香港中文大學
The Chinese University of Hong Kong

香港中文大學醫學院
Faculty of Medicine
The Chinese University of Hong Kong

40th Anniversary

Personalized Risk-based Care and Education for Early Survivors of Childhood Cancer in Hong Kong

Yin Ting CHEUNG, PhD
Associate Professor
School of Pharmacy, Faculty of Medicine
Hong Kong Hub of Paediatric Excellence
The Chinese University of Hong Kong
Email: yinting.cheung@cuhk.edu.hk

Supported by Health Bureau, The Government of the Hong Kong SAR (HMRF Research Fellowship Ref: 03170047).

Mentor: Prof Chi Kong Li (CUHK Paediatrics)
Co-investigators: Prof. Vivian Lee (CUHK CLEAR), Prof. Nelson Yeung (CUHK SPHPC), Prof. Smita Bhatia (University of Alabama at Birmingham)

School of Pharmacy CUHK
Expanding the pharmaceutical universe, Creating opportunities for life

Late Effects in Survivors of Childhood Cancer

- Survivors of childhood cancer are at-risk of developing treatment-related late effects [1-2]

- Studies have shown that survivors who had early access to a structured survivorship program are more likely to be: [3]
  - Aware of their personal health risks and potential late effects
  - Adopt health-protective lifestyles
  - Adhere to late effects screening

1. Poon LH and Cheung YT, et al. J Cancer Surviv. 2019;13(3):374-396
2. Cheung YT, et al. J Natl Cancer Inst. 2018 Apr 1;110(4):411-419
3. Signorelli C, et al. Crit Rev Oncol Hematol. 2017 Jun;114:131-138

Research Gaps (Local Setting)

- Less than half (45%) of the survivors were aware of the late effects for which they were at risk → a subset may default or skip long-term follow-up appointment [1]

- Despite the low prevalence of health-damaging behaviors, local survivors are not engaging in health-protective behaviors (e.g. physical activity, diet, vaccination) [2]

- No centralized paediatric cancer survivorship program in Hong Kong before 2019:
  - The Hong Kong Children's Hospital (HKCH) begins its operation in April 2019

1. Yang LS and Cheung YT, et al. Health Expect. 2021;24(4):1473-1486
2. Cheung YT, et al. Hong Kong Med J. 2022 Feb;28(1):33-44.

Objectives of the HMRF Research Fellowship

Training Objective:

- To develop a methodological framework for patient-specific survivorship care plan and risk-based late effects screening

Research Objective 1: (a mixed-methods approach) [1]

- To identify barriers and facilitators of the implementation of late effects screening recommendations in local/regional practice

Research Objective 2: (a prospective pe- and post-intervention study) [2,3]

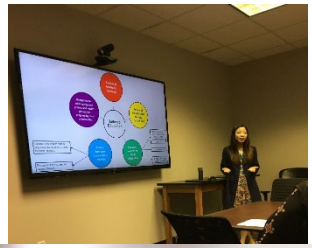
- To evaluate the short-term efficacy of a tailored education program for childhood cancer survivors in improving their awareness of personal health risks

1. Cheung YT, et al. JCO Glob Oncol. 2021;7:261-276
2. Yang LS and Cheung YT, et al. Health Expect. 2021;24(4):1473-1486
3. Ma CT and Cheung YT, et al. Pediatr Blood Cancer. 2023;70(2):e30084

HMRF Research Fellowship Training

Institute for Cancer Outcomes and Survivorship, University of Alabama at Birmingham

Children's Oncology Group (USA)



Training activity	Deliverables
Expert panel meeting	• Panel member of the Children's Oncology Group Long-term Follow-up Guidelines version 6.0
Participation at the Survivors' Clinic	• A prototype of the survivorship care plan for our local survivors • Clinical portal, features of a care plan, educational information
Sharing session on current survivorship work in Hong Kong and mainland China	• A set of recommendations to address common barriers to establishing a survivorship program

