Original Article

Emergency department and inpatient clinical decision tools for the management of febrile young infants among tertiary paediatric centres across Canada

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Abstract

Objectives: With no nationally-endorsed guidelines and the emergence of newer diagnostic tools, there exists significant variation in the management of febrile infants <90 days. We sought to evaluate the prevalence and content of clinical decision tools (CDTs) for the emergency department (ED) and inpatient management of febrile young infants across Canada.

Methods: We undertook a cross-sectional analysis of febrile young infant CDTs from ED and inpatient units at all 16 Canadian tertiary paediatric hospitals. Additional data were collected using an electronic survey of ED and inpatient representatives, characterizing their clinical settings and diagnostic test availability. Content of all existent CDTs was independently reviewed using list items determined a priori. The primary outcome was the proportion of EDs and inpatient units with CDTs.

Results: Information regarding CDTs was gathered from all 16 EDs and 16 inpatient units. CDTs were infrequently available (9/32, 28%), and were more common in the ED than inpatient setting (8/16 versus 1/16, $P=0.02$). Review of existing CDTs revealed inter-centre differences for inclusion ages, treatment regimens, lumbar puncture recommendations, diagnostic testing and normal laboratory values. Despite availability reported at nearly all centres, C-reactive protein and respiratory virus testing were recommended in 3/9 and 5/9 CDTs, respectively. Procalcitonin testing was available at only 2/16 (13%) centres, and not incorporated into any CDTs.

Conclusions: CDTs for the management of febrile young infants are infrequently available among Canadian tertiary paediatric centres, and rarely incorporate newer diagnostic tests. Heterogeneity among existent CDTs highlights the need for evidence-based unified ED and inpatient national guidelines.

Keywords: *Fever; Guidelines; Sepsis; Septic workup; Serious bacterial infection.*

Approximately 10% of febrile infants younger than 3 months of age harbour potentially life-threatening occult serious bacterial

infections (SBIs) (1,2). In the USA, several externally validated risk-stratification criteria have been developed for identifying

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febrile infants at low risk for SBI (3–5). These criteria have differing inclusion criteria based upon patient age, and provide conflicting recommendations for diagnostic testing, empiric antibiotic treatment and need for hospitalization. Importantly, these risk-stratification criteria also predate the availability of newer diagnostic tests, notably rapid respiratory virus testing (6,7), C-reactive protein (CRP) (8,9), and procalcitonin (8–10), each of which offer an enhanced ability to discriminate between low and high-risk infants.

In Canada, there are currently no nationally-endorsed guidelines for the management of febrile young infants, and no single protocol has been universally adopted. Consequently, there exists significant variation in care (11,12). With the aim of balancing the risk of under-diagnosis and the potential harms of over-investigation, a majority of freestanding US paediatric hospitals have implemented institutional evidence-based clinical decision tools (CDTs) (13). CDTs incorporate best available evidence to improve quality of care, and clinical pathways, clinical practice guidelines and order sets are among the most commonly used CDTs (14–16). CDTs specific to the management of febrile young infants have been shown to reduce practice variation while optimizing clinical outcomes and costs (6).

The primary objective was to evaluate the prevalence of CDTs available to EDs and inpatient units at all 16 Canadian tertiary paediatric centres. Secondary objectives were to 1) compare the content of existing CDTs, and 2) determine the diagnostic tests currently utilized and readily available at each of the study sites. We hypothesized that febrile infant CDTs would be available at most hospitals, but that there would exist significant variability across sites.

METHODS

Study design

We performed a cross-sectional analysis of febrile young infant CDTs from EDs and inpatient units at each of the 16 Canadian tertiary paediatric hospitals. ED site representatives were identified using the email database of site representatives for the Pediatric Emergency Research Canada (PERC) network, a research consortium aimed at facilitating multicentre studies (17). ED site representatives assisted in identifying paediatricians who would be aware of inpatient guidelines from their institutions. Representatives were asked to provide all CDTs specific for the management of febrile young infants below 90 days available at their ED and inpatient units. Content of submitted CDTs was independently evaluated using a 10-item evaluation instrument of list items determined a priori. CDT evaluation items were generated from a previously published study assessing CDT use among US paediatric EDs (13). CDT content that was assessed included inclusion/exclusion criteria, recommended diagnostic testing, low-risk laboratory value

definitions, indications for lumbar puncture and hospitalization, as well as suggested treatment regimens (drug and dosage). Existing CDTs were classified as a clinical pathway (protocol that standardizes management with detailed steps in an algorithm using time-frames or criteria-based progression), clinical practice guideline (framework that provides recommendations for diagnosis and management rather than specific protocols) or order set (predefined collections of medical orders that standardize treatment based on established guidelines) according to recognized definitions (14–16).

