BestBits of the Pediatric Hematology Oncology literature
Introduction

BestBits of the Literature is a synopsis of current literature in Pediatric Hematology & Oncology. The articles have been selected from clinical and scientific journals, and represent high impact research that may influence the current and future practice of pediatric hematology and oncology. Short summaries are presented with the reviewer’s conclusion on the impact of the findings. All articles are posted on bestbits.ca.

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Generation and optimization of the self-administered pediatric bleeding questionnaire and its validation as a screening tool for von Willebrand disease

Casey, LJ et al., 2017, Pediatric Blood and Cancer

Discriminating children who have a bleeding disorder using their personal history remains difficult and several bleeding scores have been developed to discern children at increased probability for a bleeding disorder from those without. While most bleeding questionnaires have been expert-administered, this article presents an evaluation of a newly developed self-administered bleeding score (Self-PBQ, administered by caregivers or children).

This study was set up in three different phases: Phase 1: Translation of existing pediatric bleeding questionnaire items into lay language targeting reading level grade 4 and evaluation of the correlation with expert-administered questionnaires using known patients with von Willebrand disease type I (vWD I). Phase 2: Establishment of the normal range of the bleeding scores with the Self-PBQ in children with and without vWD I. Phase 3: Evaluation of the developed Self-PBQ for screening in first-time referrals (complaint being bleeding symptoms or family history) to the hematology clinic.

Phase I was performed on 38 patients with vWD I and without bleeding disorders (controls) and showed good correlation between the Self-PBQ and expert-administered bleeding scores after several rounds of revisions. Phase 2 using 56 children with and without vWD I showed that all tested controls had bleeding scores of 0-2 which led to the definition of a bleeding score cut-off of >2 being abnormal. Phase 3 in 155 children referred to a hematology clinic showed excellent correlation of the Self-PBQ and the expert-administered PBQ. Of 23 patients referred to vWD I, 5 were assigned a negative BS, all of them had a positive family history of vWD. The negative predictive value was 91%. Median time for completion was 10 minutes.

The same limitations apply to all existing bleeding scores, they perform moderately well to rule out minor bleeding disorders (vWD I). Particularly young children might be missed as they haven’t faced major hemostatic challenges. So far, this bleeding score has only been evaluated for vWD I, it would be highly desirable to test it in other bleeding disorders. Family history seems needed to adequately assess individual patients’ risks for a bleeding disorder which is not part of the Self-PBQ.

 педиатрические симптомы в области гемостаза и дисфункции

Targeting novel mechanisms of pain in sickle cell disease

Tran, H et al, 2017, Blood

In this review article, the authors look at the underlying pathophysiological mechanisms of pain in Sickle Cell Disease and potential strategies/ targets to reduce pain in Sickle Cell Disease.
Section 2. Leukemia and Lymphoma & Bone Marrow Transplantation

Assessment of imatinib as first-line treatment of chronic myeloid leukemia: 10-year survival results of the randomized CML study IV and impact of non-CML determinants

Hehlmann R et al, 2017, Leukemia

Chronic myeloid leukemia (CML)-study IV was designed to explore whether treatment with imatinib (IMA) at 400 mg/day (n=400) could be optimized by doubling the dose (n=420), adding interferon (IFN) (n=430) or cytarabine (n=158) or using IMA after IFN-failure (n=128). Primary goals were the comparative response and long-term survival analyses of the experimental arms vs IMA 400 mg.

Patients (aged 16-88y) were recruited by 210 centers in Germany, Switzerland, and the Czech Republic. From July 2002 to March 2012, 1551 newly diagnosed CML patients in chronic phase were randomized, 1536 were evaluable. Molecular monitoring of all patients was an integral part of the study from the beginning.

After a median observation time of 9.5 years, 10-year overall survival was 82%, 10-year progression-free survival was 80% and 10-year relative survival was 92%. Survival between IMA 400 mg and any experimental treatment arm was not different. Patients reaching the molecular response milestones at 3, 6 and 12 months had a significant survival advantage. For responders, monotherapy with IMA 400 mg provides a close to normal life expectancy independent of the time to response. The authors concluded that survival with CML is currently more determined by patients’ and disease factors than by initial treatment selection.

