Did you know that your funding dollars can have a sustained impact on advancing pediatric cancer research and treatment options for kids with cancer for years after the grant money has been spent?

The impact of a research grant is like the ripples in a pond. There is an intense 2-3 years of research, or longer in the case of a clinical trial, followed by sharing of the research results. Next comes the waves of research and follow-up grants that are a direct consequence of the initial grant. Other impacts include changes to clinical practice, a new tool for testing patients, or new resources that can be used by other research teams. Running parallel to these impacts are the trainees that are behind most research programs—graduate students, medical residents, and undergraduates. Many trainees will take their knowledge to other research groups, into clinical practice, or to their own research program.

Here are some of the impacts stemming from the research funded in partnership with the Kids with Cancer Society.

**Jennifer Stinson, Hospital for Sick Children (awarded in 2010)**

I developed and tested an award-winning phone app that gives children with cancer a way to accurately record the pain they experience, which will help their healthcare team understand and effectively treat their pain. This ultimately improves the quality of life of these young patients. We have since received several grants to continue and expand this research, including expansion of the app to additional languages. The graduate student who worked with me on the C17-funded portion of this project is now an assistant professor of nursing and embarking on her own career.

**Lucie Lafay-Cousin, Alberta Children’s Hospital (awarded in 2011)**

Because of your donation I was able to focus my research on a rare group of very young brain cancer patients who need special treatment approaches to cure them, while protecting their developing brain. Our research described several types of the ATRT brain tumour at a genetic level, giving us the tool to predict each patient’s risk of aggressive disease. The goal is to use this prediction to tailor treatment intensity to risk, so that we can reduce chemotherapy and radiation exposure, and therefore reduce toxicity and brain damage in these very vulnerable little patients.

**Nancy Baxter, St Michael’s Hospital (awarded in 2013)**

As a result of our 2013 C17 grant, we were able create a database of all teens (aged 15 – 18 years) diagnosed and treated with leukemia, lymphoma, sarcoma and testicular cancer treated in all pediatric and adult hospitals in Ontario between 1992 and 2010. Research is ongoing using this database, and we have secured over $900,000 in additional grants. This database is allowing us to answer questions about how best to treat teens and their unique characteristics. For example, should a 19 year old with leukemia receive treatment closer to that of a young child or an older adult —which gives that age best chance of survival? The results of this study will inform doctors how best to treat teens and will have significant impact on health policy in order to optimize outcomes for young Canadians with cancer.
Third-party Human Umbilical Cord Perivascular (HUCPVC)-derived Mesenchymal Stromal Cells (MSC) to Treat Refractory or Steroid-dependent Acute Graft-versus-Host Disease after Allogeneic Hematopoietic Stem Cell Transplantation in Children, TUMS Phase I-II trial

Principal Investigator: Henrique Bittencourt, CHU Ste-Justine

Total award value: $120,000
KWCS 2016 Allocation: $40,000

Acute graft-versus-host disease (aGVHD) is a frequent complication after hematopoietic stem cell transplantation. Severe forms of aGVHD can lead to multiple complications and death when patient doesn’t respond to the initial treatment based on steroids. Researchers have shown recently that a type of cell found in bone marrow, called mesenchymal stromal cells (MSC), can be used with excellent results in the treatment of aGVHD that has not responded to steroids. MSCs from bone marrow are expensive (about $200,000) and require a painful procedure to extract from a donor. MSCs are also found in umbilical cords from newborns. Currently, umbilical cords are thrown away after delivery. We have developed a method to isolate and expand MSCs from umbilical cords, making them an attractive and affordable treatment for aGHD. They also have the added benefit of being compatible in any patient, so there are no rejection issues to consider.

Dr. Bittencourt’s study will include up to 38 patients (from all pediatric transplant centers in Canada) aged 21 years old or less with aGVHD that has not responded to steroid treatment. These patients will receive 8 infusions of MSC isolated from umbilical cords. The hope is that these MSCs can provide the same results as MSC from bone marrow.

Genetic profiling of killer immunoglobulin-like receptors (KIRs) of natural killer cells as predictors of ATG-conditioned HLA-matched pediatric allogeneic hematopoietic cell transplantation (HCT) outcomes

Principal Investigator: Faisal M. Khan, University of Calgary

Total award value: $115,000
KWCS 2015 Allocation: $80,000 over two years

Bone marrow transplantation (BMT) is a life-saving treatment for childhood cancer and blood disorders. Despite using donors matched as closely as possible to the patients, BMT is successful for only 35% of patients. The rest of the patients die because their cancer returns, infection, or their immune system rejecting the transplant. It is important that researchers improve BMT by finding ways to reduce transplant rejection, while at the same time enhancing the part of the immune system that fights infection and cancer.