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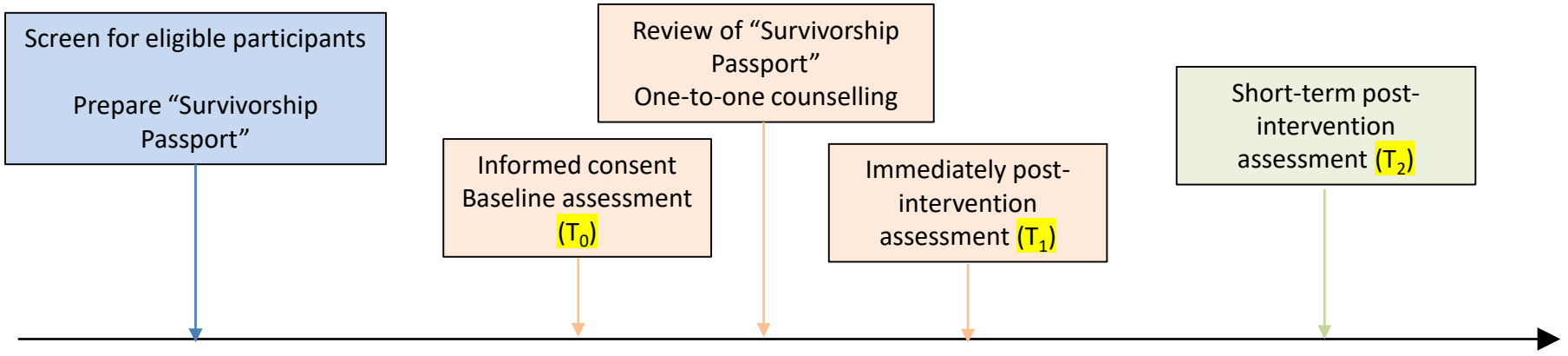
Methods

- Prospective study with pre- and post- intervention testing
- Study site: Prince of Wales Hospital Long-term Follow-up (LTFU) Clinic
- Study period: June 2019 to May 2021
- Approved by the Joint CUHK – NTEC Clinical Research Ethics Committee
  - Informed consent and assent (for pediatric survivors)
- Participants:
  - Diagnosed with cancer before 18 years of age
  - 2 years or more post-treatment
  - Cancer remission
  - Able to read and understand Cantonese

Study Procedure



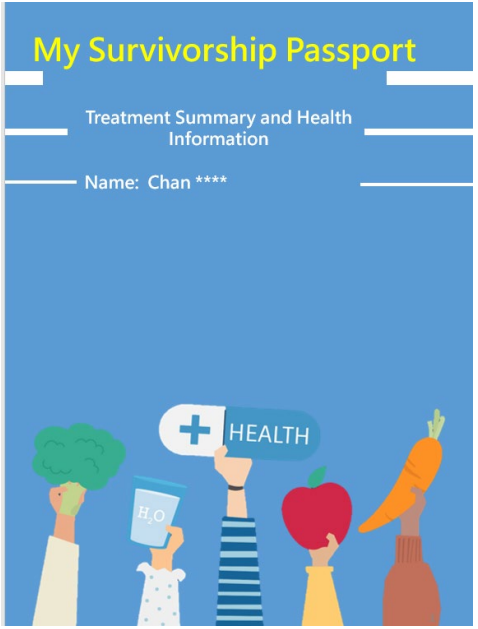
Before Survivors' LTFU clinic

At the Survivors' LTFU clinic

1 to 3 months after intervention (by mail)

“Survivorship Passport”

- A structured personalized care plan for each survivor
- Culturally adapted from the Children’s Oncology Group
- Co-developed with our patients and NGO partners



1. Landier W, et al. Clin Oncol. 2018;36(21):2216-22
2. The Children's Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers. URL: http://www.survivorshipguidelines.org/pdf/2018/COG_LTFU_Guidelines_v5.pdf.

