

A background image of a man and a young child. The man is smiling and looking down at the child. The child is laughing joyfully. The image is dimmed and serves as a background for the text.

Syllabus

Guide on How to Develop a Training Programme for the Management of Childhood Cancer at the Primary Healthcare Level

Introduction

Children (>1 year of age) and adolescents represent between 1% and 3% of cancer sufferers, yet cancer is the second or third cause of disease-related mortality among that demographic worldwide. About 80% of children with cancer living in well-resourced countries can achieve long-term survival, but this is not the case in low- and middle-income countries (LMICs), where a range of factors determine survival, such as cancer biology, host conditions, social determinants, and the delivery of cancer care. Missed and delayed diagnosis and poor-quality care are common issues for children with cancer, particularly in LMICs. Furthermore, detecting the warning signs and diagnosing cancer in children is challenging, due to the low incidence of the disease among children (100-180 cases per 1,000,000 inhabitants per year), subtle clinical presentations, and because patients often present with symptoms that mimic more common, less serious, illnesses.

Treating children effectively for cancer depends largely on intensive chemotherapy and therefore on healthcare capacity to provide support to the different life-threatening adverse events. Furthermore, survivors can suffer from a range of long-term treatment-related sequelae that not only decrease their quality of life but also their life expectancy. The purpose of City Cancer Challenge Foundation (C/Can) programmes is to positively impact cancer survival outcomes. Developing educational programmes to overcome cultural and educational barriers about childhood cancer within the medical community is essential.

C/Can cities initially carry out a Needs Assessment Process to self-evaluate the capacity, quality, and accessibility of cancer care, including childhood cancer. The needs assessment carried out by the first four C/Can cities (known as Key Learning Cities: Cali, Asuncion, Yangon and Kumasi) identified late stage at presentations, delayed referrals and high mortality due to the side effects of cancer treatment as the main barriers to improve access to quality cancer care for children. These are related to insufficient knowledge among health professionals that would enable them to suspect, refer and provide proper support to children with probable cancer or in treatment for the disease. This knowledge is mainly required by primary care physicians to impact the clinical outcomes of children with cancer. When children with cancer are achieving cure, it is of the utmost importance that health providers learn about the impact of late effects of cancer treatment. For children in need of palliative care, adequate management of pain, proper nutrition and other issues ensuring access to these services in their home town should be part of their humanised treatment of cancer.

Despite the findings of the Needs Assessment Process, childhood cancer has not as yet been included as a priority in any of the C/Can Key Learning Cities.

This is why, during the last quarter of 2021, C/Can decided to constitute a specialised task force on childhood cancer to develop a global project. Leading experts in childhood cancer from C/Can's four Key Learning Cities and representatives of C/Can partners were invited to join this group. Lorna Renner, Head of the Paediatric Oncology Unit, Korle Bu Teaching Hospital, Accra. Jaques Van Heerden, Universitair Ziekenhuis Antwerpen | UZA · Division of Pediatric Oncology and Hematology. Joyce kambugu, Head of pediatric oncology at the Uganda Cancer Institute. And the leaders of the first four C/Can cities: Aye Aye Khaing, Yangon; Angélica Samudio, Asunción; Vivian Paintsil, Kumasi; and Oscar Ramirez, Cali.

Their first initiative was to envision and draft a syllabus for a childhood cancer training programme that could be applied to different local contexts, whether in C/Can cities or others worldwide.

C/Can would like to recognize the contribution of the drafting group coordinator Oscar Ramirez, and the drafting group members: Jaques Van Heerden, Aye Aye Khaing, Angélica Samudio, and Vivian Paintsil; and extends thanks to them for authoring this Guide.

Once the final draft version is ready, the document will be put forward for a virtual consultation process with C/Can cities. Feedback from the cities will be incorporated and the final document will be disseminated as *C/Can's Guide on How to Develop a Training Programme for the Management of Childhood Cancer at the Primary Healthcare Level*.

This syllabus was constructed to help to avoid missed diagnoses, reduce the time from suspicion to diagnosis, improve early referral, reduce treatment-related mortality and provide better supportive care to survivors.

Aim

To acquire skills in childhood cancer clinical diagnosis, about management of treatment complications, supportive therapy, and long-term follow-up of children undergoing different cancer treatment modalities.

Target population

This syllabus is an educational activity for primary care, emergency care, hospital-based physicians, paediatricians, advanced nurse practitioners, and medical students.