This study provided long term outcome data for adult CML patients on long term treatment with imatinib. However, pediatric CML patients were started on treatment at a much younger age compared to this cohort and may need to continue treatment for a much longer time, therefore this data cannot directly apply to our patients. If the study can have subgroup analysis of the younger adult patients and their long-term outcome in next 2 decades, that may be more meaningful for applying our patients.

❖ There is increasing data on long-term outcome data in adult CML patients, but there is still a need for more long-term outcome information on pediatric patients.

Characteristics and outcome of patients with therapy-related acute promyelocytic leukemia front-line treated with or without arsenic trioxide

Kayser, S et al, 2017, Leukemia

This study is a retrospective review on the outcomes of patients with therapy-related acute promyelocytic leukemia (APL). Therapy-related APL is rare, and this is a multi-institutional study.

Data on 103 adult patients who were treated between 1991-2015 were collected from 11 study groups and institutions in the US/ Europe. Cox proportional hazards regression model was used to identify prognostic variables for EFS, RFS, and OS.

The study showed difference in outcome based on the APL treatment. None of the patients treated with ATRA alone survived beyond one year. Event-free survival was significantly higher after ATO-based therapy (95%, 95% CI, 82-99%) as compared to CTX/ATRA (78%, 95% CI, 64-87%; P=0.042), if deaths due to recurrence of the prior malignancy were censored.

This was not a prospective study or RCT, therefore possible to have more confounding factors / biases. Further, this study only included adult patients, may not directly be applicable for pediatric oncology patients.

❖ Therapy-related APL appears to have responsiveness to arsenic trioxide based treatments, similar to de novo APL.
CD207+CD1a+ cells circulate in pediatric patients with active Langerhans cell histiocytosis

Carrera Silva, EA et al., 2017, Blood

Langerhans cell histiocytosis (LCH) is seen as a myeloid neoplasm with an important inflammatory component. Pathological CD207+CD1a+ cells are found in the lesions among other cell types. This study investigated whether these cells could also be found circulating in the blood in active (AD) and non-active (NAD) disease patients. Further cytokines were measured that had been previously associated with LCH.

Twenty-two patients with LCH were recruited from a single center about half having active disease (AD) and the other half non-active disease (NAD). Plasma, peripheral blood mononuclear cells, and further biochemical values were collected. Flow cytometry was used to differentiate circulating cells. Cytokines were measured in the plasma. AD patients were compared with NAD and healthy adults. Plasma of AD LCH patients was incubated with healthy donor monocytes.

CD207+CD1a+ cells were found in the peripheral blood of only AD LCH patients but not NAD LCH patients, healthy adults, umbilical cord blood, or patients affected with disseminated juvenile xanthogranuloma (a non-LCH inflammatory disease). CD11b+ cells were also increased. Previously identified cytokines associated with LCH thymic stromal lymphopoietin (TSLP) and transforming growth factor b (TGF-b) plasma levels were increased in patients with AD LCH compared to NAD LCH. When incubating plasma from AD LCH patients with monocytes of healthy adults, appearance of CD11b+ and CD207+ cells was noted. The authors concluded that CD207+CD1a+ cells could be used as markers of AD in LCH.

The sample size used to draw conclusions was small. While the theory is compelling and the findings very promising, they have to be put into the clinical context of LCH patients and measured over time when AD patients become NAD and vice versa.

❖ CD207+CD1a+ cells were associated with active disease in LCH patients which is the first time that circulating LCH cells are identified in the peripheral blood and could serve as a disease marker.

Off-the-Shelf Virus-Specific T Cells to Treat BK Virus, Human Herpesvirus 6, Cytomegalovirus, Epstein-Barr Virus, and Adenovirus Infections After Allogeneic Hematopoietic Stem-Cell Transplantation


Severe viral infection post HSCT are still a major cause of morbidity and mortality. Current antivirals can be ineffective and associated with significant toxicities. Donor-derived virus-specific T cells (VSTs) have been shown to be efficacious but issues include high costs, complex manufacturing and the need of seropositive donors. This study aimed to study VSTs generated from eligible, third-party donors. Phase 2 study using generated banks of VSTs that recognized five common viral pathogens: EBV, adenovirus (AdV), CMV, BK virus, and human herpesvirus 6.

