

EDUCATION OPEN ACCESS

Aliança AMARTE: A Collaborative Network to Improve Oncologic Pediatric Care in Brazil

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Received: 29 May 2025 | **Revised:** 31 July 2025 | **Accepted:** 3 August 2025

Keywords: hematology/oncology | pediatric hematology/oncology | pediatric oncology

ABSTRACT

Introduction: In Brazil, inequalities in access to treatment and survival of childhood cancer are observed across different geographic regions. In 2014, under the coordination of Hospital de Câncer Infantojuvenil de Barretos (Fundação Pio XII), six hospitals met weekly for case discussion. In 2019, the AMARTE (Apoio Maior Aumentando Recursos e Treinamentos Especializados) Alliance officially began with the aim to improve the quality of pediatric oncology care in Brazil and became a collaborative network of innovation, research, and learning with 31 member institutions in 2024.

Methods: AMARTE follows four strategic pillars: (1) equalize diagnostics, (2) homogenize treatment, (3) epidemiological and survival studies, and (4) scientific development and innovation. Fundação Pio XII and St. Jude Children's Research Hospital provide infrastructure and human resources. Implementation resources are supported mainly by the member institution. The first strategic goal was to maintain sustainable member engagement. A semestral assessment (SCORE) monitors the progress and engagement level, based on defined indicators.

Results: Three engagement reports have been published, with an increase in members' scores: 17 hospitals increased their SCORE, 7 decreased, and 1 hospital did not change. Key achievements include a common data registry, diagnostic and

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treatment protocols, regular technical-scientific meetings, and the formation of a fundraising group to achieve financial sustainability.

Conclusion: The first decade of the AMARTE Alliance highlights the relevance of collaboration in pediatric oncology. Challenges refer to the sustainable participation of specialists and heterogeneous governance structure across members, requiring flexibility in the implementation of shared initiatives. Outcome indicators are being developed to assess long-term impact.

1 | Introduction

Cancer in childhood and adolescence represents the leading cause of death from disease in this age group. Every year, 400,000 children and adolescents develop cancer worldwide, with many not even being diagnosed. While 80% of them live in low- and middle-income countries, only 20% of these children and adolescents survive. On the other hand, the majority of pediatric patients who have this diagnosis in high-income countries are cured (> 80%) [1]. In Brazil, inequalities in access to treatment and survival are also observed between different geographic regions [2]. Survival is higher in the Southeast and South regions, where most of the treatment centers are located [3].

In 2014, Hospital de Câncer Infantojuvenil de Barretos proposed the AMARTE Project (*Apoio Maior Aumentando Recursos e Treinamentos Especializados*—in English: Increasing Resources and Specialized Training). With the participation of six Brazilian pediatric oncology sites, the AMARTE Project aimed to increase diagnostic accuracy, to optimize therapeutic proposal, and to contribute to the training of junior physicians and from the multidisciplinary team. The project's weekly meetings were a platform for experience exchange and clinical cases discussion. These encounters shed light on the heterogeneity of available technical-scientific resources affecting childhood cancer care and contributing to disparities in Brazil.

As stakeholder integration within the AMARTE Project continued, it became clear that only a collaborative effort would reduce these inequities [4]. In 2019, building on an existing technical-scientific cooperation between Fundação Pio XII, Hospital de Câncer Infantojuvenil de Barretos, and St. Jude Children's Research Hospital (St. Jude), the three organizations launched the Aliança AMARTE (AMARTE), a collaborative network of innovation, research, and education to improve care for children with cancer by reducing inequities. This article describes AMARTE's governance structure, key initiatives in the past five years, and main implementation results.

2 | Methods

This section describes the four pillars that guide AMARTE's activities, its governance structure, membership process, and monitoring and evaluation mechanisms.

2.1 | Pillars

AMARTE Alliance's statute establishes four strategic pillars: (1) equalize diagnostics, (2) standardize treatment, (3) epidemi-

ological and survival studies, and (4) scientific development and innovation (Figure 1). All activities developed within the AMARTE Alliance must follow one or more pillars.

2.2 | AMARTE Governance

Figure 2 brings the organogram of the governance structure, regulated by AMARTE's statute: The steering and executive committees manage the governance and decision-making; sub-committees, working groups, and study groups are responsible for developing and implementing collaborative initiatives; and the operation center provides administrative support to all AMARTE bodies (Figure 2).

