



# The Care of Childhood Cancer Survivors in India: Challenges and Solutions

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Ind J Med Paediatr Oncol 2024;45:167–172.

## Abstract

**Purpose** We describe the challenges faced and lessons learnt over three decades of a childhood cancer survivorship program in India.

**Methods** We provide a descriptive analysis of the challenges and barriers faced in running this program, our strategies in management, and detail the stages of development of holistic support system.

**Results** The profile of late effects in our cohort of survivors is notable for the high prevalence of psychosocial issues and metabolic syndrome. Major difficulties faced were transitioning of patients to survivorship care and attrition to follow-up, which were overcome to an extent by ensuring constant communication/rapport-building, updated databases, and peer support groups. Collaborations with nonprofit organizations and other donors have enabled financial, psychosocial, educational, and vocational rehabilitation.

**Conclusions** It is feasible to establish and sustain a survivorship program in a large-volume center in low- and medium-income country. Understanding the unique spectrum of late effects and establishing a holistic support system go a long way in ensuring the long-term physical and mental health and psychosocial concerns of childhood cancer survivors. Decentralization, development of a strong national networks, capacity building, and incorporation of sustainable technology should be priorities in survivorship care.

## Keywords

- ▶ childhood cancer survivors
- ▶ low- and middle-income countries
- ▶ survivorship care

## Key Points

In this manuscript, we describe the lessons learnt over three decades of a late effects program in India. We also describe our strategies of transitioning to survivorship care and tackling attrition to follow-up. We have found that constant communication/rapport-building, updated databases, and

peer support groups have helped tackle the problems of attrition. Collaborations with nonprofit organizations and other donors have enabled financial, psychosocial, educational, and vocational rehabilitation. It is feasible to establish and sustain a survivorship program in low- and medium-income countries (LMICs). Understanding the unique

article published online  
April 17, 2023

DOI <https://doi.org/10.1055/s-0043-1761262>  
ISSN 0971-5851.

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Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

spectrum of late effects and holistic support goes a long way in ensuring the long-term physical and mental health and psychosocial concerns of childhood cancer.

## Introduction

Survivors of childhood cancer are at risk of developing long-term health conditions; the prevalence increases with time and aging, necessitating lifelong care.<sup>1-3</sup> However, survivorship care has been a relatively underserved area in India, and the increasing interest in survivorship care in India over the past few years has been limited to the larger centers.<sup>4</sup>

As the oldest and largest survivorship clinic in India, the After Completion of Treatment (ACT Clinic at Tata Memorial Hospital, Mumbai) has successfully established and expanded a late effects program within a high-volume pediatric oncology unit.<sup>5-7</sup> All survivors are seen by pediatric oncologist and psychologist, and selected survivors are assessed by radiation oncologists, surgical oncologists, dietician and social worker, cardio-oncology, and endocrinology clinics, as required.<sup>8,9</sup> The ACT Clinic coordinates the care of over 3,600 long-term survivors of childhood cancer from all regions across India. The ACT Clinic has been instrumental in mentoring several Indian centers in starting late effects services, and we feel that the lessons learnt over the last three decades would be of use to all those interested in establishing their own survivorship program. The ACT Clinic can be a successful model that can be replicated in similar settings. The stages of development of the ACT Clinic as well as the burden of late effects in childhood cancer survivors (CCS) registered at our clinic have been published during the initial years as well as recently.<sup>5-7</sup> We describe below some of challenges that we faced, feasible solutions, and lessons learnt by us during the past three decades.

### The Need to Recognize the Unique Spectrum of Late Effects in India

An increasing body of literature suggests that survivors of childhood cancer are more likely than their siblings to develop long-term effects of cancer, with the disparity becoming more evident with increasing age.<sup>1-3</sup> In one of the largest cohorts of adult survivors of CCS, the most prevalent clinically ascertained adverse outcomes were pulmonary (65.2%), auditory (62.1%), endocrine or reproductive (62.0%), cardiac (56.4%), and neurocognitive (48%).<sup>3</sup>