Major Milestones

Milestones

Name Chan *** **Date of Birth** 02/11/2013

Sex Male

Date	Milestone		Remarks
01/01/2015	Diagnosis	Acute Myeloid leukaemia	
	Chemotherapy	NOPHO AML 2004	
01/01/2016	Hematopoietic stem cell transplant	CYC Melphalan Busulfan conditioning	Matched unrelated double unit cord blood transplant
06/2016	GVHD	Skin stage 2, stopped immunosuppressive treatment in 12/2016	
01/01/2016		BMA regenerative and 100% DNA chimerism	

Surgery	No
Radiation	No
Stem cell transplant	Yes
Chemotherapy	Yes

Date of diagnosis

Date of completion of treatment

Major treatment modalities

Stem-cell Transplant

Treatment	Late Effect	Health Topics
Hematopoietic stem cell transplantation Bone marrow transplantation	Acute myeloid leukaemia Bone marrow abnormalities Solid tumour	Reducing the Risk o Second Cancers
	Damage to liver and liver function	Liver Health Gastrointestinal Hea
	Osteonecrosis	Osteonecrosis
	Reduction in bone density	Bone Health
	ney ction	Kidney Health Cardiovascular Risk Fa
Graft-versus-host disease (GvHD)	Damage to skin	Skin Health
	Dry eyes	Eye Health
	ms	Dental Health
	ngs	Lung Health
	of oesophagus	Gastrointestinal Hea
	Joint contracture	-

Chemotherapy

Drugs	Late Effects	Health Topics
All chemotherapy	Dental problems	Dental Health
	Psychological distress associated with the treatment experience	Emotional Issues
環磷醯胺 (Cyclophosphamide) Class: Alkylating agent	Testosterone deficiency Damage to sperm-producing cells	Male Health Issues
	Acute myeloid leukaemia Bone marrow abnormalities	Reducing the Risk of Second Cancers
	Damage to urinary tract Bladder cancer	Bladder Health
米托蒽醌 (Mitoxantrone) 類別:蒽環類抗生素 Class: Anthracyclines	Acute myeloid leukaemia	Reducing the Risk of Second Cancers
	Damage to heart	Heart Health Cardiovascular Risk Factors Diet and Physical Activity

Type of treatment / chemotherapy drug

Potential late effects and health topics to refer to

Screening Recommendations

Late Effect	Recommended Screening
Psychosocial distress (Problems with emotions, school, and social skills)	Long-term follow-up once a year Test Psychosocial assessment (emotional, schoc social functioning) Frequency Once a year Referral to specialist if needed
Dental problems	Test Dental check-up, dental X-ray (when clinica needed) Frequency Once every 6 months
Testosterone dysfunction	Long-term follow-up once a year Test Blood test (male hormone levels) Frequency Based on the individual's timing of puberty female hormone levels Referral to specialist if needed
Impairment in sperm cell production	Long-term follow-up once a year Test Semen analysis (when clinically needed) Blood tests (when semen analysis is not po Frequency Based on the individual's fertility needs Referral to specialist if needed

Screening Recommendations

Late Effect	Screening Recommendation
Kidney problems	Long-term follow-up once a year (blood pressure test and urine test) Test Kidney function and electrolytes (blood test) Frequency A baseline assessment upon entry into long-term follow-up Repeat assessment as recommended by your doctor
Damage to the liver or liver function	Long-term follow-up once a year Test Liver function test (blood test) Frequency A baseline assessment upon entry into long-term follow-up Repeat assessment as recommended by your doctor
Lung problems Pulmonary Fibrosis	Long-term follow-up once a year Test Lung function test Frequency A baseline assessment upon entry into long-term follow-up Repeat assessment as recommended by your doctor

- Type of screening test and its frequency for each late effect
- Based on the Children's Oncology Group recommendations
- Adapted to local context