The steering committee is responsible for the governance, strategic planning, strategic decisions, approval of statutes, by-laws and overseeing of all the AMARTE initiatives. It is composed of two representatives (a pediatric oncologist and a hospital manager with decision-making authority) from each of the five member institutions. In 2019, the 13 AMARTE members reached a consensus and selected three institutions with the longest engagement in AMARTE to compose the first steering committee: Hospital de Câncer Infantojuvenil de Barretos, Hospital Erastinho, e Hospital da Criança de Brasília José de Alencar. The by-laws suggest that, in case of an increased number of institution entries, two new steering committee institution members should be included.

Potential members would be evaluated by the current steering committee based on:

- Length of participation in AMARTE,
- Case volume,
- Pediatric oncology unit existence years,
- Number of pediatric/hematology oncologists,
- Participation during the second AMARTE meeting,
- Participation in the executive committee coordination between 2020 and 2022.

In 2022, with the entry of 12 new institutions, and following the established criteria, Hospital Pequeno Príncipe and Grupo de Assistência à Criança com Câncer Vale do Paraíba were subsequently invited and joined the steering committee. The steering committee convenes weekly.

The executive committee is responsible for tactical decision-making and overseeing the progress of AMARTE initiatives. It

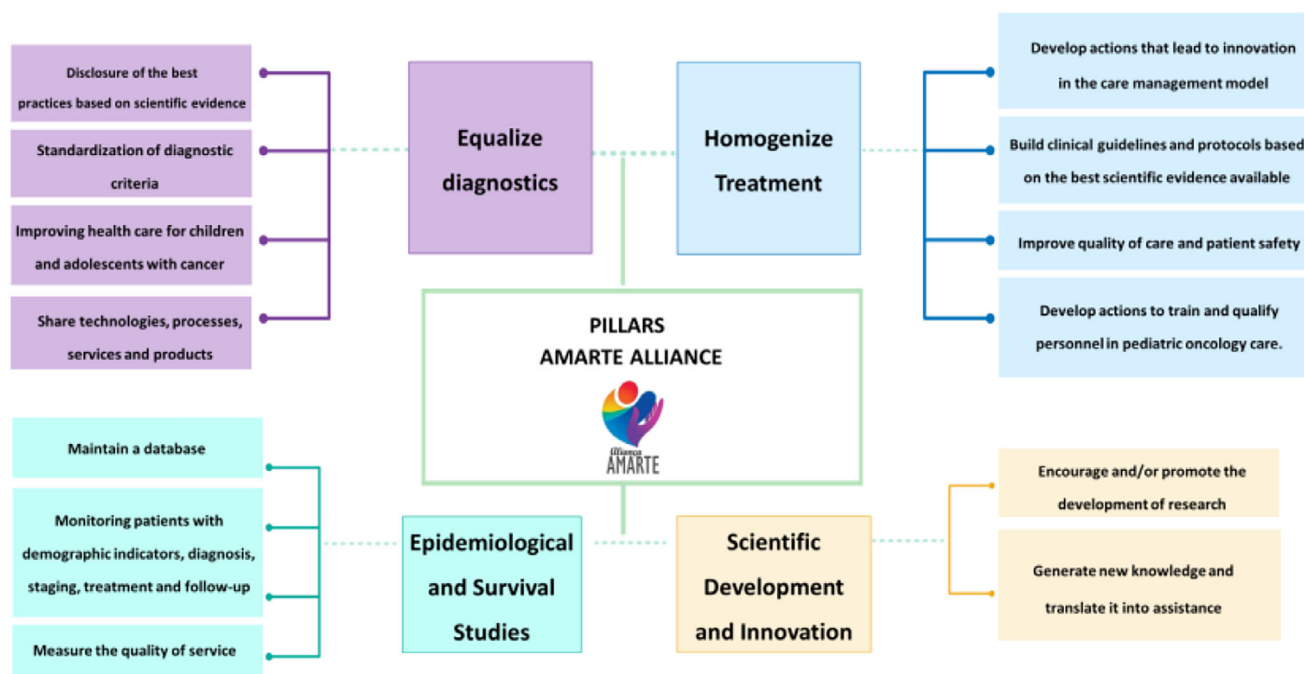


FIGURE 1 | AMARTE Alliance pillars.