The prevalence and spectrum of late effects in our cohort have been published.<sup>5-7</sup> The high prevalence of transfusion-transmitted viral infections and metabolic syndrome or its components have been noted from several centers in India.<sup>4,7-10</sup> Psychosocial issues (including scholastic issues and school dropouts) are multifactorial and need holistic and consistent assessment and interventions.<sup>7,11</sup> Survivors of certain cancers—retinoblastoma, brain tumor, and nasopharyngeal carcinoma—who had the highest cumulative incidence of chronic and disabling late effects need special attention and multidisciplinary monitoring and rehabilitation.<sup>7</sup> However, a national survey to assess delivery of services to CCS found poor

availability of extended service providers such as endocrinologists and psychologists.<sup>12</sup>

### Transitioning from Acute Care to Survivorship Care: Catch them Early, and Catch them Young

One of the major challenges that we have faced is to streamline and increase recruitment to the ACT Clinic in our high-volume center. Children who complete treatment are followed up in the routine outpatient department until they are eligible to enroll in the ACT Clinic, that is, 5 years from start of treatment and 2 years from completion of treatment. Care of the survivors is then continued in the ACT Clinic. Of eligible survivors who initiated anticancer treatment between 2010 to 2012 and 2013 to 2016, only 65 and 53% (respectively) have transitioned to long-term care. Large numbers (600–1000 patients completing treatment/year) of patients and limited days of ACT Clinic functioning (2 days/week) necessitate additional stay for patient contribute to this discrepancy.

Another concerning finding was that at entry to the survivorship care, several children have scholastic and health issues (including overweight in 10% of child/adolescent survivors) unaddressed during routine outpatient visits, or have not been reimmunized as advised.<sup>8,9</sup> Additionally, certain “late” effects, such as endocrinopathies in survivors of brain tumors, may start during or soon after treatment, which necessitates special care.<sup>13</sup>

To avoid missing on such crucial, preventable, and actionable issues, we have started the “Early Reintegration Program,” which focuses on the transitional period between completion of treatment and survivorship care. Children are screened by a team of nurse, dietician and psychologist for growth, scholastic and adjustment issues, and advised regarding healthy lifestyle, the need for disciplined follow-up and reimmunization. This screening is done on the same day as scheduled outpatient clinic visit. Children with concerns picked up on screening receive detailed evaluation and intervention by specialists.

The C2S study, under the aegis of Indian Pediatric Oncology Group (InPHOG), a multicenter registry of children completing cancer treatment—which attempts to streamline the process of transition to survivorship care—is a welcome step in this direction.<sup>14</sup>

### Tackling the Problem of Attrition to Follow-Up, Especially in Adult and High-Risk Survivors

Attrition to follow-up with passing time continues to be a major cause for concern at our clinic. Of 3,067 survivors, 720 (22.5%) have not returned for follow-up at the ACT Clinic for 5 years or more.<sup>7</sup> Expectedly, a far higher proportion of survivors (60% of survivors treated prior to 2000) from the earlier decades are lost to follow-up. Analysis of our cohort also showed that 36% of survivors treated prior 2000 had a late effect requiring intervention (grade 2 and higher) compared with 16.2% treated after 2000.<sup>7</sup> This phenomenon has been noted world-over.<sup>2,15</sup> A recent audit at our clinic found that the major causes for attrition to follow-up include gaps in awareness, financial toxicity, and “social stigma,” similar

to results of a nationwide survey.<sup>12,16</sup> At registration into the ACT Clinic, the gender ratio of 2.5:1 (male preponderant), while skewed, was similar to that at initial cancer diagnosis at our center. However, several female survivors discontinued clinic visits into adulthood and marriage. Societal pressures, often gendered, significantly influence health-seeking behaviors across the cancer continuum in India, and are challenging to overcome.<sup>17</sup>

Our approach to tackling this has been multipronged:

- a) Repeated reinforcement by the pediatric oncologists and psychologists in ACT Clinic at each visit regarding long-term follow-up. There is emphasis on “high-risk” survivors, specifically older survivors, those with pre-existing health concerns and those with treatment exposure likely to necessitate longer and more intensive health monitoring
- b) Proactive follow-up: Our clinic policy has been to send out postal letters once every 5 years to the last known postal address of survivors. This is often an exercise in futility due to outdated and incomplete postal addresses for the older patients. Recently, we have started flagging delayed follow-ups in our database and contacting them over telephone and email. Despite the effort involved, even a single response is gratifying in 2020, we contacted 480 and received 45 responses; the median age of these survivors was 28 years with a median lost-to follow-up duration of 8 years.
- c) Updated contact information: At each follow-up visit, the contact information (at least 2 telephone numbers, email and postal address) of all survivors are updated in the ACT Clinic Database. Survivors are provided the corresponding contact information of ACT Clinic at each follow-up and actively encouraged to keep in touch by email, telephone or WhatsApp.
- d) Establishment of a holistic support model (described below).