38 patients with 45 drug-refractory infections received the VST +/- antivirals depending on physician preference. A single infusion produced a cumulative complete or partial response rate of 92% (95% CI, 78.1% to 98.3%) overall and the following rates by virus: 100% for BKV (n = 16), 94% for CMV (n = 17), 71% for AdV (n = 7), 100% for EBV (n = 2), and 67% for HHV-6 (n = 3). Infusions were safe, and only two occurrences of de novo graft-versus host disease (grade 1) were observed. Small, single centre, adult study thus unknown if these results can be replicated in pediatric HSCT patients. Not an RCT.

❖ New methods to decreased morbidity and mortality associated with viral infections post HSCT are needed and banked VSTs may be a feasible, safe, and effective approach but more studies needed, in particular RCTs on paediatric populations.
Philadelphia chromosome–like acute lymphoblastic leukemia

Tasian, SK et al, 2017, Blood

❖ This review illustrates the entity of Philadelphia chromosome-like ALL, encountered driver mutations, and potential targeted treatment with tyrosine-kinase inhibitors.

Pathophysiology of Chronic Graft-versus-Host Disease and Therapeutic Targets


❖ An excellent review of chronic GVHD pathophysiology accompanied by illustrations.
A Children’s Oncology Group and TARGET initiative exploring the genetic landscape of Wilms tumor

Gadd, S et al, 2017, Nature Genetics

This study was performed to gain a better understanding of the genetic changes which lead to the development of Wilms tumours. 117 high-risk Wilms tumors (favorable histology tumors which had relapsed, or tumors with diffuse anaplasia were evaluated through whole genome sequencing, analysis of mRNA and miRNA expression, DNA copy number, and DNA methylation status.

Commonly affected genes were those previously known - CTNNB1, DGCR8, DROSHA, MLLT1, MYCN, SIX1, SIX2, TP53, WT1, and AMER1. Other mutations not previously described were also reported here. CTNNB1 was the gene most commonly mutated in Wilms tumors. Germline mutations were found in 10 % of patients with Wilms tumors. Subgroups were proposed based on expression patterns and DNA methylation patterns. While some mutations and copy number variations segregate with these groups, they do not have any clear clinical significance. This study was based on genetic and methylation analysis of Wilms tumor, and did not evaluate protein expression profiles. The extent of DNA methylation analysis was limited. Only "high risk" tumors were investigated.

❖ The results demonstrate that many different genetic changes occur in Wilms tumors, which may converge on common pathways. The epigenetic regulation of transcription in early renal development is likely an important area to explore in future studies.

MIBG avidity correlates with clinical features, tumor biology, and outcomes in neuroblastoma: A report from the Children’s Oncology Group


Neuroblastomas that are MIBG non-avid may have more favorable characteristics compared with MIBG avid tumors. Prior work from this group demonstrated that MIBG non-avid tumors lead to superior event-free survival (EFS) compared to MIBG avid tumors in high-risk disease. The goal of this study was to compare clinical features, tumor biology, and clinical outcomes between patients with MIBG avid and non-avid disease for patients with intermediate- and high-risk disease. This study was conducted by the COG.

Patients had metastatic high- or intermediate-risk neuroblastoma and treated on COG protocols A3973 or A3961. Clinical and biologic features according to MIBG avidity were compared. EFS and overall survival (OS) were compared. Three-hundred and six patients had high-risk disease, and 37 had intermediate-risk disease. Thirty of 343 patients (8.7%) had MIBG non-avid disease. Non-avid tumors were less likely to have adrenal primary tumors, bone metastases, and positive urine catecholamines compared with MIBG avid tumors. Non-avid tumors were more likely to be MYCN amplified and had lower norepinephrine transporter expression. The 5-year EFS for MIBG non-avid tumors was 50% compared with 38.7% for MIBG avid tumors (p=0.028). In high-risk patients, MIBG avidity was the sole adverse prognostic factor for EFS. This analysis was limited to patients with metastatic disease. It is not clear if these results can be generalized to non-metastatic disease.

❖ Patients with MIBG non-avid tumors had superior outcomes compared with MIBG avid disease, despite a higher likelihood of MYCN amplification.
Phase I study of oral sonidegib (LDE225) in pediatric brain and solid tumors and a phase II study in children and adults with relapsed medulloblastoma

Kieran, M et al, 2017, Neuro-Oncology

This is a phase 1/2 study of sonidegib, an inhibitor of upstream components of the sonic hedgehog pathway (Hh, PATCH and Smoothened-driven tumors) in patients with relapsed disease (MB and other solid tumors). For the phase 2 component, this agent was tested in children/adults with relapsed MB.