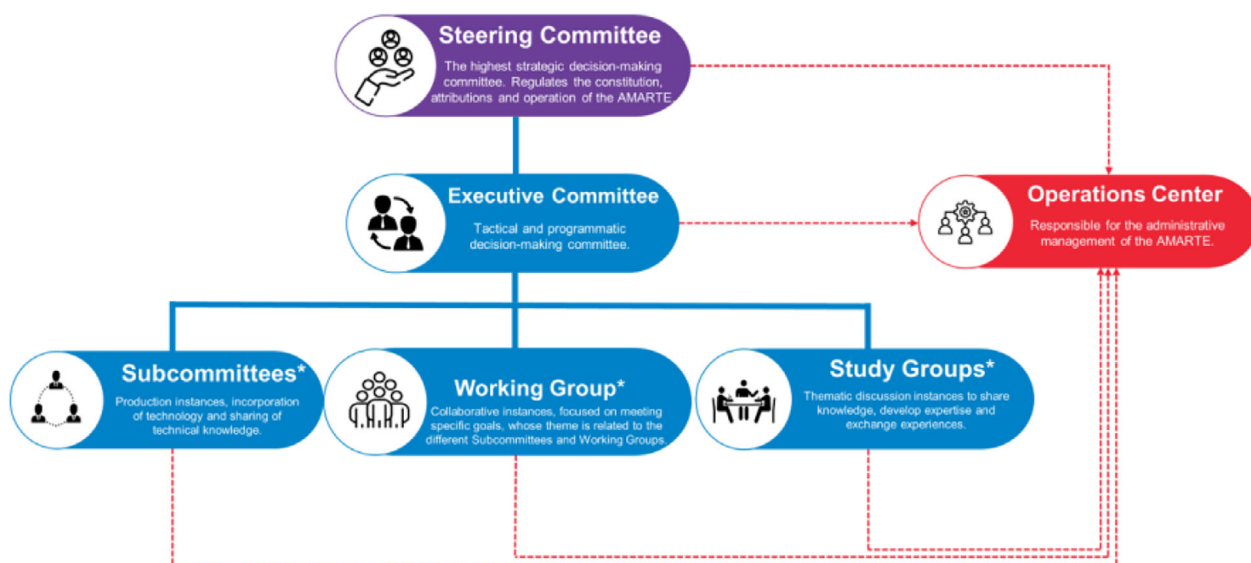


FIGURE 2 | AMARTE Alliance's governance structure.

***Subcommittees:** Cytology and flow cytometry, epidemiological data and registry, nursing, palliative care, pathology, radiology, and surgery.

Working Groups: Diagnostics, treatment, education, fundraising, infectious diseases and patients' rights.

Study Groups: Social work, psychology, pediatric, dentistry, nutrition, pharmacy, bioethics, occupational therapy, central nervous system tumors, education and training, infectious diseases, critical care, molecular biology, bone marrow transplantation, radiotherapy, physiotherapy.

is composed of two representatives from each member institution with voting rights. Representatives are indicated by the member institution delegates (appointed in the collaboration agreement) and should be a pediatric oncologist and a hospital manager.

The subcommittees offer a platform for specialists to exchange experiences, discuss clinical cases and literature review, produce

technical notes, and develop guidelines and protocols. A semestral activity report must be delivered to the governance bodies. Today, AMARTE has seven subcommittees: cytology and flow cytometry, epidemiological data and registry, nursing, palliative care, pathology, radiology, and surgery.

The working groups are project-based groups from member institutions working together to develop and implement a project

within AMARTE. These groups must be approved by the steering and executive committees and submit a semestral activity report. Currently, AMARTE has six active working groups: (1) diagnostics, (2) treatment, (3) education, (4) fundraising, (5) infectious diseases, and (6) patients' rights.

The study groups were created to generate and disseminate knowledge, facilitate experience exchange between partner institutions, and expand professional relationships. These groups flow more organically, with groups being created or closed based on the specialists' demand. Study groups do not require a defined project, mandatory participation from representatives, or activity reports. These groups usually use the AMARTE structure for case discussions and needs assessment. If the members from the study group mobilize and propose a project, they can also request to transform it into a working group.

Finally, the operations center provides administrative support that includes managing meeting schedules, minutes, maintaining records, project coordination and monitoring, and accountability of AMARTE's budget. It also oversees the onboarding process, keeps track of the semestral activity reports delivered by the subcommittees and working groups, and coordinates the semestral member engagement score. The operations' center staff and equipment are hosted at Hospital de Câncer Infantojuvenil de Barretos, and financially supported by Fundação Pio XII and St. Jude. The operational budget includes staff and in-kind administrative support, office space, and supplies. Project implementation resources in each site are supported by the member institution. Moreover, all professionals who participate in AMARTE activities do so additionally with their routine work, aiming to improve the care provided.

