Original Article

The Cost-Effectiveness of Treating Childhood Cancer in 4 Centers Across Sub-Saharan Africa

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BACKGROUND: The treatment of childhood cancer often is assumed to be costly in African settings, thereby limiting advocacy and policy efforts. The authors determined the cost and cost-effectiveness of maintaining childhood cancer centers across 4 hospitals throughout sub-Saharan Africa. **METHODS:** Within hospitals representing 4 countries (Kenya, Nigeria, Tanzania, and Zimbabwe), cost was determined either retrospectively or prospectively for all inputs related to operating a pediatric cancer unit (eg, laboratory costs, medications, and salaries). Cost-effectiveness was calculated based on the annual number of newly diagnosed patients, survival rates, and life expectancy. **RESULTS:** Cost per new diagnosis ranged from $2400 to $31,000, attributable to variances with regard to center size, case mix, drug prices, admission practices, and the treatment abandonment rate, which also affected survival. The most expensive cost input was found to be associated with medication in Kenya, and medical personnel in the other 3 centers. The cost per disability-adjusted life-year averted ranged from 0.3 to 3.6 times the per capita gross national income. Childhood cancer treatment therefore was considered to be very cost-effective by World Health Organization standards in 2 countries and cost-effective in 1 additional country. In all centers, abandonment of treatment was common; modeling exercises suggested that public funding of treatment, additional psychosocial personnel, and modifications of inpatient policies would increase survival rates while maintaining or even improving cost-effectiveness. **CONCLUSIONS:** Across various African countries, childhood cancer treatment units represent cost-effective interventions. Cost-effectiveness can be increased through the control of drug prices, appropriate policy environments, and decreasing the rate of treatment abandonment. These results will inform national childhood cancer strategies across Africa. ***Cancer* 2020;0:1-7**. © *2020 American Cancer Society*.

KEYWORDS: childhood cancer, cost-effectiveness, strategies, sub-Saharan Africa.

INTRODUCTION

Approximately 397,000 children aged birth to 14 years are diagnosed with cancer annually, of whom >90% reside in low-income and middle-income countries (LMICs).[1] Although cure rates for children with cancer residing in high-income countries (HICs) now exceed 80%, cure rates are substantially lower in LMIC settings, ranging from 55 to 60%.[2-4] As infectious-related childhood mortality continues to decline, childhood cancer accounts for a growing percentage of childhood morbidity and mortality.[3] In recognition of the magnitude of this problem, the World Health Organization (WHO) launched the Global Initiative for Childhood Cancer in 2018, which aims to improve childhood cancer survival globally to 60% by 2030.[5] A key component of reaching this goal will be the widespread development and adoption of national childhood cancer plans by LMICs.

A major barrier to the adoption of such plans is the perception on the part of many policymakers that childhood cancer treatment is too expensive for LMIC health systems. A recent systematic review demonstrated that although the few studies conducted to date uniformly concluded that childhood cancer treatment in LMICs is cost-effective,

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many did not comprehensively capture all the associated costs of treatment.[6] In addition, to our knowledge, very few rigorous studies were conducted in sub-Saharan Africa, which will account for nearly one-half of the total global childhood cancer burden by 2030 and where health systems routinely face acute resource constraints, resulting in difficult decisions concerning how best to allocate scarce public funds.[1,7,8] Previous work by our team demonstrated that operating a childhood cancer treatment center in Accra, Ghana, is very cost-effective by international standards.[9] Whether those results can be generalized to a wider range of sub-Saharan African treatment centers is unknown.

Therefore, the objective of the current study was to determine the cost and cost-effectiveness of sub-Saharan childhood cancer treatment centers across a range of diverse settings to: 1) generate policy-relevant data that can inform decision making in each jurisdiction regarding how to prioritize childhood cancer interventions in the face of competing health priorities; and 2) contribute robust evidence regarding the economic dimensions of childhood cancer treatment to the existing literature, including a comprehensive accounting of relevant costs.