General learning objectives

1. To increase knowledge and awareness of childhood cancers.
2. To identify children with an increased risk for developing cancer, including the genetic and molecular bases of the different types of cancers.
3. To improve on the level of knowledge of main signs and symptoms of childhood cancers, both leading and early.
4. To encourage prompt and early referrals for diagnosis and treatment
5. To gain insight into different treatment complications, with emphasis in the most important acute toxicities related to chemotherapy, including those that should require immediate referral and other that could be managed locally.
6. To recognise clinical warnings of severe complications due to the disease and/or the treatment, and when to refer to specialist cancer care centres
7. To learn about treating long-term effects, follow-up and requirements of adult survivors of childhood cancer

Time proposed

for the development of this Syllabus

Twelve hours of lectures (**theory**)

Six hours of practical exercises (**study cases**)

Specific objectives by Modules

Module I

Early detection and warning signs of childhood cancers



**Proposed duration time: three hours of lectures
and two hours of practice exercises (clinical cases)**

1. Epidemiology of childhood cancer and burden of the disease worldwide and at the city/region/country (depending on the coverage area of the training programme).
 2. Basic pathology features of each tumour group and diagnostic methods.
 3. Clinical outcomes of children with cancer.
 4. Children with an increased risk for developing cancer.
 5. When to suspect a cancer in children: clinical assessment and differential diagnosis.
 6. Establishing Childhood Cancer awareness program.
 7. How to apply early detection tools and referral.
 8. Psychological and social aspects of cancer diagnosis.
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Module II

The child with an oncologic emergency and adverse effects of its treatment



Proposed duration time: four hours of lectures and two hours of practice exercises (clinical cases)

1. Identifying the most frequent and life-threatening oncologic emergencies in children with cancer.
2. Understanding the basic diagnostic and therapeutic approaches of the oncologic emergencies.
3. Overview of the paediatric early warning score.
4. Identifying the most common life-threatening adverse effects associated with the treatment of children with cancer.
5. Identifying other (non-life-threatening) common adverse effects related to therapy that affects quality of life of children with cancer.
6. Identifying other (non-life-threatening) common adverse effects related to therapy that can be managed at PHC level and how to manage them.

Module III

Childhood cancer survivors



Proposed duration time: five hours of lectures and two hours of practice exercises (clinical cases)

1. Approaching late effects in a child treated for a specific cancer.
2. Understanding the principles in the follow up of late effects in children treated for cancer and how to plan/perform it.
3. Providing guidelines related to the screening and treatment of late effects.
4. Understanding late effects impact on families.

Module I

Early detection and warning signs of childhood cancers

Demographics

- A brief overview of the world, country and the C/Can city.
- Up-to-date information of the total population for the country and the city.
- What total percentage of this population are children?

Epidemiology

- General epidemiological and biological features of childhood cancer.
- An in-depth overview of the childhood cancer burden in the country and then the city using appropriate local data or references.
- International childhood cancer classification (ICCC-3), rationale and structure.
- Particular epidemiological features by ICCC-3 grouping.
 - I. Leukaemia, myeloproliferative diseases, and myelodysplastic diseases.
 - II. Lymphomas and reticuloendothelial neoplasms.
 - III. CNS and miscellaneous intracranial and intraspinal neoplasms.
 - IV. Neuroblastoma and other peripheral nervous cell tumours.
 - V. Retinoblastoma.
 - VI. Renal tumours.
 - VII. Hepatic tumours.
 - VIII. Malignant bone tumours.
 - IX. Soft tissue and other extraosseous sarcomas.
 - X. Germ cell tumours, trophoblastic tumours, and neoplasms of gonads.
 - XI. Other malignant epithelial neoplasms and malignant melanomas.
 - XII. Other and unspecified malignant neoplasms.

Pathology and diagnosis

- Basic pathology features of each tumour group.
- Basic methods for diagnosis.

Clinical outcomes of children with cancer

- Overview of survival statistics interpretation.
- General survival of each tumour group, by WHO region, country and C/Can city.

Psychological and social aspects of cancer diagnosis

- How to give bad news? Speaking about cancer diagnosis with the family.
- “Talking about death”.
- Family and patient mourning after diagnosis.
- Identifying and activating the families’ social network support.

Children with an increased risk for developing cancer

- Congenital syndromes associated with cancer.
- Acquired and congenital immunosuppression diseases predisposing to cancer.
- Birth-weight, breastfeeding, infections, and other acquired risk factors.
- When and how to do genetic screening in children and parents with increased risk of developing cancer.
- Screening siblings of patients with a cancer diagnosis.