2.3 | Member Institutions

The preliminary selection of participant institutions in 2019 took into consideration previous participation in the AMARTE Project, and academic relationships established with Hospital de Câncer Infantojuvenil de Barretos and the geographical dispersion of the member institutions. Thirteen hospitals were invited to and accepted to join the AMARTE Alliance, which has expanded since (Figure 3). As of April 2024, there are 31 AMARTE members. In Brazil, there are 78 hospitals certified by the Ministry of Health to treat childhood cancer [5]. AMARTE members are distributed across the five regions: 33% of total hospitals in the North (1 out of 3 certified hospitals); 60% of total hospitals in the Northeast (9 out of 15 hospitals); 40% in the West Center (2 out of 5 hospitals); 25% of total hospitals in the Southeast (9 out of 36 hospitals); and 37% of total hospitals in the South (7 out of 19 hospitals). Three members are processing their certification and were not included in this distribution.

With the increased interest from hospitals around the country to participate in AMARTE initiatives, a stepwise membership process was formally defined in 2023:

1. First, the institution must submit a letter of interest to the Operations Center. Hospitals must be certified by the Ministry of Health to provide pediatric oncologic care and be in good order with applicable legal and tax matters.

2. A meeting to present AMARTE is scheduled with the hospital management, multidisciplinary team, and clinical staff.
3. The institution shares the required documents for the preparation of the cooperation agreement. At this point, the institution is also invited to join the St. Jude Global Alliance [6].
4. After approval from all parties, the institution signs a cooperation agreement with Fundação Pio XII and Hospital de Câncer Infantojuvenil de Barretos, in which they reinforce the commitment to AMARTE's shared goal and formally appoint two delegates to serve as points of contact at the member institution.

Interested institutions may submit their application at any time, and the signature process happens twice a year: February and September.

2.4 | Monitoring and Evaluation

Twice a year, the steering and executive committees assess (1) the progress of each group, using a standardized activity report, and (2) the engagement level of each member institution with the AMARTE Alliance initiative, measured by an engagement score.

Subcommittees and working groups submit semestral activity reports for evaluation of the steering and executive committees. The reports collect information on institution participation, meetings and agenda, barriers and facilitators to the group's activities, and status of projects and indicators. These groups are invited at least once a year to present their status during one of the executive committee meetings. In this article, data about the barriers and facilitators for AMARTE implementation were collected from the three reports issued between September 2022 and February 2024.

The engagement score (SCORE) aims to measure the adherence level to AMARTE by each member institution, to celebrate the institutions with high engagement, and to identify strategies to support low adherence levels. The operations center coordinates the SCORE composed of seven variables, which were consolidated by the steering committee based on AMARTE's statute and priority projects (Table 1). Measures have different values, with those related to priority projects being doubled. As per Table 1, measures related to participation in meetings and appointment to the specialists' subcommittees equal 10 points each (five subcommittees regularly met and had their participation tracked). Being the priority project, measures related to the AMARTE Registry project are worth 20 points each. Finally, participation in AMARTE Workshops is worth 6 points. The engagement score is calculated twice a year, in February and September. In this article, data for the AMARTE SCORE come from the 25 member institutions that began the 2022–2024 biennium. Three reports have been issued, respectively, in February 2023, August 2023, and February 2024. While there is no minimum SCORE required, members are encouraged to improve their results from one semester to the next. In this manuscript, we use the software JAMOVI Cloud [7] to run a mixed-design ANOVA test in the three SCORE reports.