To obtain complementary data regarding site- and physician-level characteristics which could be associated with the presence of febrile infant CDTs, representatives from each unit were asked to complete a 14-question self-administered electronic survey between September and October of 2017 (www.limesurvey.org online platform, Hamburg, Germany). Previously published methods were employed for the survey design (18,19) and dissemination (20), which was developed in both English and French and piloted for clarity among 8 medical professionals not involved in the study. All survey fields were mandatory and required complete responses with no missing data. ED and inpatient representatives were asked multiple choice and open-ended questions to characterize their ED and inpatient settings as well as available diagnostic tests. For sites reporting existing CDTs, respondents were asked questions regarding development, implementation and adherence. Participants were not surveyed regarding content of existing CDTs.

Statistical analysis

The primary outcome was the prevalence of CDTs in ED and in inpatient settings. We additionally compared the availability of CDTs between ED and inpatient settings, using a chi-squared test; a two-tailed P-value < 0.05 was considered statistically significant. Descriptive and comparative analyses were performed using STATA v14 software (College Station, TX). The study was approved by the Research Ethics Board of the McGill University Health Centre and by the PERC Scientific Committee.

RESULTS

ED and inpatient unit characteristics

All 16 ED and inpatient study sites responded. Annual ED volume varied among centres with 11/16 (68.8%) reporting ≥40,000 patient visits/year (range <10,000 to >80,000 visits/year). Ten of the 16 (62.5%) EDs were staffed predominantly by physicians certified in Pediatric Emergency Medicine (PEM) by the Royal College of Physicians of Canada (RCPC). Among inpatient units, 10/16 (62.5%) reported ≥40 general paediatric medical beds, (range <10 to >60), and

all were staffed predominantly by physicians RCPC-certified in Paediatrics. Five of 16 (31.3%) EDs reported having dedicated short stay units in which eligible, nonadmitted febrile infants can be observed for ≥ 12 hours, and 11/16 (68.8%) reported access to a medical day hospital offering follow-up to discharged febrile infants. Respondents were asked about access for discharged febrile infants to next-day outpatient follow-up with primary healthcare providers; this was reported to be readily available to a majority of children on weekdays by only 6 of 32 of representatives (18.8%) and on weekends by only 2 of 32 (6.3%).

CDT prevalence across Canadian tertiary paediatric hospitals

Overall, CDTs of any type were available among 9 of 32 units (28.1%) at 8 of 16 (50.0%) hospitals. CDTs were more often available in the ED (8/16, 50.0%) than the inpatient setting (1/16, 6.3%, $P=0.02$); one site had both ED and inpatient CDTs. By CDT type, clinical pathways, practice guidelines and order sets were available at 5/32 (15.6%), 2/32 (6.2%), and 4/32 (12.5%) units, respectively. ED CDTs were available at 1/5 (20.0%), 3/5 (60.0%), and 4/6 (66.7%) of centres with $<40,000$, $40- <70,000$, and $\geq 70,000$ annual visits, respectively. Similarly CDTs were present in 2/6 (33.3%), 3/6 (50.0%),

and 4/6 (66.7%) EDs with $<50\%$, $50- <80\%$, and $\geq 80\%$ PEM-trained physicians.

CDT development and implementation processes

Nearly all CDTs (8/9, 88.9%) were implemented after 2002, and all but one have been updated more recently than 2012. Few reported tracking of provider adherence or audits of impact (3/9, 33%). All eight of the ED CDTs were developed locally by PEM physicians in consultation most frequently with infectious disease specialists (6/8, 75%; Figure 1A). Few ED CDTs were developed in consultation with inpatient physicians (3/8, 37.5%). Strategies most commonly employed to implement CDTs in the ED were the circulation of materials to Department members and creation of Internet-based reference documents (both 5/8, 62.5%; Figure 1B).