如何減低繼發性癌症的風險

了解發生繼發性癌症的風險可能令人沮喪和焦慮。之後，你最害怕得知的或許就是在成年期發生繼發各種原因，隨著年齡的增長，每個人的癌症風險都明，隨著兒童癌症康復者年齡的增長，與普通人（繼發性）癌症的風險略高。可能導致這種風險的療時的年齡，治療方法，以及遺傳和家族史。

甚麼人會較容易患上繼發性癌症？

接受過某些化療藥物的人：一些治療會險。有些人治療後或會患上急性骨髓性病通常發生在原始癌症治療後的前10年烷化劑（如環磷酰胺 Cyclophosphami Mustard），表鬼臼毒素（如依托泊苷 苷 Teniposide）和蒽環類化療藥物（如或柔紅黴素 Daunorubicin）治療及自體的患者，發生繼發性白血病的風險尤高

接受放射治療的年輕人：患上繼發性實年齡增長的。最常見的部位包括皮膚，（大腦和脊柱），甲狀腺和骨骼。與繼發性實質固態瘤最常出現在治療後10年劑量和大面積的放射性治療後，繼發性增加。

在家庭中有癌症病史的人：有時，癌症些基因變化（突變），更容易患上繼發這些遺傳性變化不算常見，佔癌症患者家族史在每一代年輕人中發現多種癌症兩側（例如眼睛，呼吸，腎臟等）發生致癌基因的可能性。如果你有任何疑問能患有癌症，你應該諮詢你的醫護人員你會知道是否需要進行遺傳諮詢或檢測

Reducing the Risk of Secondary Cancers

癌症治療後的白內障

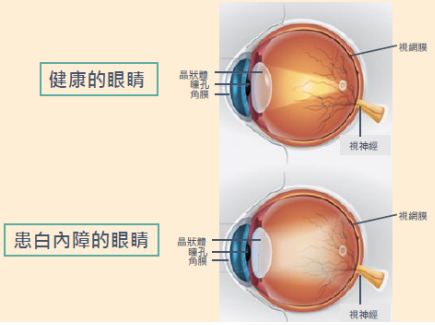
兒童癌症治療使用的藥物或放射療法，或會增加患白內障的風險。 因為視力會對日常生活產生重大影響，所以曾接受這些治療的康復者定期睛很重要。

什麼是白內障？

白內障使眼睛的正常透明晶狀體混濁。白內障往往發展緩慢，但加，視力就會受到影響。

白內障如何影響視力？

眼睛是個非凡的器官，它們轉換光線成傳遞給大腦的脈衝，而大圖像的地方。光通過一層透明的組織進入眼睛，又叫**角膜**。角膜焦光線，並通過已知的眼睛開口發送，此開口為**瞳孔**。瞳孔控制的光線量。瞳孔後面是眼睛的**晶狀體**，它將光線聚焦在**視網膜上**後壁的膜。視網膜中的神經細胞將光線轉換成電脈衝並將它們經傳遞到大腦感知圖像的地方。當**晶狀體因白內障而變得渾濁時**視網膜的圖像會變得模糊。



Cataracts after Cancer Treatment

健康飲食和定期運動

足夠的營養和定期運動可以給予兒童癌症康復者很多的好處。這些好處有：

- 促進受到癌症及其治療損害的器官或組織的痊癒
- 提升肌肉力量與肌肉耐力
- 減低患有某些癌症和其他疾病的風險
- 減低心理壓力及給予幸福感

兒童癌症對營養和運動的影響

兒童癌症對營養和運動的影響對每位康復者都不一樣。癌症可以從不同的方面影響人體內的營養。有些康復者會有提升體重的困難，亦有些康復者會過重。運動對維持健康體重十分重要，雖然受到不同因素影響，每位康復者的運動能力都會不一樣。