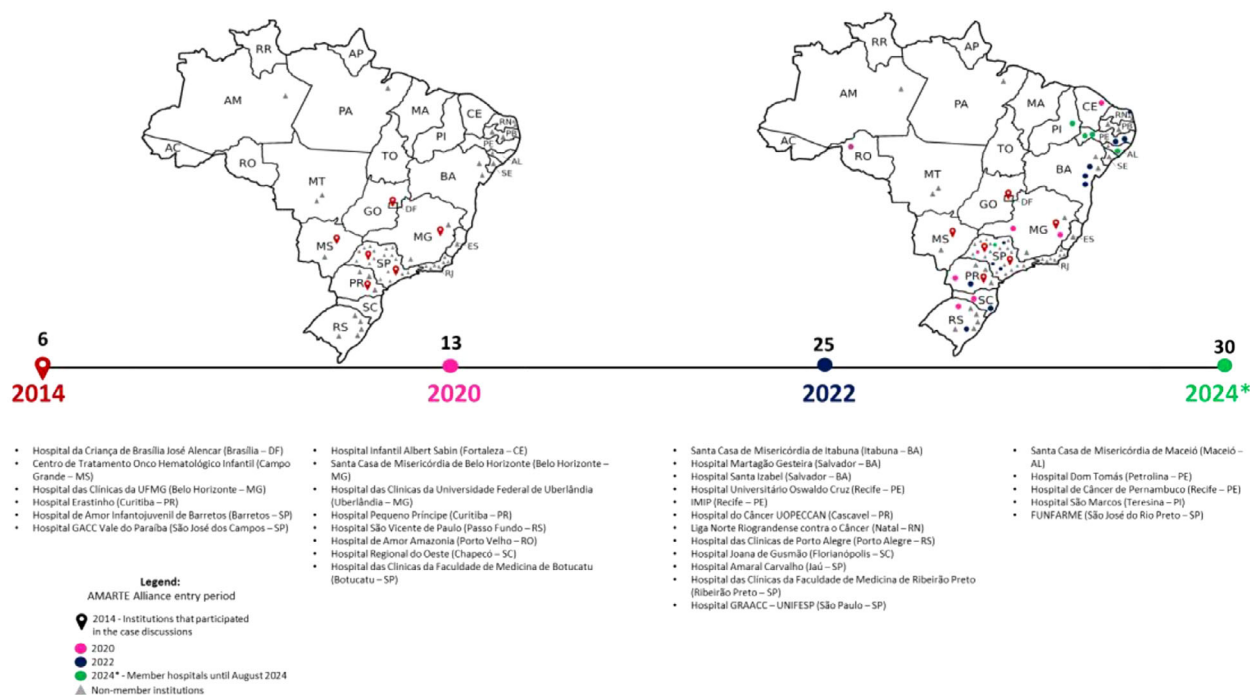


FIGURE 3 | AMARTE expansion: 2014–2024.

2.5 | Strategic Planning and Project Prioritization

In 2021, the first 13 AMARTE institutions applied the Abbreviated ProFILE (St. Jude Pediatric Oncology Facility Integrated Local Evaluation Tool), a tool for evaluation of health-system delivery and resources [8]. ProFILE helps teams define an improvement strategy to increase childhood cancer survival by offering a guided institutional self-assessment. The Abbreviated ProFILE was translated into Portuguese for individual member assessment and report.

In May 2021, over 140 representatives from the 13 members gathered for a virtual three-day workshop. The workshop aimed to share the AMARTE ProFILE aggregated results, prioritize collective initiatives for five multidisciplinary working groups (diagnostics, treatment, advocacy and fundraising, palliative care, epidemiological data) and develop an action plan by August 2022. During the exercises, each group prioritized one recommendation, analyzed its impact, causes, and resources required.

In September 2022, the II AMARTE–St. Jude Global Meeting took place in Barretos, Brazil, and via Zoom. The workshop welcomed new members, analyzed the results of the first biennium (2021–2022), and planned the goals for 2023–2024. Attended by over 180 people (in person and virtual), the seven groups (advocacy and fundraising, surgery, social rights, nursing, epidemiological data, surgery and pathology) established their goals through design thinking activities.

The AMARTE strategic plan is reviewed biannually. During the period, each subcommittee, working group and study group may identify a shared need in the network and propose a new project aligned with AMARTE pillars. The project must be presented to the steering committee for feedback and approval.

3 | Results

In this session, we describe the activities developed in AMARTE in each pillar.

3.1 | Pillar 1: Equal Diagnostics Deliverables

3.1.1 | Standardization of Pathology Records

The Diagnostics Working Group developed six models for pathology report—brain tumors, kidney tumors, bone tumors, sarcomas, lymphomas, and neuroblastomas—which are being reviewed by specialists from AMARTE centers.

3.1.2 | AMARTE Diagnostic Guidelines

3.1.2.1 | Surgery. The Surgery Subcommittee agreed on a list of topics to develop pocket guidelines to share knowledge and standardize care. So far, nine pocket guidelines were developed and discussed among surgeon members. The group is currently working on a standardized surgical report.

