatment. The transition from 2-D to 3-D treatment planning has moved the practice to more precise radiotherapy, which will hopefully result in improved outcomes with decreased morbidity.

During the 2012–2017 period, NCI Paraguay made significant improvements in treatment access and workflow for cervical cancer (Fig. 1), moving from practice consistent with a “basic setting” to practice consistent with an “enhanced setting”. While the center requested external consultation, the changes were driven and implemented by the leadership and physicians at NCI Paraguay. The process included obtaining additional resources and training, better organization of existing resources and communication between specialists, and partnerships with private and international organizations.

### 3. Discussion

Standard of care treatment for advanced cervical cancer is concurrent cisplatin-based chemotherapy plus brachytherapy. The recommendation for concurrent chemoradiation is based on several large

randomized clinical trials (Josefson, 1999). Brachytherapy has been shown to be an important component of definitive radiation, providing a method to deliver high-dose radiation to the tumor with decreased dose to adjacent normal structures. A National Cancer Database study demonstrated that patients who received treatment with external radiation and brachytherapy in the United States had significantly improved overall survival compared with patients who were treated with external beam radiation alone. Han et al. (2013) noted a decrease in cause-specific survival in patients when brachytherapy was omitted. Delays in initiating treatment have a detrimental effect on local control (Chen et al., 2008). Total treatment duration has also been identified as a prognostic factor in cervical cancer outcome. Treatment time longer than 7–9 weeks has been associated with increased pelvic failures and decreased overall survival. A retrospective institutional study found a higher incidence of pelvic failures in patients who had a treatment duration longer than 56 days and identified delay in brachytherapy as a major contributing factor (Song et al., 2013).

Overall survival in patients with cervical cancer is associated with stage at presentation and treatment efficacy. Delays in diagnosis and initiating therapy contribute to higher stage disease. Resource limitations affect the ability to deliver effective treatment.

The treatment of invasive cervical cancer is multimodal and requires radiotherapy, surgical and medical oncology, access to chemotherapy, and supportive care. Unfortunately, the burden of cervical cancer is highest in LMIC, where these skills and resources are scarce.

Radiotherapy facilities are expensive to initiate and maintain and require highly trained personnel and physicians and dependable access to power and water. Currently, 33% of the world’s external beam units

are available in LMIC to treat 60% of the world's cancer patients (Datta et al., 2014). The lack of radiation facilities in LMIC is well documented, and multiple solutions have been proposed (Abdel-Wahab et al., 2017). In the absence of financial incentives to provide radiation oncology services, strong governmental support is required.

NCI Paraguay's approach to improve cervical cancer management was pragmatic and addressed significant barriers to treatment outcomes. The project goals were to reduce delays in initiating treatment, provide timely access to external beam radiation with chemotherapy and brachytherapy, improve the quality of radiotherapy, and reduce the time from diagnosis to completion of therapy.

Compared with treatment barriers described in some LMIC (Kivut-Bitok et al., 2013; Makau-Barasa et al., 2017; Haque et al., 2017), NCI Paraguay had several strengths. The facility leadership and physicians were aware of the shortcomings of the treatment process and committed to improving it. Treatment in this public facility is paid for by the government, eliminating the barrier of treatment cost to the patients. The physicians were well trained and have access to current medical information. The facility initiated the process and used multiple strategies and partners to accomplish the improvements in care. This included inviting an outside organization to provide assessment and recommendations. While not all recommendations were put into action, those implemented were directly related to reducing treatment delays and improving multidisciplinary communications. The government purchased an HDR brachytherapy treatment device and obtained training from the vendor. IAEA served as a resource for positioning devices. A staff radiation oncologist obtained regional training and implemented 3-D planning. Additional radiation oncologists and a physicist were hired.

Cancer treatment facilities in LMICs have strengths and opportunities unique to their individual settings. The process described may not be applicable to other institutions. However, the key factors that contributed to an improved process of care are applicable to other settings. The first is that the leadership and staff of the center were committed to improving care and led the process. The second is that the institution used a variety of partners and techniques to improve care and did not depend on a single source for expertise and resources.

#### 4. Conclusion

While Paraguay continues to have insufficient radiation oncology facilities for the population, the leadership of NCI Paraguay improved access and care at this major public cancer hospital. Between 2012 and 2017, NCI Paraguay improved the treatment process and quality of care for cervical cancer patients with reduced delays in initiating and completing treatment and attainment of an enhanced standard of care.

#### Conflicts of interest

The authors have no conflict of interest.

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