建立一個健康飲食計劃

健康飲食的建議包括：

1. 在所有食物種類中選擇多樣的食物，利用 *www.choosemyplate.gov* 內的互動及個人化的指引去建立一個均衡飲食及活動計劃
2. 每天進食五份或更多的水果及蔬菜，包括柑橘類水果和深綠及深黃色的蔬菜
3. 當飲用蔬果汁時，選擇百份百的果汁或蔬菜汁，一天不要飲用多於150毫升一天
4. 進食高纖維食物，如全穀類麵包、飯、意粉和麥片
5. 減少進食精製的碳水化合物，如糕點、有糖麥片、汽水和糖

Diet and Physical Activity

Personalized set of health information based on each survivor's risk profile:

- Symptoms
- Risk factors
- Screening strategies
- Prevention and treatment

Patient Support Groups and Non-governmental Organizations

Children's Cancer Foundation

生命小戰士會

生命小戰士會於 2002 年成立以來，一直由病童、康復者、家長及醫護人員組成，是現時本港唯一一所註冊兒童血液及癌症病人互助組織，旨在改善對患上癌症、嚴重血病及曾接受骨髓移植的病童提供的服務和促進他們的福利，至今服務超過 2,700 名會員。過去 17 年來，會員間相互交流，以貼身服務迎合癌症病童與家人的需要。而自香港兒童醫院於 2018 年底啟用後，兒童癌症的個案將會於該院集中處理。本會於 2019 年 5 月完成全港五間兒童癌症互助組織的合併工作，日後將更有效地為病童及其家屬在面對疾病的路途上提供全面及適切的支援。

本會服務包括：

我們的願景 Our VISION

- 同心互助　戰勝癌症
- 活出新生　回饋社會

Little Life Warriors Society

兒童癌症康復護理相關機構

香港也有不同機構，可以為癌症康復者提供各類服務和資訊。以下為各機構可提供的服務：

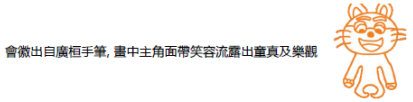
鮑廣桓兒童慈善基金

兒子廣桓於一九九八年因血癌的離世，驅使鮑廣桓兒童慈善基金於同年年底成立，鮑潔鈞夫婦憑著過來人的經驗及熱誠，開展了服務香港非住院兒童癌症家庭的義務工作。在香港的服務內容包括:

~ 協助兒童癌症康復者勇闖明天，邁向豐盛未來
~ 鼓勵癌症病童家長建立正面人生
~ 舉辦兒童癌症康復者研討會，為康復者及醫護建立溝通渠道

基金於二零零四年加入國際兒童癌病協會 (Childhood Cancer International，以下簡稱CCI)為成員，因此亦展開於國內及亞洲兒童癌症家長組織發展的工作。二零一八年CCI成為世界衛生組織正式關係的非政府機構，藉此基金亦參與世衛於二零一八年全球改善兒童癌症的倡議。

CCI是全球最大關注兒童癌症的非醫學組織，在五大洲九十個國家代表一百六拾七個關注兒童癌症的機構成員。成員在歐洲及部份亞洲國家均已推出癌症康復護照，以便提醒康復者需要注意事項及醫療團隊對康復者作出適時適切的跟進。



網址:

鮑廣桓兒童慈善基金

Childhood Cancer International

Pau Kwong Wun CharitableFoundation

Childhood Cancer International

Pao Kwong Wun Charitable Foundation

Outcomes Assessment

- Primary Outcome: Awareness of treatment-related late effects score [1,2]
  - Self-reported by young adult survivors (> 15 years old)
  - Proxy-reported by parents – for paediatrics survivors (≤ 15 years old)
  - Structured assessment rubrics
  - Number of correctly identified late effect risks
  - 0 to 100 points

- Generalized estimating equation was used to test for changes in the primary outcomes (awareness scores) over the three time points of assessment
  - Adjusting for current age, sex, cancer diagnosis, time since treatment completion, treatment, and chronic conditions