Phase 1: Children with histologically confirmed recurrent MB, rhabdomyosarcoma, neuroblastoma, hepatoblastoma, or high-grade glioma were eligible. Sonidegib was given once daily orally. Recommended phase 2 dose (RP2D) was the highest tolerated dose with at least 6 patients evaluated. Phase 2: Children and adults with recurrent MB were included for study at the RP2D. Tumor response was assessed every 8 weeks.

Sixty pediatric patients were enrolled (59 on phase 1, 1 on phase 2). Thirty-nine of these patients had MB. For phase 2, 16 adults were enrolled. RP2D was found to be 680 mg/m2/dose. Median treatment exposure was 55 days for pediatric patients and 97 days for adults. Grade 3/4 CPK elevation occurred in 2 pediatric patients and 5 adults, with no evidence of renal dysfunction in the pediatric patients. Three children showed evidence of growth plate closure while on study. Response was seen in 2/60 pediatric patients and 3/16 adult patients (2 CRs and 1 PR), all of whom had MB. All 5 responses were within the SHH group. Both pediatric patients with CR stopped treatment after 9 months. Duration of response was 21 months in one of these patients, and the other remains in remission at 49 months. For the adult responders, duration was 1.6 and 8.7 months for the patients in CR and 4.8 for the patient in PR. Stable disease was seen in 11 patients (5 pediatric, 6 adult, all with MB). All other patients had progressive disease.

Not all tissue was evaluated for SHH activation. The tissue that was evaluated could not differentiate between upstream vs downstream activation of the SHH pathway (sonidegib inhibits in the upstream portion of the pathway). The study did not require tissue from the time of recurrence to assess for additional alterations, so archival tissue may not represent changes as a result of radiation or chemotherapy. It is unclear why some patients had stable disease in the absence of SHH pathway activation.

Sonidegib has activity as a targeted agent for some patients with recurrent SHH MB in this phase 1/2 trial. Toxicities observed include CPK elevation without organ impairment and concern for premature growth plate closure in pediatric patients.

Intracystic interferon-alpha in pediatric craniopharyngioma patients: an international multicenter assessment on behalf of SIOPE and ISPN

Kilday, JP et al, 2017, Neuro-Oncology

Craniopharyngioma is a hypothalamic tumor in children with difficult treatment due to the location of this tumor given the neurologic, endocrine, metabolic and optic complications that can arise from surgery or radiation. Given that most craniopharyngiomas in children are cystic, and the epithelial cells share their origin with squamous epithelium, intracystic interferon (IFN) has been used. Institutional reports have previously been published demonstrating some promise of activity, but this is the first international cohort published. The report describes efficacy with delay or prevention of progression as well as toxicity and clinical outcome. Patients from SIOPE and ISPN from 0-18 years of age with histologically proven or radiologically suspected craniopharyngioma who were treated with intracystic IFN alpha were included for the study.

Fifty-six patients from 21 centers were included. Twenty-two patients had purely or predominantly cystic lesions. Intracystic IFN was first line therapy in 13 patients, with remaining patients treated with cyst fenestration/aspiration, surgical excision, radiation or radioisotope therapy upfront. Seventeen patients had been treated with radiation prior to intracystic IFN with median time to progression 2 years (range 0.3-9 years). Median follow up after IFN therapy was 2.7 years. Five patients died (2 from tumor progression, 1 from endocrinopathy induced electrolyte imbalance and 2 from unrelated infections). IFN seemed to delay time to progression compared to each child’s previous treatment. Further review revealed that delay was seen only in the group with predominantly cystic lesions,
compared to those solid/cystic lesions. Forty-two patients had disease progression following IFN, median time 14 months (range 0-8 years). Twenty-three patients had no adverse side effects.

This is a retrospective study with limited patient numbers. Most patients had been previously treated and different regimens and number of cycles of intracystic IFN were used across different centers. The use of interferon was based on physician and patient preference. This is largely descriptive and it is difficult to make definitive conclusions based on this data.

❖ Intracystic IFN remains a promising agent, and this study shows a prolonged PFS in predominantly cystic lesions compared to previous treatments with less morbidity than current standard therapy.

Perioperative management of hypertensive neuroblastoma: A study from the Italian Group of Pediatric Surgical Oncologists (GICOP).