Dr. Khan’s research focuses on a set of genes known as ‘KIR’ that influence how blood cells and immune cells recover after BMT. Dr. Khan is proposing that the KIR genes can be used to help make better matches between donors and patients; better matches should result in improved success rates for BMT patients.

Research Update: This C17-funded research is focused on a gene system known as ‘KIR’ that control the function of a type of white blood cell called natural killer cells. These are one of the first type of blood cell that recover after BMT. Natural killer cells are an important
part of the body’s ability identify and eliminate pathogens (e.g. viruses) and other cells (e.g. tumour cells) that do not belong.

Dr. Khan’s research group has analyzed the KIR genes from over 250 pediatric BMT patients, the matching 250 donors, and over 60 healthy individuals. They have found that some specific KIR gene ‘signatures’ in donors are strongly linked to protection from a BMT complication known as graft versus host disease, as well as a herpes virus related to often fatal complication known as post-transplant lymphoproliferative disease. If the findings are confirmed in the final analyses, it may lead to refinement of donor selection algorithm for pediatric BMT. This should lead to improved survival and quality of life of pediatric BMT patients.

“We would like to thank the funding partners and their supporters for funding the present study. The preliminary findings are very encouraging and we are hopeful that the study, when completed will lead to improved patient care practice for pediatric allogeneic BMT patients.” Dr. Faisal Khan

Genetic Characterization of Pediatric Papillary Thyroid Carcinoma

Principal Investigator: Jonathan Wasserman, Sick Kids Research Institute

Total award value: $149,518
KWCS 2014 Allocation: $50,000

Thyroid cancer is the most common cancer among adolescent and young-adult women. Although similar to thyroid cancer in older adults, there are several significant distinctions when the disease appears in this younger population. Younger patients are more likely to have widespread (metastatic) cancer when they are first diagnosed and the cancer is more likely to recur than in older patients. Even though a diagnosis of thyroid cancer in younger patients is associated with excellent odds of survival, understanding these age-related differences is important. Dr. Wasserman is studying tumour tissue removed at the time of surgery from patients under 18 years of age. He is looking for cancer-associated genetic changes that may explain the different behaviour between thyroid cancer in adolescents and older patients.

Research Update: Dr. Wasserman’s research has progressed well, with patient participation that has allowed him to collect more than the minimum number of tumour samples required for his research. Using these samples, he has found that, yes, there are significant differences between pediatric and adult thyroid cancer. For example, 60% of pediatric tumours have none of the several genetic changes that have been shown to drive thyroid cancer—these are called “dark matter” tumours. Further investigations into these tumours led to the discovery of a new genetic change associated with pediatric thyroid cancer, and there is a possibility that this genetic change may be related to treatment resistance. In addition, Dr. Wasserman found that 25% of “dark matter” tumours have mutations in the DICER1 gene. This is an exciting discovery because it identifies DICER1 as a frequent mutation in pediatric, but not adult, thyroid cancer and a potential target for new drug development. His research team is now performing in-depth testing to detail these genetic differences and to see if any connects to differences in the patients (such as age and sex) and their tumours (such as size and aggressiveness). Ongoing characterization of ‘dark matter’ tumours will unmask further genetic changes that are behind the development of pediatric thyroid, potentially identifying additional new treatment options.

“We are profoundly grateful to C17 and its funding partners for the opportunity to conduct this research and we hope that our research will contribute to improved outcomes for patients affected by this tumour.”