Attrition to follow-up has definitely decreased over the last two decades, with only 2% of survivors diagnosed after 2010 being lost-to follow-up, and will hopefully become negligible in the future.

### The Importance of Holistic Support

Financial hardship in long-term survivors of childhood cancer is being increasingly recognized, especially in those with chronic late effects.<sup>18,19</sup> State schemes may cover a substantial part of treatment in children with cancer, but survivors of childhood cancer (CCSs) in countries like India which lack established universal healthcare coverage may incur significant out-of-pocket expenditures. While travel and basic investigations are heavily subsidized and supported by our public funded hospital, survivors need funding for costs of medical treatment, food, lodging, etc. Certain late effects of treatment incur heavy expenditure—the average annual cost of growth hormone treatment is INR 300,000 (USD 4000) and antiviral treatment is INR 30,000 (USD 400) at our center; the per capita income in India is USD 6600 in terms of purchasing power parity, but only close to USD 2200 in actual terms.<sup>20</sup>

The expense precluded growth hormone treatment in most patients prior to 2015 since treatment funding is generally available only to patients on active anticancer treatment. Long hospital visits may lead to loss of daily wages for adult survivors and parents of child survivors. Until recently, medical insurance was not available to survivors of cancer in India.

Since 2016, the pediatric foundation—ImPaCCT foundation—at our hospital has been receiving funding specifically for survivors of childhood cancer.<sup>21</sup> From 2016 to 2020, these survivorship funds (totaling INR 56.6 million; USD 6,80,000) have enabled us to support the cost of late effects surveillance and treatment in 450 survivors—including growth hormone supplementation in 100 survivors, second malignancy management in 20 survivors, antivirals therapy in 38 survivors, and other hormonal treatments/ assisted reproduction. The inclusion of in-house cardio-oncology, endocrinology, and hepatitis clinics also helped co-ordinate the management of medical costs and reduce costs, including out-of-pocket expenditure. Funding for education of survivors and patients on maintenance treatment via pediatric foundation, nonprofit organizations and individual donors has immensely benefited our survivors.<sup>4</sup> Multiple nonprofit organizations partner with us to provide medical and vocational rehabilitation. The addition of foundation-employed dietician, nurse, and data manager to our team has led to improved quality of services and streamlined functioning. The evolution of the multidisciplinary, holistic support offered by the ACT Clinic has been described elsewhere.<sup>7</sup>

The holistic care available at our clinic (detailed in ref. <sup>7</sup>), predominantly financial assistance and educational/vocational guidance, has possibly played a part in improved follow-up.

### Barriers to Communication and the Need for Rapport Building

The sociocultural barriers to effective education and communication with survivors and families tend to be multiple and complex in India.<sup>22</sup> Overprotective families, lack of autonomy for adolescent and young adult survivors, societal pressures, and taboos surrounding issues such as fertility and sexual health often preclude discussion and effective communication with survivors and families.<sup>23</sup> Thus, awareness and sensitization regarding potential late toxicities are often lacking, and we often need to “start from scratch” when survivors are independent and autonomous adults.

Establishing a strong relationship with constant communication, especially in adolescent/ young adult and aging survivors, is crucial.<sup>24</sup> Patient education should start with newly diagnosed patients with cancer and extend through survivorship, modified to suit individual understanding and adjusted for mental health and cultural preferences. All survivors are seen by either of the two pediatric oncologists at the ACT Clinic, and all older adult survivors are seen by the senior pediatric oncologist and senior psycho-oncologist who are familiar with their medical and psychosocial concerns. This rapport-building has helped immensely in ensuring continuity of care and adherence to follow-up in a large

proportion of survivors, who often refer to the medical team as their extended family.