MATERIALS AND METHODS

Study Setting

Four childhood cancer treatment centers, each located within a different sub-Saharan African country, participated in the current study. The 4 participating centers included: 1) Kenyatta National Hospital (KNH) in Nairobi, Kenya; 2) Bugando Medical Centre (BMC) in Mwanza, Tanzania; 3) University College Hospital (UCH) in Ibadan, Nigeria; and 4) Parirenyatwa Hospital (PH) in Harare, Zimbabwe. These centers were chosen based on a combination of purposive and convenience sampling considerations, including geographic and socioeconomic diversity, variations in institutional size and service capacities, and the presence of strong collaborative relationships with institutional leaders in pediatric oncology. The 4 countries represented different regions (1 in West Africa, 2 in East Africa, and 1 in southern Africa) and a range of country income levels (1 low-income country and 3 lower middle–income countries using World Bank categories). Participating sites also varied with regard to characteristics such as patient volume, catchment area, infrastructure, available services, and financing (see Supporting Table 1). KNH, BMC, and PH all treated between 130 and 155 new cases of childhood cancer per year, whereas UCH represented a smaller volume center, seeing approximately 40 new diagnoses annually. Although Kenya, Nigeria, and Tanzania have multiple childhood cancer centers, PH represents the only treatment center for children with cancer in Zimbabwe. In PH, radiation availability was limited, whereas surgery was referred out to another local hospital. Similarly, the BMC transfers children requiring certain treatments to 1 of the other 2 centers in Tanzania. Treatment protocols are based on international standards, but usually are modified to account for a greater risk of toxicity or lack of resources.

All 4 centers face common challenges in funding the diagnosis and treatment of childhood cancers. Although public health insurance is available in all 4 jurisdictions, significant gaps exist in the coverage of key diagnostic investigations and treatments. All 4 sites rely on philanthropic funding to some extent, although the amount of such funding available varied. Important sources of such funding included the Hope for Cancer Kids in Kenya, the International Cancer Care and Research Excellence Foundation (iCCARE [http://i-ccare.org/]) in Tanzania, and KidzCan Zimbabwe (https://www.kidzcanzimbabwe.org/). Out-of-pocket expenses still are significant in all 4 centers, but are most extensive in Nigeria, in keeping with its higher reliance on the private sector for health services and financing compared with many other sub-Saharan African countries.

Data Collection

The current study took the perspective of the health care system. Cost data were collected using an instrument originally piloted in a pediatric cancer center in El Salvador.[10] The instrument also was used previously in sub-Saharan Africa for a study conducted at the Korle Bu Teaching Hospital in Ghana.[9] Each of the 4 participating centers nominated a small team, usually comprised of 2 individuals, to collect the required data. The team typically included a senior oncologist along with another researcher to support the detailed data collection process. Team members participated in 3 structured webinars regarding basic methods for costing and how to measure and interpret cost-effectiveness. This was followed by a 1-day in-person meeting to discuss the details of data collection, harmonize data collection procedures, and, when necessary, make minor modifications to the instrument to adapt it to local contexts. Local piloting did not identify additional necessary modifications.

Costs were compartmentalized, including such categories as personnel (medical and support), room and board for patients and their families ("hoteling"), outpatient clinic, shared services (pharmacy, pathology, surgery, radiation, imaging, and blood bank), other services (information technology and training), and other central hospital services (utilities, human resources, and administrative costs). All costs were collected and included regardless of the source of funding (government vs philanthropic vs out-of-pocket funding).

Cost data sources varied. Medical personnel costs were determined by multiplying salary figures for relevant health care personnel by the self-reported percentage of their time dedicated to pediatric oncology care. A broad range of personnel were included, such as social workers and data registrars when present. In rare cases, staff personnel who were not remunerated (eg, unpaid pediatric residents) were assigned appropriate salaries by local leads. Information regarding the time devoted by nonmedical personnel (eg, clerical staff registering patients to inpatient or outpatient units or other administrative personnel) to pediatric oncology services was more difficult to estimate. In the absence of such information, we thus used the same ratio of the cost of nonmedical to medical personnel (25:75) as for the pediatric cancer unit at the Hospital Nacional de Ninos Benjamin Bloom in San Salvador, El Salvador, which maintains separate financial statistics for their pediatric cancer unit and to the best of our knowledge produced the first published estimates of the cost of running a pediatric cancer unit in a LMIC.[10]