Retrospective multicenter survey of patients with Neuroblastoma and hypertension from the Italian Registry of Neuroblastoma who underwent surgical resection between 2006 and 2014. Hypertension (HT) defined as BP higher than 99th percentile + 5mm Hg. Of 1126 patients with NB, only 25 patients had HT (2.2%). Of 25 patients with HT and NB, 21 patients underwent surgical resection and were included in the analysis

Median age 15 months, Stage 1 (24%), Stage 2 (43%), Stage 4 (34%), MYCN amplification neg. in 95%, VMA/HVA – 57% normal. 89% of normal BP patients had elevated VMA/HVA versus 43% of HT patients. Norepinephrine only analyzed in 3 high BP patients – all elevated. Renal pedicle involvement – 38%. Renal size – normal in all patients. No evidence of cardiac HT-related complications on preop echo analysis. 86% received an antihypertensive treatment (various agents). Intraoperative HT peaks treated predominantly with alpha1 blockers (5 patients). 6 patients had persistent HTN despite complete tumor resection in 4. Small number of patients, no analysis of renal artery stenosis, renal flow etc. so while no evidence of renal parenchymal size change, incomplete analysis. Heterogenous treatment of HT preoperatively means no definite therapeutic protocol can be recommended.

❖ Given limited number of patients, this retrospective review doesn't add markedly to the literature, however, the incidence of postresection HT and the risk factors for same (renal pedicle involvement) might be helpful for prognostication.
Section 4. Supportive Care, Survivorship, General Pediatrics & other updates

Clinical and Genetic Risk Prediction of Subsequent CNS Tumors in Survivors of Childhood Cancer: A Report From the COG ALTE03N1 Study

Wang, X et al., 2017, Journal of Clinical Oncology

Survivors of childhood cancer are at risk for developing subsequent CNS tumors. Recent adult studies identified inherited predispositions to glioma and meningioma. This study aimed to use genetic information from adult studies and clinical information (including radiation exposure, age) to create a prediction model that identifies survivors of childhood cancer at high or low-risk of developing CNS tumors.

Multicentre COG study ALTE03N1. Eligible participants were individuals diagnosed with a primary cancer at age 21 years or younger who subsequently developed a histologically distinct CNS tumor. For each participant, four controls were selected from a pool of survivors of childhood cancer with no evidence of subsequent neoplasms. All participants provided blood or saliva for germline DNA to identify specific single nucleotide polymorphisms (SNPs).

Phase 1: multivariate analysis to study association between SNPs and subsequent tumors in 82 participants and 228 matched controls. Phase 2: developed prediction models to identify survivors at high or low-risk for subsequent CNS tumors. Phase 3: validated these models in an independent matched case-control sample with 25 participants and 54 controls.

Association between six previously published SNPs and subsequent CNS tumors in survivors of childhood cancer. Prediction model applying genetic variants with primary cancer, sex, cranial radiation had a sensitivity of 87.5%, specificity of 83.5%, PPV was 60.9% and NPV was 95.8% for predicting survivors at highest of lowest risk of subsequent CNS tumour. Validated in independent sample.

Survival bias as only living survivors included in this study. Survivors who already died due to CNS tumour were missed in this study thus underestimation of the effect size for genotypes associated with increased lethality. Slightly different cohort and control groups in the validation group but not statistically significant.

❖ Developed prediction tool can identify childhood cancer survivors at lowest and highest risk of subsequent CNS tumors but need genetic information to apply this tool. Identifying survivors at highest risk may allow for a more intense individualized approach to screening and early detection in this patient population.

Guideline for the prevention of acute chemotherapy-induced nausea and vomiting in pediatric cancer patients: A focused update

Patel, P et al, 2017, Pediatric Blood and Cancer

❖ This article is a focused update of the 2013 guideline for prevention of nausea and vomiting in children receiving chemotherapy, illustrating the role of aprepitant and palonosetron.

Cancer incidence and mortality among young adults aged 20–39 years worldwide in 2012: a population-based study


Population based study with the aim of quantifying the global burden of cancer in young adult patients (20-39y). Young adult cancers have not received the same amount of study as cancer in children or adults.