Ugam—a support group of CCS from ACT Clinic, initiated by the Indian Cancer Society—has been active for over a decade in peer support, empowerment of survivors, and advocacy.<sup>25</sup> The ACT-Ugam model has been successfully replicated by the Indian Cancer Society to provide holistic care to cancer survivors across the country.<sup>26</sup>

### Telesurvivorship and Distant Follow-Up are Feasible and Effective

Since 2017, due to the large volumes at our center, we have actively incorporated distant follow-up and shared care; this stood us in good stead during the COVID pandemic. Our strategy during the first 15 months of the COVID pandemic has been described in detail.<sup>27</sup> Analysis of the trends at our center points toward increasing use of telesurvivorship, especially in survivors with no/few late effects, easy access to technology, and stay in places distant from Mumbai.<sup>27</sup> However, in-person follow-ups will continue to remain high, especially in those who stay in Mumbai and surrounding areas, and those with medical/psychosocial concerns who depend on our in-house onco-endocrinology, cardio-oncology and hepatitis services, which offer subsidized care. While the majority of urban survivors have access to WhatsApp and internet, there is a small proportion of survivors who lack access, and an even smaller proportion (mainly rural and semi-literate) who are uncomfortable with distant follow-up. Overall, telesurvivorship has been successful, and multiple modalities may be effective depending on the survivors' access to technology. We actively encourage in-person follow-ups at present.

### The Need for Adapted Treatment Guidelines

Current guidelines for the follow-up of survivors originate from large collaborative groups in North America and Europe.<sup>28,29</sup> While these surveillance guidelines are comprehensive, evidence-based and thoroughly scrutinized by experts, their direct application in resource-limited settings might not be feasible or cost-effective. There is very little long-term data that can help direct the specific requirements for CCS from LMICs. Ethnic, racial, cultural, and sociodemographic variations necessitate adaptation of international guidelines to suit local needs.<sup>30</sup>

To decentralize survivorship care, it is essential to have several levels of adapted treatment guidelines which can be used at each level of care. While adapted treatment guidelines and levels of care for various tumor types and supportive care have been laid down by the International Society for Pediatric Oncology, these do not include survivorship.<sup>31</sup> Despite efforts by individual centers and special interest groups among pediatric oncologists in India, there have been no national consensus guidelines for survivorship care till date.

At our center, we ensure risk-stratified and exposure-based screening using an adapted version of standard guidelines that focuses on history, physical examination, basic

laboratory investigations, and higher diagnostics used only as indicated.

### Future Directions for the ACT Clinic and Survivorship Care in India

a) Decentralization of care and capacity building: Decentralization of care, with a shift toward shared-care and remote follow-up, especially in low-risk survivors, is a main priority for us, especially considering our large patient volume of diverse geographical origin. This could be facilitated by the development of a strong multicentric network of late effects clinics providing holistic, standardized care as well as a network of support groups/supportive care services. Successful efforts in this direction are already being spearheaded by nonprofit organizations, namely Cankids Survivor Passport2Life clinics and Project PICASSO of the Indian Cancer Society.<sup>4,26</sup>

b) Incorporation of technology: With over 50% of our survivors being adolescent and young adults—who are internet-savvy—technology can be leveraged in multiple ways to greatly expand the scope of survivorship care. Internet-based, individualized survivorship care plans that may be accessed securely by the survivor or local designated physicians can help effective decentralization of care.

Several ongoing interventions—psychosocial, cardiometabolic health, educational—can be sustainably performed individually or in groups via videocalls. The existing online support groups can be expanded to include all categories of survivors as well as parents and caregivers. The past few months have greatly improved our capabilities of online communication and greatly broadened the scope of digital interventions.<sup>32</sup>

c) Education: There is a definite need for improved education and sensitization of patients/survivors, families, and healthcare professionals regarding potential late toxicities. There should be an increased focus on minimizing avoidable late toxicities and adopting best practices in treatment. Pediatric oncologists need to be sensitized toward simple interventions such as semen cryopreservation and monitoring for cardiac and ototoxicity during treatment.

d) Research: A strong understanding of the profile of late effects and other concerns faced by survivors of childhood cancer is required, both for development of adapted guidelines and for relevant interventions. The projects and collaboration within the multicentric Late Effects subcommittee of the InPHOG<sup>33</sup> are a welcome step in this direction. However, interventional research relevant to our population needs to be the priority focus. While there have been several attempts to minimize neurocognitive issues and azoospermia, late effects amenable to intervention like cardiometabolic complications, frailty and psychosocial toxicities are other areas in urgent need of pre-emptive and innovative solutions.<sup>34–37</sup>

## Funding

None declared.

## Conflict of Interest

None declared.

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