Content of existing CDTs

All nine units with existing CDTs submitted these for independent content review and comparative summaries are available in online-only materials. Review of existing CDTs revealed inter-centre differences for inclusion ages, exclusion criteria, and high-risk clinical features and diagnostic testing recommendations (Table 1). All CDTs defined fever as a rectal temperature $\geq 38.0^\circ\text{C}$. Hospitalization and empiric parenteral antibiotic

Figure 1. Clinical decision tool development (upper panel, A) and implementation processes (lower panel, B).

Table 1. Clinical decision tool content by institution

	Hospital sites							
	9	10	11	12	13	14	15	16
Setting	ED	ED	ED	ED	ED	ED	ED	ED
Type of CDT	Clinical pathway	Clinical pathway, Order set	Clinical pathway	Clinical practice guideline	Clinical pathway, Order set	Clinical pathway	Clinical practice guideline	Order set, Medical directive
Age Range for Inclusion	0–90 days	0–60 days	0–3 months	0–90 days	1–90 days	1–90 days	≤60 days	0–90 days
Exclusion Criteria	N/A	Focal infection OR sepsis	Focal infection, sepsis OR recognized viral infection	High risk clinical features	Fever <38°C (rectally), unreliable fever history OR not well-appearing	High risk clinical features	N/A	Temp <38°C, temp not taken rectally, no fever in the last 8 h, CTAS-1 (Resuscitation), first immunization within 48 h, confirmed diagnosis (UTI, meningitis, pneumonia) OR pre-existing condition (cardiac, resp or metabolic)
High-Risk Clinical Features	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
Prematurity	Yes	Yes	No	No	No	No	No	No
Ill/toxic appearance	Yes	Yes	Yes	Yes	Yes	No	Yes	No
Chronic illness	History of previous complicated hospitalization	Perinatal antibiotics, treated for unexplained jaundice, history of previous hospitalization, not discharged with mother, intrapartum history of maternal fever, Group B streptococcus, or maternal antibiotic treatment	Fever >40°C, perinatal antibiotics, active antibiotic therapy or in the last 7 days, immunosuppression, sickle cell anemia	Immunosuppression, sickle cell anemia	Current or previous antibiotics, previous hospitalization, not discharged with mother	Previously in ICU for any reason, previously on antibiotics,	Perinatal antibiotics, not discharged with mother	No
Other						previously been assessed for this fever		No
Temperature grade	≥38°C Rectal	≥38°C Rectal	≥38°C Rectal	≥38°C Rectal	≥38°C Rectal	≥38°C Any body site	≥38°C N/A	≥38°C Rectal
Measurement site	Rectal	Rectal	Rectal	Rectal	Rectal	Any body site	N/A	Rectal
Recommended diagnostic testing	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
CBC	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
UA	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
CRP	No	Yes	No	No	Yes	Yes	No	No
AST/ALT	No	No	No	No	No	No	No	Yes
PCT	No	No	No	No	No	No	No	No