1. Landier W, et al. Clin Oncol. 2018;36(21):2216-22
2. Yang LS and Cheung YT, et al. Health Expect. 2021;24(4):1473-1486

Study Population (n=248)

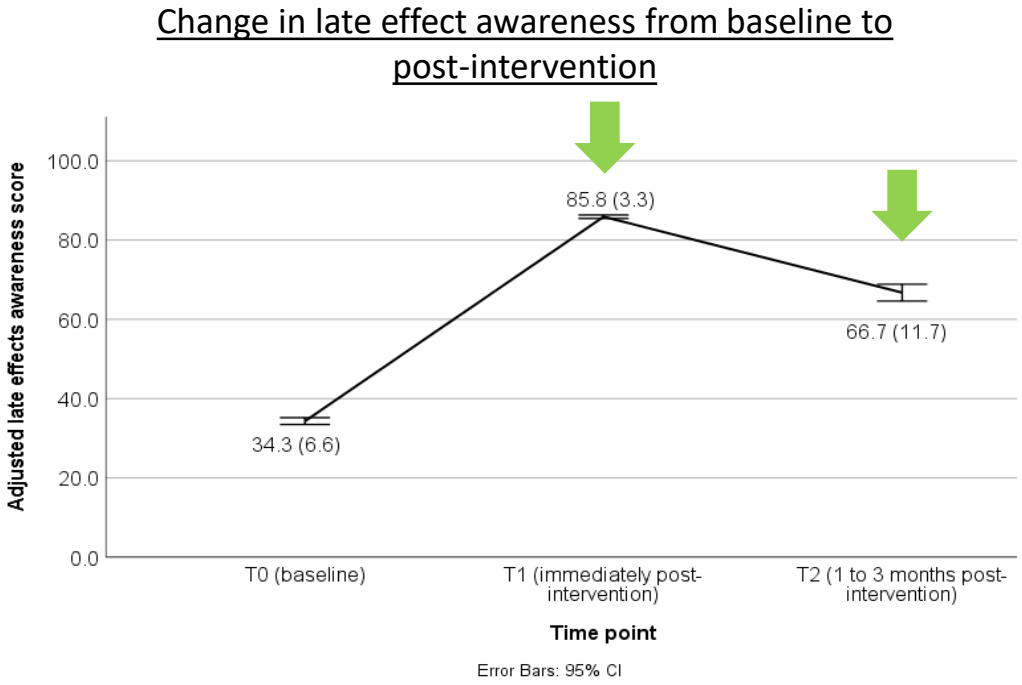
Socio-demograhics	All survivors
Age at interview	19.4 [SD = 6.7] years
Young adult survivors	164 (66%)
Pediatric survivors	84 (34%)
Sex	
Male	138 (54%)
Female	110 (43%)
Household income *	
<HKD 30,000	117 (47%)
>HKD 30,000	120 (48%)

*Missing (n=11)

Clinical	All survivors
Diagnosis	
Hematological cancer	164 (66%)
Non-CNS solid tumor	72 (29%)
CNS tumor	12 (5%)
Relapse	18 (7%)
Age of diagnosis (years)	7.2 [5.5] years
Years from treatment completion (years)	10.2 [SD = 5.2] years