Detailed financial records generally were not available at participating sites. Thus, for the majority of items, including laboratory tests, medications (supportive and chemotherapeutic), diagnostic imaging, surgical services, and blood products, all services used by pediatric oncology patients, both inpatients and outpatients, were recorded prospectively for a defined period of time: 4 weeks in Nigeria, Tanzania, and Zimbabwe and 2 weeks in Kenya given the higher volumes and resource limitations in that country. A small number of cost items, such as radiation services, were captured retrospectively. Tests that were ordered but not completed were not included. Unit costs were obtained from appropriate hospital sources and, in the case of medications, adjusted based on dosage. Unit costs for diagnostic services incorporated the costs of personnel (eg, pathology or laboratory technicians) involved in providing the service. Unit costs and volumes were multiplied to determine the total associated cost of treating children with cancer over the time period, and then multiplied by the appropriate factor to determine annual costs.

Operating room (OR) costs associated with pediatric oncology patients were determined by obtaining OR records for a 4-week period within the last calendar year and determining the number of OR hours used by pediatric oncology patients. OR hours were categorized as major versus minor based on the length of time in surgery (ie, >1 hour vs ≤1 hour) and by the type of surgery (procedures involving extensive surgical resections, thoracotomies, the central nervous system, or cardiopulmonary region all were considered major). Total hours were annualized, and then multiplied by the cost of an average hour of OR time in the local country to provide an estimate of the annual OR budget attributable to children with cancer.[11] Costs associated with radiotherapy were captured in a similar manner.

For the cost of central administration, we again used data from El Salvador, which, by determining the cost of utilities and central administration and the pediatric cancer unit's share of inpatient admissions, were able to determine that such costs came to 11.8% of the total cost of the pediatric cancer unit. Such assumptions were necessary to include some estimate of administrative and indirect costs and thus avoid gross underestimates of total cost.

All costing parameters were summed to determine the overall annual cost associated with operating each pediatric oncology treatment center.

Cost-Effectiveness Analyses

We compared current treatment provided by the treatment centers with the alternative of no treatment at a childhood cancer center. Because specialized knowledge, equipment, and personnel are necessary to treat childhood cancer,[3] we therefore assumed that all children with cancer who did not reach a childhood cancer treatment center would die. Other groups have made this assumption when modeling childhood cancer survival.[12] Each site collected 1-year survival data for 2017, with the exception of KNH, in which a medical staff strike occurring in 2017 rendered those data unrepresentative, necessitating the use of 2016 data instead. Treatment refusal and abandonment are major issues in LMICs.[13-16] When feasible, efforts were undertaken by investigators to contact families who had abandoned therapy to ascertain outcome, but when such efforts were unsuccessful, patients were conservatively assumed to have died. The ratio of 5-year survival

to 1-year survival was assumed to be 0.62 based on data from Chennai, India, a lower-middle income setting.[17] Given uncertainty in applying the ratio to the African context, it was varied in sensitivity analyses.

The cost per life saved was converted into cost per DALYs averted using the life expectancy of each of the 4 countries, assuming a mean age at diagnosis of 6 years. Although data regarding the health status of childhood cancer survivors in Africa who are >5 years from diagnosis are lacking, impacts on life expectancy for those who have survived for 5 years most likely are substantially less pronounced than in HICs given the far lower treatment intensity used. However, we did consider a sensitivity analysis in which the number of additional years survived beyond 5 years after diagnosis was reduced by approximately 15%.[18,19] Similar to previous studies,[9,10] the mean treatment duration was assumed to be 1 year with no gain in usefulness noted during treatment. Future years of life saved were discounted at 3%, as recommended in the WHO CHOosing Interventions that are Cost-Effective (CHOICE) guidelines, with sensitivity analyses using rates of 0% and 6%.[20]

We used WHO thresholds for cost-effectiveness suggesting that interventions costing less than the per capita income per DALY averted were "very cost-effective," and those costing <3 times the per capita income per DALY averted were "cost-effective."[20] These thresholds are not universally accepted, with ratios of 0.5, 0.7, and 1.5, respectively, suggested and some authors arguing against such ratios altogether.[21-23] Regardless of specific thresholds, interventions that are below per capita income per DALY averted are likely higher priorities and more feasible from a budgetary standpoint than those that are <3 times the per capita income. Key parameters discussed in this section for each of the 4 countries are shown in Table 1.