Table 1. Continued

Setting	Hospital sites								
	9	10	11	12	13	14	15	16	16
	ED	ED	ED	ED	ED	ED	ED	ED	Inpatient
Indications for lumbar puncture	If ≤28 days OR high-risk factors, otherwise consider LP	If ≤28 days OR high-risk factors perform LP if stable, otherwise consider LP	If <1 month OR If <3 months and high risk factors OR If ≤3 months with elevated leukocytes or elevated absolute neutrophil count	If ≤28 days OR 29–90 days with signs of severe infection perform LP. If not consider LP according to age, clinical condition and paraclinical assessments	If 1–28 days OR high risk clinical features OR high risk laboratory criteria (elevated CRP, positive urinalysis, infiltrate on CXR)	If 1–28 days OR if 29–90 days and unwell appearing or elevated leukocytes, elevated absolute neutrophil count, elevated CRP	If ≤28 days OR if 29–60 days and high risk clinical features or elevated leukocytes, positive unialysis, positive stool cytology	If ≤28 days OR 29–60 days without bronchiolitis	If ≤42 days and not completed or unsuccessful in ED
Indications for HSV testing and treatment	N/A	If compatible history or symptoms, consider HSV testing	N/A	If <28 days consider HSV testing	If HSV risk factors (maternal infection prior to delivery, intrapartum genital lesions, postnatal contact, vesicular skin rash, eye or mouth manifestations; hepatosplenomegaly, seizures, CSF pleocytosis with negative gram stain, thrombocytopenia, elevated transaminases)	If conjunctivitis or vesicles on skin or month, hepatitis or bleeding from venipuncture sites, seizures or unexplained CSF pleocytosis, maternal genital lesions, prepartum, intrapartum or postpartum OR after 24 h antibiotics, CSF cultures negative and infant fails to improve	N/A	If ≤28 days consider HSV testing	If ≤42 days and not completed or unsuccessful in ED consider HSV testing
Indications for viral testing	N/A	Consider if ≤60 days and no focal infection	N/A	N/A	Consider NP swab if significant respiratory symptoms	Obtain if 1–28 days OR if 29–90 days and clinical picture atypical for bronchiolitis	N/A	Consider for infants ≤28 days	Consider if respiratory symptoms
Indications for chest radiography	If respiratory symptoms, fever ≥39.5°C OR elevated leukocytes	Consider if no focal infection	If tachypnea (RR > 50/min), respiratory distress, abnormal pulmonary auscultation, SaO2<95%, or elevated leukocytes	If respiratory symptoms	If significant respiratory symptoms	If SaO2< 96%, cough, tachypnea OR any respiratory or cardiac findings	If respiratory symptoms	Consider for infants ≤28 days	Consider for infants ≤42 days

Table 1. Continued

Setting	Hospital sites							
	9	10	11	12	13	14	15	16
	ED	ED	ED	ED	ED	ED	ED	Inpatient
Hospitalization and empiric antibiotic treatment criteria	If ≤28 days: Hospitalization and parenteral antibiotics	If ≤28 days: Hospitalization with parenteral antibiotics (within 1 h of physician assessment)	If <1 month: Hospitalization with parenteral antibiotics	If ≤28 days: Hospitalization with parenteral antibiotics (within 1 h of physician assessment)	If ≤28 days: Hospitalization and parenteral antibiotics	If ≤28 days: Hospitalization and parenteral antibiotics	If ≤28 days: Hospitalization with parenteral antibiotics (within 1 h of physician assessment)	If ≤28 days: Hospitalization and parenteral antibiotics
Minimum discharge criteria	N/A	Reliable follow-up within 24 h, adequate caregiver education, drinking well, consider outpatient ceftriaxone	Negative investigation or no investigation needed, viral etiology more likely, reliable parent or guardian AND available telephone and transportation AND ability to consult within 24 h AND absence of neutropenia AND no need for oxygen or IV hydration	Well appearing, low-risk laboratory results, reliable parents, accessibility to a physician within 24 h	Low-risk testing criteria and no barriers to 12-24 h follow-up, tolerating PO, no antibiotics	If clinically well, good social supports, no indication for acyclovir, low-risk laboratory criteria and no focus apparent. Consider discharge with dose of ceftriaxone. infant must be reassessed within 24 h even if remains afebrile or if positive cultures	Well appearing, normal vital signs, well hydrated, tolerating PO, good understanding of education and follow-up plan	N/A

AST/ALT Aspartate transaminase/alanine transaminase; CBC complete blood count; CDT Clinical decision tool; CRP C-reactive protein; ED emergency department; PCT procalcitonin; PO oral route; UA urinalysis.

treatment was recommended for infants ≤ 28 days at all sites. Only two CDTs suggested consideration of outpatient management with intravenous antibiotic coverage (ceftriaxone) for infants > 28 days. Discharge criteria were similar among CDTs with 5/9 (55.6%) specifying that follow-up within 24 hours should be ensured. Antibiotic treatment regimens differed between sites (Table 2).