SD, standard deviation

Results

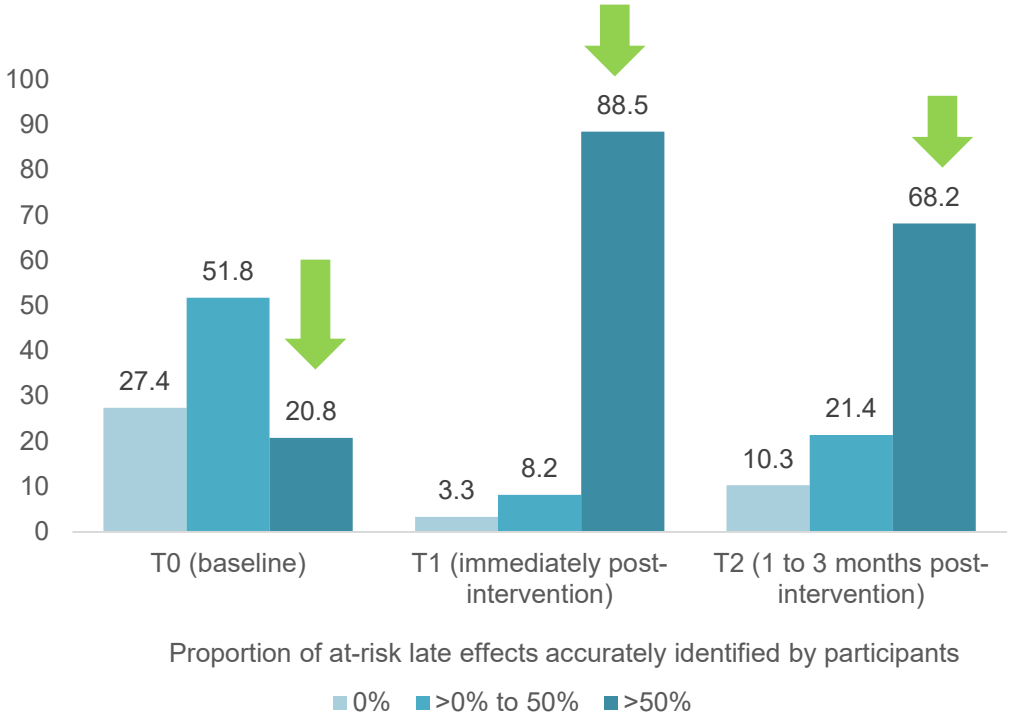


Overall significant gain in late effects awareness score from T_0 to T_2 ($P < 0.001$)

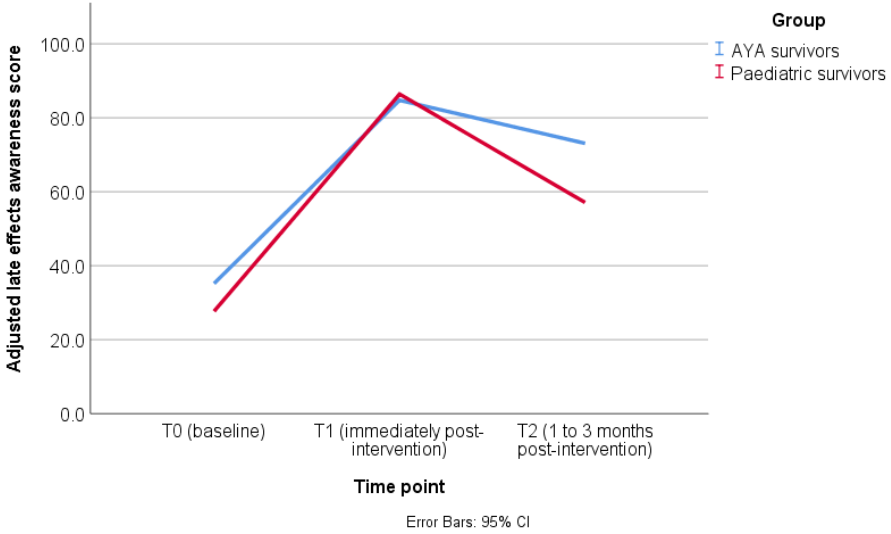
- But a drop from T1 to T2 → Need for reinforcement of the educational materials during subsequent follow-up visits