Potential factors contributing to cost-effectiveness also were explored. Unit costs for commonly used chemotherapeutic agents were compared between centers. We also attempted to model the impact of treatment abandonment on cost-effectiveness by modeling a scenario in which no child abandoned therapy. In this particular analysis, the 5-year survival of children completing therapy was applied to the entire cohort. We then assumed that there would be additional treatment costs for those children who completed rather than abandoned treatment. The ratio of cost per DALY averted to the per capita income was recalculated under the assumption that the average cost of treatment incurred by children abandoning therapy was 10%, 20%, or 25% of the average cost of treating a child who completed therapy.

RESULTS

The annual operating costs of the pediatric oncology centers varied considerably between centers, from $229,000 in the smallest center (UCH in Nigeria) to just over $4 million (KNH in Kenya) (Table 2). Personnel constituted the largest cost item in 3 centers, accounting for between 39% and 57% of the total expenditures, and represented the second largest expense in the fourth center (KNH, 24%). Medication and administrative costs also represented major expenses across all centers (Table 2) (Fig. 1). OR-related costs were the second most expensive item in UCH. Hoteling costs accounted for approximately 15.6% of the total expenditures in KNH compared with between 1.3% and 5.7% in the other centers. Other components (eg, pathology, imaging, and blood services) individually accounted for <5% of the total cost across centers.

Costs per newly diagnosed patient varied substantially, ranging from $2338 in PH in Zimbabwe to >10 times higher in KNH ($31,344) (Table 3). The 1-year survival rate also varied, ranging from 12.5% in UCH to 43.0% in the BMC in Tanzania. Cost per DALY averted thus varied from $323 in BMC to $5783 in KNH. For BMC and PH, the ratio of cost per DALY averted to the per capita GNI was 0.3; both thus were considered to be "very cost-effective." The ratio for UCH was 1.4 (cost-effective) and that for KNH was 3.6 (just above the threshold for being considered "cost-effective"). The results of sensitivity analyses of varying parameters such as 5-year survival and discounting rates are shown in Supporting Table 2.

Table 4 compares unit costs of selected chemotherapies between the 4 centers. In some cases, the unit costs varied substantially. For example, the cost of 50 mg of 6-mercaptopurine (6MP) ranged from $0.35 in BMC to $1.98 in KNH and $5.47 in PH. The results of sensitivity analyses modeling the impact of eliminating treatment abandonment are shown in Supporting Table 3. Assuming that the current average cost associated with treating children who abandoned treatment is 25% of that associated with children who completed therapy, eliminating treatment abandonment would decrease the ratio of cost per DALY averted to the per capita GNI from 3.6 to 2.7 in KNH and from 1.4 to 0.9 in UCH.