Diagnostic test availability and CDT recommended testing

Urinalysis and complete blood count (CBC) testing was recommended in all CDTs (Table 3). Despite availability reported at all centres, CRP was rarely incorporated into existent CDTs (3/9, 33.3%). Multiplex respiratory virus testing was included among 5/9 (55.6%) of CDTs, but indication varied by institution depending on patient age and presence of respiratory symptoms. Five of nine CDTs (55.6%) address cerebrospinal fluid (CSF) testing for herpes simplex virus infection (HSV), though with differing recommendations. Liver transaminases, imperfect but potentially important markers for disseminated HSV (6,21,22), were never included among existing CDTs. Procalcitonin, the laboratory test with highest sensitivity and specificity for detection of SBI in febrile young infants (8,10), was reported available at only 2/16 (12.5%) centres, and was not incorporated into any CDTs. CSF testing, which is universally available, was recommended in all CDTs for infants in the first month. Most CDTs (7/9, 77.8%) did not endorse routine lumbar puncture for infants beyond 28 days, however indications and ages for lumbar puncture varied for this older age group between centres, and between ED and inpatient CDTs at the same site. Low-risk laboratory values to guide management were inconsistently included among CDTs, and frequently differed between centres when specified.

DISCUSSION

This cross-sectional analysis of all Canadian tertiary paediatric ED and inpatient units revealed that CDTs for the management of febrile young infants are more frequent in the ED setting, but not widely available overall. Among existent CDTs, there exists considerable inter-institution variation, which differ by inclusion criteria, high-risk clinical and laboratory findings, diagnostic testing, antibiotic treatment regimens, and indications for lumbar puncture. When present, existent CDTs rarely incorporate information on newer, higher performing diagnostic tests, such as procalcitonin (8–10).

The overall paucity of institutional CDTs nationwide was counter to the *a priori* hypothesis of this study. In Canada, evidence for management of febrile young infants was last examined by the Canadian Paediatric Society in 1996 and excluded neonates (23), and there are currently no nationally-endorsed

guidelines. A 2009 study from six Canadian tertiary paediatric EDs demonstrated significant practice variation for febrile young infants, particularly in terms of CSF testing and antibiotic treatment (11). Few existing CDTs, compounded with heterogeneity of those that exist, may in part underlie ongoing practice variation. A study of 37 freestanding US children's hospitals in 2014 similarly found substantial patient- and hospital-level variation in the management of febrile young infants (2). Twenty-one of 33 of these centres (64%) reported institutional clinical practice guidelines, and while they show relative uniformity in recommendations for infants under 1 month, there is significant heterogeneity for the management of older infants (13). In a systematic assessment of all 25 hospitals providing paediatric care in Israel in 2014, only 9 (36%) were found to have written protocols regarding febrile young infants, and significant differences were noted among those in use (24).

Clinical practice guidelines can improve healthcare quality and outcomes while reducing utilization of low-value clinical services (25). Implementation of CDTs for febrile young infants has been shown to reduce the time to diagnostic test collection (26), time to antibiotic administration (26,27), decrease practice variation, and ensure appropriate testing (6). A set of febrile young infant CDTs implemented across a healthcare system in Utah decreased variability with excellent clinical outcomes and reduced costs (6). Importantly, the presence of CDTs does not ensure knowledge of, or adherence to guidelines (28).

In the current context of widespread immunizations and antenatal Group B streptococcus screening/prophylaxis, there has been a shift in SBI epidemiology among febrile young infants (29,30). There is broad consensus on the need for new evidence-based guidelines for the management of febrile young infants (31). Important work remains toward establishing updated national guidelines incorporating newer diagnostic tests (9,32). At present, the highest performing laboratory tests are infrequently incorporated into Canadian CDTs and procalcitonin testing is not widely available. There was a trend towards CDTs existing at higher volume centres with more PEM-trained physicians. CDTs would likely be of particular benefit in smaller, nontertiary and nonpaediatric centres where febrile young infants may be managed less frequently. We have provided summaries of existing CDTs that centres can use to compare or as a starting point for development.