Symptoms and signs of childhood cancer mimicking normal childhood illnesses

- Generalised malaise, fever, adenopathy, night sweating.
- Headache, nausea, vomiting.
- Febrile seizure.
- Earache, ear secretion.
- Rhinitis, epistaxis, pharyngitis.
- Diarrhoea, vomiting, hepatomegaly, and/or splenomegaly.
- Haematuria.
- Trouble voiding.
- Musculoskeletal pain, limb tenderness, bony mass.

Symptoms and signs in children that warrant immediate consultation

- **General**
 - Petechiae, purpura, bleeding without evidence of trauma.
 - Sudden onset weight loss.
 - Hypertension.
 - Soft tissue mass.
- **Central nervous system**
 - Headache, early morning vomiting, cranial nerve palsy, ataxia, dilated pupil, papilledema, afebrile seizures, hallucinations, aphasia, unilateral weakness, paralysis.
 - Failure to thrive, sexual abnormalities, electrolyte disturbance. Cushing's syndrome.
 - Regression of milestones.
 - Macrocephaly.
- **Ocular**
 - Eye white spot (leukocoria), proptosis, blindness, wandering eye, intraorbital haemorrhage.
- **Otorhinolaryngology**
 - Bulging mass from the external auditory canal, mastoid tenderness, swelling.
 - Puffy face and neck, pharyngeal mass, periodontal mass, loose teeth.
- **Thorax**
 - Costal mass, haemoptysis, new onset of persistent bronchospasm without history of asthma.
 - Gastrointestinal
 - Hepatomegaly, splenomegaly, ascites, abdominal mass, haematochesia, melaena, haematemesis, constipation or inability to pass stool.
- **Genitourinary**
 - Testicular induration or mass, scrotal mass, haematuria.

Peripheral blood cell count interpretation as a basic tool in the diagnosis of children with cancer

- Cytopenias.
- Abnormal cells.

Warning signs

- **General**
 - Use the general warning signs to identify cancers.
 - Use acronyms like:

For example

Child Cancer

(C ontinued, unexplained weight loss, H eadaches, I ncreased swelling or persistent pain in bones, L ump or mass, D evelopment of excessive bruising, bleeding, C onstant infections, A whitish colour behind the pupil, N ausea which persists or vomiting without nausea, C onstant tiredness or noticeable paleness, E ye or vision changes which occur suddenly and persist, R ecurrent or persistent fevers of unknown origin)

Siluan

(Seek help for persistent symptoms, Eye signs, Lumps and masses, Unexplained fever, weight loss and pallor, Aches and pains, Neurological signs).

How to apply early detection tools and referral

- PAHO childhood cancer early detection tool. (<https://iris.paho.org/handle/10665.2/34850>)
- Discuss referral systems in place at the C/Can city.
- To discuss early referral on suspected cases using appropriate referral systems to the main paediatric cancer treatment centre.
- To discuss guidelines of candidate patients for contra-referral and which relevant information is needed.

Module II

The child with an oncologic emergency and adverse effects of treatment

Oncologic emergencies

- **Metabolic emergencies**
 - Tumour lysis syndrome.
 - Electrolyte derangements.
 - Hyperleucocytosis.
 - Hypercalcemia of malignancy.
 - Diabetes insipidus.
- **Cardiothoracic emergencies**
 - Superior vena cava syndrome.
 - Superior mediastinal syndrome.
 - Pericardial effusion and cardiac tamponade.
 - Massive pleural effusion.
 - Haemoptysis.
 - Pulmonary embolism.
 - Hypertensive crisis.
- **Abdominal emergencies**
 - Massive abdominal masses with increase intraabdominal pressure and/or alterations of the ventilatory mechanics.
 - Intestinal obstruction and intussusception.
 - Gastrointestinal perforation, tumour rupture, and intraabdominal haemorrhage.
- **Genitourinary emergencies**
 - Acute kidney failure secondary to obstructive uropathy.
 - Haematuria.

- **Neurological emergencies**
 - Spinal-cord compression.
 - Seizures.
 - Raised intracranial pressure.
 - Cerebrovascular accidents.
 - Alterations in mental status.
- **Haematological emergencies**
 - Severe bleeding.
 - Disseminated intravascular coagulation.