3.1.2.2 | Flow Cytometry. During the meetings of the hematopathology and flow cytometry subcommittee, significant variability was identified in the analysis and administration of intrathecal chemotherapy between Brazilian centers. This disparity impacts diagnostic accuracy and proposed therapeutic strategies. Based on consolidated references, a comprehensive guide was developed for cerebral spinal fluid (CSF) collection, chemotherapy infusion, cytological laboratory analysis, and immunophenotyping by flow cytometry.

TABLE 1 | AMARTE Alliance engagement SCORE indicators.

Name	Operational description	Nominator	Denominator	Data source
Executive committee attendance	Percentage of executive committee meetings with participation of ≥ 1 hospital representative	Number of meetings attended by the hospital during the semester	Number of executive committee meetings in the semester	Registration lists for each meeting via Zoom platform
Appointed representatives in subcommittees	Percentage of subcommittees with a hospital-appointed representative	Number of subcommittees with at least one appointed representative	Total number of subcommittees	Database of the operation center of AMARTE and Coordinators of each subcommittee
Subcommittees participation	For each subcommittee, participation percentage of at least one appointed representative of the hospital in the subcommittees meetings	Number of meetings attended by the hospital during the semester	Number of subcommittee meetings in the semester	Registration lists for each meeting via Zoom meetings platform
AMARTE workshops attendance ^a	Participation of professionals in thematic workshops in person or virtually	Attendance of the professional appointed by the hospital at the workshop	Number of professionals invited to participate in workshops	Database of the operation center of AMARTE
Registered cases on REDCap	Percentage of registered cases in the AMARTE Registry compared with the total number of patients received of each hospital	Number of cases the hospital registered during the semester	Number of cases the hospital received during the semester	Database (REDCap) of the registry and epidemiological data subcommittee
Data manager training completion	Measures if the data manager appointed by the institution has completed the three mandatory courses about REDCap and REGISTRY	Sum of courses completed by the data managers	Number of Data Managers appointed by the institution multiplied by 3 (total number of mandatory courses)	Database of the registry and epidemiological data (REDCap) subcommittee coordination
Medical monitor training completion	Measures if the medical monitor appointed by the institution has completed the three mandatory courses about REDCap and REGISTRY	Sum of courses completed by the medical monitors	Number of Medical Monitors appointed by the institution multiplied by 3 (total number of mandatory courses)	Database of the registry and epidemiological data (REDCap) subcommittee coordination

^aNot included in last score as no workshop took place in the evaluated period.

3.2 | Pillar 2: Standard Treatment Deliverables

3.2.1 | Improving Children's Onco-hematology Nursing (ICON) Project

Over ten months, the research team from St. Jude Global Nursing and AMARTE's Nursing Subcommittee explored nursing regulations in Brazil, nursing literature reviews, situational analysis of pediatric hematology/oncology nursing practice, and reviewed institutional policies within 26 AMARTE members. Together, the team identified 25 gaps for improvement and created an action plan with eight (8) goals:

1. Create and implement a policy on cleaning toys for infection prevention;
2. Create and implement pain (re)assessment policy for pediatric oncology;
3. Create a policy on end-of-life care assessment for pediatric oncology;
4. Create a tool for initial inpatient nursing (re)assessment on pediatric oncology;
5. Create and implement a policy on peripheral vascular access devices;

6. Create and implement a policy on the safe administration of chemotherapy and manage the availability of personal protection equipment in Brazil;
7. Develop and test a patient classification tool applicable to pediatric oncology-hematology patients;
8. Train pediatric oncology-hematology nurses on courses/programs.

Currently, the nursing subcommittee is developing an implementation plan for the six nursing guidelines developed for Goals 1–6, adapting a classification system for pediatric oncology patients, and disseminating an educational program that includes courses focused on pediatric oncology nursing.

3.2.2 | Palliative Care Family Guide

The palliative care subcommittee developed a guide to increase awareness regarding palliative care for newly diagnosed patients and their families. After validation by the AMARTE Steering Committee, the AMARTE members requested legal authorization locally to begin distributing the letter. The subcommittee is monitoring adherence.

3.2.3 | AMARTE Treatment Guidelines

3.2.3.1 | Tumor Lysis Syndrome (TLS) Guide. The creation of a treatment guide for TLS involved a multidisciplinary team that, based on a literature and practice review, developed a tool applicable in different institutions in Brazil.