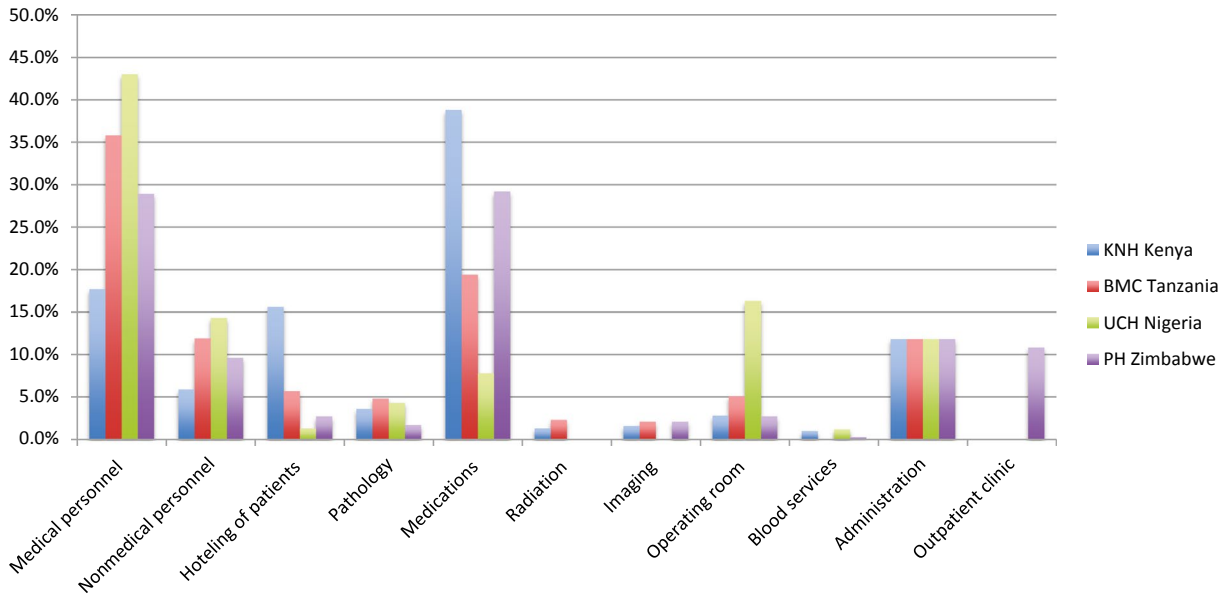

FIGURE 1. Percentage of expenditures attributable to various cost items compared between the participating centers. BMC indicates Bugando Medical Centre; KNH, Kenyatta National Hospital; PH, Parirenyatwa Hospital; UCH, University College Hospital.

DISCUSSION

A systematic review by Fung et al[6] identified 30 studies regarding the cost of childhood cancer treatment in LMICs, of which only 12 provided either the cost per DALY averted or data from which this could be calculated. The cost per DALY averted ranged from $100 to $4475 in the 4 studies of individual cancers in which the majority of the key cost components were included.[6] These costs per DALY averted were substantially under the per capita GNI and thus considered to be very cost-effective. It is likely that the cost-effectiveness of treating individual cancers varies, and that existing studies do not cover the full range of common childhood cancers. These findings underscored the need for additional rigorous cost-effectiveness analyses, particularly in relatively neglected areas such as sub-Saharan Africa.

In the current study, we found that the cost-effectiveness of the 4 participating childhood cancer treatment centers varied substantially, with ratios of cost per DALY to the per capita income of as low as 0.3 in BMC in Tanzania and PH in Zimbabwe. These ratios not only fall below the WHO CHOICE thresholds for "very cost-effective" but also more stringent definitions proposed by other health economists.[21-23] In contrast, the ratio of KNH in Kenya was 3.6, which is above the WHO CHOICE threshold for being "cost-effective." Identifying the causes of such variations across centers is key to optimizing both the effectiveness and efficiency of childhood cancer care across the continent.

Previous studies of both chemotherapeutics and nonchemotherapeutics have demonstrated substantial variations in drug prices.[24-26] Because medication costs accounted for substantial percentages of the total expenditures across centers, even small differences in unit prices may contribute to major differences in overall cost and thus cost-effectiveness. For example, the price of 6MP, an oral antimetabolite chemotherapeutic that is used for a prolonged period of years in the treatment of patients with acute lymphoblastic leukemia, was >6 times higher in Kenya than in Tanzania. Because recent modeling has demonstrated that because of its high usage, 6MP accounts for greater than one-half of global childhood cancer chemotherapy budgets,[27] such differences may have outsized impacts on treatment center budgets. It is interesting to note that although unit drug costs generally were highest in Zimbabwe, medications accounted for nearly 40% of the costs in KNH in Kenya, which is a substantially higher percentage than that of any other center. Comparative data of this nature help to isolate areas for targeted research and policy attention: in this case, evidence of inflated drug prices, potentially secondary to the inefficient procurement practices. The findings of the current study underscore the need for future work to delineate the determinants of cancer drug prices,

availability, and patient access for children with cancer in Africa and other LMIC settings.