The present study has limitations. We solicited participation from the site representatives most appropriate to comment on febrile young infant management, though it possible that these representatives did not have perfect knowledge of the CDTs in place. As such, we cannot completely exclude the possibility of misclassification resulting from answers provided by site representatives regarding CDT implementation processes. However, we collected CDTs when existent for independent analysis to minimize recall bias of CDT content. Our primary outcomes

Table 2. Treatment regimens by institution

Treatments		Age		Hospital sites						
		9	10	11	12	13	14	15	16 (ED)	16 (Inpatient)
Ampicillin	< 1 month	<ul style="list-style-type: none">If < 1 month with hospitalization: combine with Gentamicin	<ul style="list-style-type: none">If < 1 week: 50 mg/kg/dose q8h	<ul style="list-style-type: none">If < 1 month: 50 mg/kg/dose combine with Gentamicin		<ul style="list-style-type: none">0–7 days and > 2 kg: 50 mg/kg/dose IV q8h. If serious bacterial infection combine with Tobramycin	<ul style="list-style-type: none">1–14 days: admit and start with Gentamicin1–14 days: admit and start with Cefotaxime if evidence of meningitis		<ul style="list-style-type: none">0–7 days: 100 mg/kg/dose q8h combine with Tobramycin0–7 days and Meningitis: 300 mg/kg/day combine with Tobramycin	<ul style="list-style-type: none">≤ 7 days: 100 mg/kg/dose q8h combine with Tobramycin≤ 7 days and Meningitis: 300 mg/kg/day combine with Tobramycin
	> 1 month	<ul style="list-style-type: none">If > 1 month with hospitalization: combine with Cefotaxime		<ul style="list-style-type: none">If ≥ 1 month and < 2 months and suspicion of Listeria combine with Ceftriaxone		<ul style="list-style-type: none">8–28 days and > 2 kg: 50 mg/kg/dose IV q6h. If serious bacterial infection combine with Tobramycin	<ul style="list-style-type: none">15–28 days: admit and start with Cefotaxime		<ul style="list-style-type: none">8–28 days: 75 mg/kg/dose q6h combine with Tobramycin8–28 days and Meningitis: 300 mg/kg/day combine with Tobramycin	<ul style="list-style-type: none">8–28 days: 75 mg/kg/dose q6h combine with Tobramycin8–28 days and Meningitis: 300 mg/kg/day combine with Tobramycin
	No age specification			<ul style="list-style-type: none">50 mg/kg/dose q6h				<ul style="list-style-type: none">Normal renal function: 200 mg/kg/day q6hIf meningitis suspected and normal renal function: 300 mg/kg/day	<ul style="list-style-type: none">50 mg/kg, once (Max 12g/day)	
Cefotaxime	< 1 month		<ul style="list-style-type: none">If < 1 week: 50 mg/kg/dose q12h				<ul style="list-style-type: none">1–14 days: admit and start with Ampicillin if evidence of meningitis		<ul style="list-style-type: none">0–28 days and gram-negative organism is suspected: 75 mg/kg/dose q6h	
	> 1 month	<ul style="list-style-type: none">If > 1 month with hospitalization: combine with Ampicillin				<ul style="list-style-type: none">9–90 days: 50 mg/kg/dose q6h, max 4 g/dose. If serious bacterial infection combine with Ampicillin	<ul style="list-style-type: none">15–28 days: admit and start with Ampicillin		<ul style="list-style-type: none">0–28 days and Meningitis with gram-negative on CSF: 300 mg/kg/day	