Dr. Jonathan Wasserman
Development and Validation of Distress Screening Tools for use by Canadian Adolescent and Young Adult (AYA) Cancer Patients & Survivors

Principal Investigator: Anne Klassen, McMaster Children’s Hospital

Total award value: $149,554

KWCS 2014 Allocation: $50,000

The first part of Dr. Klassen’s study produced a distress screening tool for the adolescent and young adult (AYA, 15-29 years of age) cancer population. By distress, we mean feelings and worries about cancer that a person may have that make it hard to deal with day-to-day activities. The tool is a questionnaire that asks a person to circle the level of distress (none, mild, moderate, severe) they have been feeling in the following areas: physical, emotional, social, cognitive, practical, education, employment, cancer worry, and impact of experience. Some examples of items in the tool are: appearance, eating, feeling sad, missing out on social events and living expenses. This tool is different from the distress tools normally used in the cancer population because it focuses on the concerns that AYA have which may be different than concerns in younger children or older adults with cancer. The tool developed Dr. Klassen and her research team is the first measure of distress for the AYA cancer population in Canada. This tool is important because the Canadian Partnership Against Cancer (CPAC) looks at how many patients receive distress screening as a way to see how well our cancer system is working for patients. Currently in Canada, cancer patients are screened with the Edmonton Symptom Assessment Scale (ESAS) that does not include concerns necessarily important for AYA.

In the second part of the study, this tool was tested in 164 patients and 332 survivors in three provinces. The resulting information will be used to see how well the tool measures distress in the AYA cancer population. This information will also be used to see if any items on the tool are really the same, these items can then be removed to make the tool shorter. These initial results will be important because they will be the first data reported on AYA cancer distress in Canada using a tool made for this age group. The data will also be comparable to current research projects using the Australian version of the AYA distress screening tool in Australia, United Kingdom and the United States, helping us to understand how distress levels in the Canadian AYA cancer population compare to AYA cancer distress in other countries.

Although this project is still in progress, there is already impact beyond the scope of the funded grant.

AYA are an understudied group of cancer patients—there are significant gaps in knowledge and their cancer survival rates lag behind their younger, more studied, counterparts. The Canadian Partnership Against Cancer (CPAC) released a System Performance Report on Adolescent and Young Adults with Cancer. This report presented data on indicators throughout the cancer journey, and noted the lack of useful indicators for psychosocial care in what has been called a “lost tribe” of cancer patients. The distress screening tool developed in this study was mentioned as a potentially important metric for use in future reports. CPAC followed up on their interest in the distress screening tool by inviting the research team to present our work at the first meeting of its new AYA cancer network for Canada.

To learn more about the AYA and cancer see the CPAC report at www.systemperformance.ca/report/adolescents-young-adults-cancer/

The indicators of psychosocial care be found on page 69 of the AYA Reference Report, found on the link above.
A Phase I and Enrichment Cohort Study of Low-Dose Metronomic Topotecan and Pazopanib in Pediatric Patients with Recurrent or Refractory Solid Tumours and CNS Tumours (TOPAZ)

Principal Investigators: Drs. Jim Whitlock, Daniel Morganstern, Arif Manji & Sylvain Baruchel, The Hospital for Sick Children

Total award value: $149,066
KWCS 2014 Allocation: $50,000
KWCS 2013 Allocation: $74,533
Research remains active using allocated funds

Childhood tumours are often able to survive and spread by creating new blood vessels, which in turn supply tumour cells with the nutrients required to support tumour growth. Certain drugs are known to prevent the formation of these new blood vessels and can prevent tumour growth or even cause tumours to shrink. The first goal of this study is to determine the safe maximum dosage for two drugs, Pazopanib and Topotecan, when used in combination in children with solid tumours that have continued to grow or spread despite treatment. The second goal is to see if tumour growth is slowed by this drug combination. This study, TOPAZ, will examine how the body absorbs and breaks down these two drugs when used together, and whether or not factors in the blood that help create new blood vessels are changed by these drugs. These two drugs are both taken by mouth and can be taken at home, making this treatment a good option for patients diagnosed with solid tumours if it can be shown to be safe and effective.

Research Update: TOPAZ is an early phase study that aims to develop new treatments for children who have exhausted standard treatment options. The TOPAZ study is available at eight pediatric cancer treatment centres, with two addition centres opening soon. We are excited to report that 21 patients have participated in this study, allowing the research team to test higher treatment doses and different combinations. It is too early in the study to know if this new treatment will slow tumour growth, but so far the treatment has been well tolerated and there have been some responses. For example, one patient has remained on the TOPAZ study since the summer of 2015, which is exciting for a patient who started the study with relapsed or refractory disease.

TOPAZ represents a major milestone—a made-in-Canada early phase pediatric trial written by a junior physician mentored by a senior investigational researcher, funded in Canada, and now being conducted in the C17 Developmental Therapeutics Network across Canada. This study accomplishes a major goal of improving access across the country to early phase trials for patients when they are facing relapsed or refractory disease and want treatment options closer to home.