Authors gathered data on cancer diagnosis and cancer mortality in patients aged 20-39 from 184 different countries using the International Agency for Research on Cancer’s GLOBOCAN 2012 database. They calculated age-standardised incidence and mortality rates at the global and country level. Case fatality rates were approximated by dividing the age standardized mortality rate by the age standardized incidence rate. Results are also presented by geographic region and regional development level (Human development index, HDI).
975,396 cancer cases and 358,392 cancer-related deaths were estimated to have occurred worldwide in 2012. Cancer and cancer-related death was more common among women (male:female ratio of 0.5 and 0.8 for incidence and mortality respectively). There was a higher risk of cancer in young adults than in adolescents (four-fold increase) but lower than in middle-aged adults. Breast cancer was the most common cancer type in young adults worldwide (19.6% of total estimated new cases). Cervical cancer was the second most common cancer type (11.4%). Thyroid cancer was the most common cancer type in young adults in Canada.

The largest contributors to cancer-related deaths worldwide were breast (13.6%), leukemia (10.1%), and liver cancer (10.1%). Breast cancer and cervical cancer were the most common cancers in the low, medium, and high-HDI levels. At very high-HDI levels, breast cancer was most common and cervical cancer was fifth most common. Thyroid cancer, melanoma and testicular cancer were more frequent in very high-HDI regions. Cancers linked to infectious agents were more common in lower HDI settings. Mortality decreased with increasing HDI. Data are based on estimates from GLOBOCAN database and rely on quality of source information. There is a lack of uncertainty intervals provided, which is addressed by the authors. Bone and soft tissue sarcomas were not addressed. Globally, the most common cancers in young adults (20-39y) are breast cancer, cervical cancer and thyroid cancer. Cancer and cancer-related death is more common among women than men. Cancer risk is increased for young adults relative to adolescents.

❖ Young adults with cancer represent an underserved population with cancer. Future research should address the questions of prevention, surveillance and treatment.

REMAP: A Framework for Goals of Care Conversations

Although oncologists frequently have conversations about goals of care with patients, these conversations remain challenging and junior physicians may feel they lack the training to have these discussions effectively and in a timely manner. Because of this, the authors of this paper propose a guiding framework around which to structure the discussion: REMAP – Reframe, Expect emotion, Map out patient goals, Align with goals, Propose a plan.

Reframe refers to setting up the conversation to deliver bad news (often that cancer treatments will not result in a cure) and to gauge a patient’s understanding. Expect emotion involves actively attending to the patient’s emotional response and providing appropriate reflective statements (“I know this is not something you wanted to hear”). The emotional response will guide if the patient is ready to move forward with a plan. Mapping patient values steers the discussion towards the patient’s goals for themselves and reflective statements ensure alignment. Finally, a plan can be proposed to meet those goals, which can simultaneously include further life-sustaining chemotherapy (including clinical trials) and supportive care.

This paper was limited by its adult focus and did not include discussion of some of the essential differences between pediatric and adult end of life care (specifically the challenge of transitioning away from cure-directed therapy). Regardless, many of the concepts are still relevant to the pediatric population.

❖ The REFRAME mnemonic aims to promote patient centered decision making during a very difficult but critical conversation. It emphasizes that the conversation be guided by the patient, allowing oncologists to be flexible in their approach and ultimately aligned with the expectations of the patient in that moment. Ultimately, better communication should lead to better end of life care.
Pediatric-Specific End-of-Life Care Quality Measures: An Unmet Need of a Vulnerable Population


There continues to be a concern about the quality of end of life (EOL) care that both children and adults receive, with upwards of 45% of pediatric patients reporting distressing symptoms such as pain and fatigue at the EOL. To this effect, quality of EOL care warrants ongoing measurement in order to influence best practice guidelines which are currently lacking. This is compounded by the fact that current literature on this topic focuses on adult measures, which may not always be relevant to pediatrics. The authors of this paper explore some of the notable differences in EOL measures between children and adults, propose modifications to existing measures and suggest the formation of a task force to address this gap.

Some notable differences relevant to pediatrics include longer disease trajectories, the higher preference of a death in hospital, desire for high intensity therapy, the difficulty of symptom assessment in young children, variable access to pediatric specific palliative care, and the need to measure bereavement in parents/care givers and siblings. This was a commentary and a paper focused specifically around American measures of quality (some of which are tied to funding. Not necessarily relevant to Canada).

❖ End of life care in pediatrics is notably different than in adults, hence what constitutes ‘good quality care’ is not the same, and should be measured differently to ensure that care provided is in line the needs of children and families.