Abandonment of treatment represents a major cause of treatment failure in LMICs, with rates of between 5% to 80% reported.[13-16] Participating centers also experienced high rates of treatment abandonment. Such cases represent a highly inefficient outlay of resources; costs associated with initial diagnosis, workup, and treatment prior to abandonment are "wasted," and patients and their families suffer the costs of treatment, both physical and financial, without reaping its potential benefits, including an improved quality of life and long-term survival. Abandonment is particularly prevalent in areas in which parents are required to pay for diagnosis and treatment out of pocket. Several authors have demonstrated that even when these costs are covered, interventions such as financial coverage for meals and accommodations and the funding of psychosocial personnel are associated with a reduction in rates of treatment abandonment.[13,28] Together, direct and indirect costs, the latter of which were not considered in the current study, result in unacceptably high rates of "financial toxicity" in both LMIC and HIC settings.[13,29,30] The sensitivity analyses in the current study suggested that the modest cost increases associated with these interventions could result in substantial improvements in cost-effectiveness, particularly in Kenya. Ultimately, the creation of universal health insurance schemes that include coverage of childhood cancer treatment is essential to improving both survival and cost-effectiveness. For example, Nigeria experienced notably high rates of treatment abandonment, most likely because of its reliance on out-of-pocket spending for essential aspects of diagnosis and treatment.

Several other potential contributors to the variations in cost-effectiveness merit mention. At KNH in Kenya, families are kept in the hospital throughout the treatment course because of inadequate outpatient clinic capacity and outpatient accommodations, as well as hospital billing policies. As a result, hoteling costs at KNH were found to be far higher than those at the other 3 centers. Economies of scale may place limits on the cost-effectiveness of UCH in Nigeria, which experienced approximately 25% of the number of new diagnoses as the other 3 centers. Differences in case mix also may have contributed; the costs of chemotherapy and supportive care are relatively higher for patients with leukemia and lymphoma, whereas the costs associated with surgery are higher for patients with solid tumors and central nervous system tumors, a finding that explains marked differences in the cost shares of these items in Nigeria compared with the other centers. Finally, efforts to deliberately control cost outlays also may be important. The BMC in Tanzania is supported by a foundation that supports costs for families that are not covered by the new national insurance program. This foundation strictly prioritizes the types of diagnostics and treatments that can be covered to ensure that financial resources reach as many children as possible and are as effective as possible.

Despite the comprehensiveness of the undertaken costing, several study limitations are worth noting in addition to those mentioned above. First, many annual expenditures were derived through the extrapolation of focal periods of data collection, which may not properly account for fluctuations in patterns of care. Second, indirect costs shouldered by caregivers were not considered, which can be significant in both HIC and LMIC settings, as shown by emerging evidence of "financial toxicity."[13,29,30] However, together, these are unlikely to change our conclusions, especially in centers with ratios of the cost per DALY averted to the per capita GNI that are far below 1. Third, as noted above, several assumptions were necessary, including the ratio of 5-year to 1-year survival and the ratio of medical to nonmedical personnel costs. Although the validity of these assumptions is unknown, sensitivity analyses of some of these assumptions did not change our overall results. Fourth, costing exercises in Zimbabwe face additional difficulties given the high inflation and a contracting economy, making comparisons using exchange rates less reliable. Fifth, although the 4 included centers represented different sub-Saharan African settings, the generalizability of the results of the current study to specific African countries is unknown. Sixth, we did not incorporate utility weighting, instead treating children as either alive or dead. Utility weights assign a value between 0 (death) and 1 (perfect health) to various disease states, and may be particularly relevant in childhood cancer survivorship.[31] Future cost-utility studies incorporating weighting are warranted. Finally, and more generally, interventions that are cost-effective are not necessarily affordable. Further studies identifying the most appropriate financing streams for childhood cancer treatment, whether through expansions of universal health insurance schemes, philanthropy, or a combination of both, are warranted.

The results of the current study have demonstrated that the treatment of childhood cancer can be very cost-effective in both low-income and lower middle–income countries within sub-Saharan Africa. The control of drug prices, enhancement of outpatient care capabilities including outpatient accommodations for caregivers

and patients, and interventions targeting the abandonment of treatment will not only improve clinical outcomes but cost-effectiveness as well. These results should inform both regional advocacy efforts and health policies prioritizing childhood cancer.

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CONFLICT OF INTEREST DISCLOSURES

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AUTHOR CONTRIBUTIONS

Jessie Githang'a, **Biobele Brown**, **Inam Chitsike**, **Kristin Schroeder**, **Avram E. Denburg**, **Sue E. Horton**, and **Sumit Gupta** all conceived of the study and contributed to study planning. All authors were involved in the conduct of the study, analyses, and interpretation of the results. **Sumit Gupta** wrote the first draft of the article; all authors contributed to the article and approved the final version. **Sumit Gupta** is the guarantor for the content of the article.

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