Results

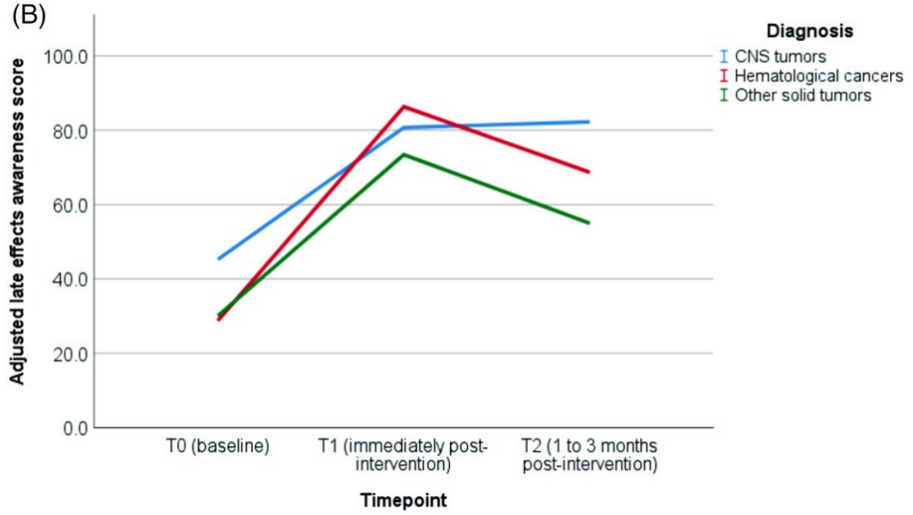
Proportion of potential late effects accurately identified by participants



Interaction Analysis



Young adult survivors demonstrated a larger overall gain in awareness of late effects than the parents of pediatric survivors (P = 0.013)



Survivors of non-CNS solid tumors only showed a modest uptake of knowledge (P = 0.032)

Conclusion

- The provision of a personalized survivorship care plan and counselling showed short-term effectiveness in increasing the awareness of personal health risks and potential late effects among childhood cancer survivors in Hong Kong
  - The need for continual reinforcement of personalized education

- Young adult survivors demonstrated the most benefits from the program
  - May reflect young adult survivors' growing interest in their health risks

Short-term Impact and Future Work

- Since Oct 2023, the “Survivorship Passport” is part of routine care in the Long-term Follow-up Clinic at the Hong Kong Children’s Hospital
  - Future work: digitalization and incorporation into clinical management system

- Resources developed through this HMRF project are shared with:
  - Local NGOs
  - Institutions from mainland China
  - Children’s Oncology Group portal

Talks organized by Local NGOs

儿童肿瘤康复随访手册

Children’s Oncology Group

Resources for a NGO in mainland China

Short-term Impact and Future Work

- Extension – “Safe Use of Chinese Medicine in Childhood Cancer Survivors”
  - Supported by the Chinese Medicine Development Fund (19B1-2/017A_R1)

Lam CS and Cheung YT, et al. J Cancer Surviv. 2022;16(3):568-581.

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- Doctors and Nurses of PWH and HKCH
  - Dr. Frankie Cheng (Head of Service) and Dr. Jeffrey Yau (Head of LTFU Clinic)
- Survivors, Patient Partners and NGOs
  - Children's Cancer Foundation, Little Life Warrior Society, Pau Kwong Wun Charitable Foundation
- CUHK Office of Research and Knowledge Transfer Services (ORKTS)
- Health Bureau Research Fund Secretariat, Consultants and Scientific Officers (past/present)

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香港中文大學醫學院
Faculty of Medicine
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Yin Ting CHEUNG, PhD
Associate Professor
School of Pharmacy, Faculty of Medicine
The Chinese University of Hong Kong
Email: yinting.cheung@cuhk.edu.hk

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Mentor: Prof Chi Kong LI (CUHK Paediatrics)
Co-investigators: Prof. Vivian Lee (CUHK CLEAR), Prof. Nelson Yeung (CUHK SPHPC), Prof. Smita Bhatia (University of Alabama at Birmingham)

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