3.2.3.2 | Febrile Neutropenia Guideline. A fever and neutropenia national guideline was a priority selected by 50 participants from 15 Brazilian hospitals during the I St. Jude Global–Brazil Workshop, held in Recife in 2019. A volunteer working group composed of pediatric oncologists, infectious disease specialists, nurses, and pharmacists reviewed guides and international literature to create a guideline that could be incorporated and adapted to the reality of each unit. Experts from St. Jude and the AMARTE Infectious Diseases Study Group reviewed the guide.

3.3 | Pillar 3: Epidemiological and Survival Studies Deliverables

3.3.1 | Implementation of a Pediatric Cancer Registry (AMARTE Registry)

Thirteen institutions started to insert data in the AMARTE Registry in June 2022, and new members joined in May 2024. The registry counts 2,386 eligible new cases. Following the requirements of the Brazilian Data Protection Law (LGPD), the legal department of Hospital de Câncer de Barretos developed a free and informed consent form for data collection and storage. Barretos also supports the REDCap [9] database that contains the AMARTE Registry. In total, 46 data managers and 28 medical monitors have completed the two required training courses (REDCap usage and Registry variables). Preliminary

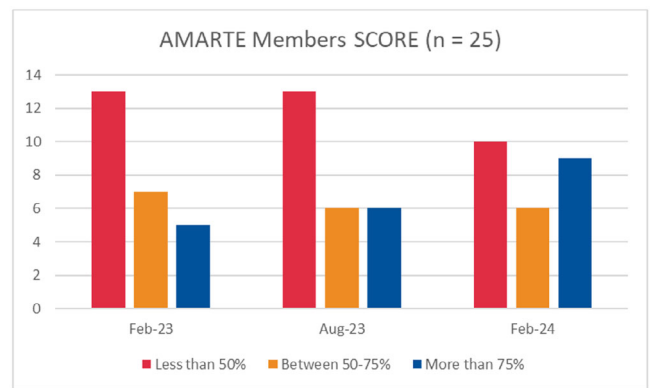


FIGURE 4 | Comparative SCORE results (February 2023 × August 2023 × February 2024).

results of the eligible cases registered and monitoring indicators have been presented in different meetings and conferences [8, 10]. As the alliance evolves, the AMARTE Registry will be an important tool to monitor patient-level outcomes and provide a comprehensive picture of AMARTE's contribution to improving pediatric oncology care.

3.4 | Pillar 4: Scientific Development and Innovation Deliverables

Collaborative Fundraising Task Force. Thirteen institutions collaboratively participated in the 2022 Giving Tuesday movement, promoting experience exchange and encouraging members to join a global campaign, three for the first time. Actions aimed to promote a donation culture (69%), to raise funds (54%) and to increase public engagement with the foundation or hospital on social media (30%). Most (54%) institutions established a goal. The campaigns lasted on average 19 days (range, 1–72 days) and raised on average USD 3,260 in funds. Donations in kind include food, clothing, hygiene, and cleaning products. Institutions highlighted the experience exchange and collaboration as the most positive outcomes from the exercise.

3.4.1 | Academic Dissemination

The collaborative work developed in AMARTE has been shared in four conferences and eight abstracts [10, 11].

3.5 | AMARTE SCORE

Between the first and third reports, there was a 10% increase in members' average, and those with a score higher than 75% almost doubled (Figure 4). Seventeen hospitals increased their SCORE, seven decreased, and one kept the same SCORE.

Two variables (participation in the executive committee meetings and subcommittees) saw a decrease in the average points between both scores (Table 2). Comparing results over time and by hospital type (academic hospitals, general hospitals, oncology hospitals, and pediatric cancer hospitals), SCORE results remained fairly

TABLE 2 | AMARTE SCORE's aggregated results per indicator.

Indicator	Max points	Average			Median		
		Feb-23	Aug-23	Feb-24	Feb-23	Aug-23	Feb-24
Participation in executive committee meetings	10	9.5	7.0	6.5	10	10	8
Participation in AMARTE workshops	6	4.6	5.0	N/A ^a	5	6	N/A ^a
Specialists appointed to Subcommittees	10	7.0	9.8	10.0	8	10	10
Participation in subcommittee meetings	50	29.8	28.4	24.6	28	28	24
Percentage of registered cases in 2023	20	7.2	12.2	11.2	0	16	16
Data manager completed trainings	20	11.0	12.6	14.2	20	20	20
Medical monitor completed trainings	20	5.1	6.9	9.9	0	0	16

^aThere were no workshops during the report period, so the variable was not included.

stable, did not differ significantly by hospital type, and did not show different trends over time across hospital types.