Overview of the paediatric early warning score (PEWS)

Treatment-associated life-threatening adverse effects

- **Infection in the immunosuppressed host**
 - Fever with and without neutropenia.
 - Pneumonia.
 - Typhlitis (Neutropenic enterocolitis).
 - Fever in patients after haematopoietic stem cell transplant.
- **Anaphylaxis and hypersensitivity to chemotherapeutic agents**
 - Asparaginase, etoposide, platinum, bleomycin, monoclonal antibodies.
- **Cytokine release syndrome**
 - High-dose cytarabine, Bispecific T-cell engagers, CAR-T cell therapy, Monoclonal antibodies, immune checkpoint inhibitors, HSCT.
- **Differentiation syndrome in acute promyelocytic leukaemia**
- **Therapy associated diabetes mellitus**
 - Dexamethasone, asparaginase, cyclosporine, immune checkpoint inhibitors.
- **High-dose methotrexate associated toxicities**
- **Asparaginase associated toxicities**

Common treatment adverse effects and supportive care

- **Gastrointestinal symptoms**
 - Nausea, vomiting prevention and treatment, emetogenic potential of common paediatric chemotherapeutic agents.
 - Mucositis recognition, grading, prevention and treatment.
 - Constipation and ileus.
- **Respiratory symptoms**
 - Dyspnoea.
- **Systemic symptoms**
 - Asthenia.
 - Cachexia and anorexia.
 - Nutrition assessment and intervention.
- **Myelosuppression (Leukopenia and neutropenia, Anaemia, Thrombocytopenia).**
- **Pain**
 - Definition, classification, assessing pain using the pain scales, management.
- **Skin changes and alopecia.**
- **Basic care of CVC in the outpatient setting.**
- **General care associated with the outpatient treatment**
 - Fundamental facts about infection control to be carried out at the home of the immunosuppressed patient.
 - General hygiene advice for parents with children undergoing treatment.
 - Nutritional guidelines.
 - Management of pain at home.
 - Psychological support.

Module III

Childhood cancer survivors

The aims of late effects monitoring

- Decrease the severity of late complications of treatment.
- Reduce excess morbidity.
- Reduce mortality.
- Screening for known risks.

The surveillance of patients

- Extensive history of patients (physical, physiological and psycho-emotional).
- Full physical examination.
- Disease and treatment specific screening.
- Identification of emerging, established and chronic effects.
- Quality of life assessments (questionnaires, etc.).
- Nutritional screening.

Needs of patients

- Social, psychological, sexual health and rehabilitative support.
- Ongoing health education.
- Health promotion advice.
- Transitional strategies for adolescent and adult survivors to more age-appropriate care provider.
- Education, employment, disability and life insurance planning.

Organs and systems affected

- **The central nervous system**
 - The brain and spinal cord.
 - The peripheral nervous system.
 - Eyes and ears.
- **Endocrine system**
 - Hypothalamus-hypophysis axis.
 - Thyroid gland.
- **Reproductive system**
 - Gonads (fertility).
 - Uterus.
- **Genito-urinary system**
 - Kidneys.
 - Bladder and lower urinary tract.
 - Genitalia.
- **Cardiovascular system**
 - Heart.
 - Vascular system (including hypertension).
- **Respiratory system**
- **Gastro-intestinal and hepatobiliary system**
- **Musculoskeletal**
 - Muscular system.
 - Bones including spine.
- **Skin**
- **Cranio-fascial and dental.**
- **Secondary malignancies and immune deficiencies.**

Functional quality of life assessments

- Neuropsychological wellness (including neuro-developmental, behavioural and emotional well-being).
- Growth.
- Sexual maturity.
- Exercise capacity and physical well-being.
- Metabolic syndromes (hypertension, diabetes, cholesterol and lipidaemias).

Aetiology of late effects

- Chemotherapy toxicity to major organs
- Radiotherapy effects to organ systems
- Surgery
 - Anatomical effects.
 - Functional effects.
- Post stem cell transplant
 - Combination of chemotherapy and radiotherapy.
 - Immunological effects.
- Multifactorial

Timing of onset

- Early onset effects – within the first year after treatment.
- Late onset effects – from one year to decades after treatment.

Severity of effects

- Mild – usually treatable.
- Moderate – usually reversible or manageable.
- Severe – usually irreversible with significant impact to the quality of life.
- Life-threatening.

Complexity of effects

- A single effect.
- Compounded effects with numerous consequences.

Scope of care

- Multi-disciplinary teams depending on the degree and complexity of effects.
- Timing of screening interventions.
 - According to type of treatment.
 - According to organ system.

Impact of late effects on families

Evaluation

A pre and post-test will be done before each module to have an insight of knowledge gaining. At the course's final, the students will be evaluated on the topics of the modules. This final evaluation will include clinical cases to solve "real-life" problems.

We would like to take this opportunity to thank all C/Can partners, especially Foundation S – The Sanofi Collective, for their support in this initiative.



<https://citycancerchallenge.org/>