4 | Discussion

From weekly case discussions, the AMARTE Alliance evolved into a collaborative network connecting hospitals from all regions in Brazil, whose main impact was the transition to an innovative paradigm transcending institutional actions. In Latin America, collaboration in childhood cancer has a long story, especially for clinical trials and standardizing protocols.⁴ AMARTE adds to the regional experience by offering a model for integrating the multidisciplinary team and for allowing specialists to propose, develop, and implement projects to improve care. Emphasis is placed on building collective approaches that simultaneously benefit several hospitals. Supported by AMARTE's structure, subcommittees and working groups transform these collective aspirations into practical reality, applying cooperative principles in decision-making and creating a forum for exchanging experiences.

For example, the growing participation in the Fundraising Working Group allowed for the collective construction of the group's mission and vision. Participants with a proactive and leadership profile played crucial roles in achieving the proposed goals, contributing significantly to the results achieved. Similarly, the nursing subcommittee has stood out in the development of protocols adapted to the diverse reality of members and promoting best evidence-based practices through the ICON project. Finally, the epidemiological data and registry subcommittee saw an improvement in the interaction between data managers and medical monitors during meetings, reflecting positively on the quality of data collected. The presentation at international conferences evidences the recognition of ongoing efforts and disseminates the results. These data will allow us to measure AMARTE's impact at the patient level in the future, while projects' specific outcome and process indicators will demonstrate the impact in additional outcomes.

Challenges relate to sustainable engagement and participation in AMARTE's recurring meetings, resulting from work over-

load and employee turnover. Professionals face challenging care conditions, working with small teams and with a high volume of assignments. Some hospitals work with third-party specialists who may be employed by other organizations or are not exclusive to childhood cancer, leaving them with limited time to participate in AMARTE activities. In order to support these hospitals, AMARTE encourages hospitals to engage all the multidisciplinary team and share the activities across multiple collaborators. The steering committee also has an important role in advocating with hospitals' administration to incorporate AMARTE in their routine and prioritize projects to participate.

A second challenge is the corporate governance diversity of the AMARTE members, which includes academic hospitals, general hospitals, oncology hospitals, and pediatric cancer hospitals. This heterogeneity has contributed to the stagnation of some institutions that, despite being engaged, face difficulties in adhering to AMARTE processes or projects.

Given this scenario, the challenge lies in maintaining efforts to build collective solutions that consider the needs of AMARTE members. The steering committee and the executive committee host feedback sessions (general and individual) to hear back from the member institutions and identify areas of opportunity for AMARTE to help with their challenges, especially for those institutions with a low SCORE. Upon request, site visits have been scheduled to better understand the challenges, increase awareness about AMARTE with the multidisciplinary team and hospital administration, and help the member to develop an engagement plan. This joint effort is essential to consolidate a truly cooperative approach and continue AMARTE's positive impact.

5 | Conclusion

The first 10 years of AMARTE reveal the need for pediatric oncology services in Brazil to establish collaboration for the technical, scientific, and managerial development of their teams in order to meet the demands of their audience. The 30 centers that currently make up AMARTE are eager to participate in this forum. Among the intangible benefits, the formation of a new

culture, based on collaboration between institutions, is highly significant for the intended advancements. As for the initial concrete outcomes, the following stand out: the establishment of a common data registry, essential for decision-making; the development of diagnostic protocols; the development of treatment protocols; systematic technical-scientific meetings among peers in specialist subcommittees; and the establishment of a fundraising group, which is undergoing training and development aimed at achieving financial sustainability for the institutions involved. Technical products developed by AMARTE are available to all members, and the network structure facilitates the development of collaborative projects that improve childhood cancer care across the country.

Acknowledgments

The authors would like to thank all professionals who participate in AMARTE Alliance for their engagement, dedication, and for believing in the impact of working together.

The Article Processing Charge for the publication of this research was funded by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brasil (CAPES) (ROR identifier: 00x0ma614).

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data are from the AMARTE Alliance (there is no patient information in the manuscript).

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