Table 2. Continued

Treatments	Age	Hospital sites								
		9	10	11	12	13	14	15	16 (ED)	16 (Inpatient)
Ceftriaxone	No age specification		<ul style="list-style-type: none">50 mg/kg/dose q8h				<ul style="list-style-type: none">Normal renal function: 200 mg/kg/day q6h	<ul style="list-style-type: none">50 mg/kg, once, infuse over 30 min		<ul style="list-style-type: none">Gram-negative organism is suspected: 75 mg/kg/dose q6h
	> 1 month	<ul style="list-style-type: none">If > 1 month with hospitalization		<ul style="list-style-type: none">If ≥ 1 month: 50 mg/kg/dose for 24 h (max 4 g/day) IV or IM.						
		<ul style="list-style-type: none">If 29–60 days: 50 mg/kg with 2^o dose after 24 h (Ambulatory)		<ul style="list-style-type: none">If suspicion of <i>Listeria</i> combine with Ampicillin			<ul style="list-style-type: none">If meningitis suspected and normal renal function: 300 mg/kg/day			<ul style="list-style-type: none">Meningitis with CSF pleocytosis or gram-negative on CSF: 300 mg/kg/day
Gentamicin	No age specification		<ul style="list-style-type: none">Consider IV or IM if not admitted				<ul style="list-style-type: none">Normal renal function: 100mg/kg/day q 24h	<ul style="list-style-type: none">80 mg/kg, once		
	< 1 month	<ul style="list-style-type: none">If < 1 month with hospitalization: combine with Ampicillin		<ul style="list-style-type: none">If < 1 month: 3 mg/kg/dose (max 300 mg/day) combine with Ampicillin			<ul style="list-style-type: none">If meningitis suspected and normal renal function: 100mg/kg/day q12h			
	> 1 month			<ul style="list-style-type: none">If <1 week: 2.5 mg/kg/dose q12h			<ul style="list-style-type: none">1–14 days: admit and start with AmpicillinIf <28 days: 4.5 mg/kg q24h			
Tobramycin	No age specification		<ul style="list-style-type: none">2.5 mg/kg/dose q8h				<ul style="list-style-type: none">If 28–90 days: 7.5 mg/Kg q24h	<ul style="list-style-type: none">2.5 mg/kg, once		
	< 1 month					<ul style="list-style-type: none">0–7 days (gestational age + chronological age>37weeks): 3 mg/kg/dose IV q 18h. If Serious bacterial infection combine with Ampicillin	<ul style="list-style-type: none">Obtain prelevel 0–60 min prior fourth dose if used for more than 3 doses		<ul style="list-style-type: none">0–7 days: 3 mg/kg/dose q18h combine with Ampicillin. Renal dysfunction: obtain prelevel at 24 h before next dose	<ul style="list-style-type: none">0–7 days: 3 mg/kg/dose q18h combine with Ampicillin.

Table 2. Continued

Treatments	Age	Hospital sites								
		9	10	11	12	13	14	15	16 (ED)	16 (Inpatient)
	> 1 month					<ul style="list-style-type: none">8–28 days (gestational age + chronological age>37 weeks) and > 1kg: 2.5 mg/kg/dose IV q8h. If serious bacterial infection combine with Tobramycin			<ul style="list-style-type: none">8–28 days: 5 mg/kg/dose q24h combine with Ampicillin. Renal dysfunction: 3 mg/kg and obtain prelevel at 24 h before next dose9–42 days: 7.5 mg/kg/dose q24h combine with Ampicillin. Obtain prelevel 30 to 60 min prior to third dose.	
Vancomycin	< 1 month						<ul style="list-style-type: none">If 1–28 days and gram-positives in CSF gram stainIf 29–90 days and CSF: >10 WBC, too bloody to interpret, gram-positive in gram stainIf 29–90 days and infant too sick to obtain LP			
Meropenem	< 1 month			<ul style="list-style-type: none">If meningitis suspected				<ul style="list-style-type: none">15 mg/kg, once over 1 hr		
	No age specification									
Meropenem	< 1 month						<ul style="list-style-type: none">If 1–28 days and gram-negative growing in blood or CSF 120 mg/kg/day q8h			
Acyclovir	< 1 month			<ul style="list-style-type: none">If <1 month and certain conditions	<ul style="list-style-type: none">Consider in 0–28 days	<ul style="list-style-type: none">1–28 days: If indicated	<ul style="list-style-type: none">1–28 days and suspicion of HSV		<ul style="list-style-type: none">0–28 days and suspicion of herpes encephalitis: 20 mg/kg/dose q8h	
	> 1 month						<ul style="list-style-type: none">29–42 days and suspicion of HSV			
No age specification			<ul style="list-style-type: none">20 mg/kg/dose q8h	<ul style="list-style-type: none">20 mg/kg/dose		<ul style="list-style-type: none">20 mg/kg/dose q8h	<ul style="list-style-type: none">Consider Acyclovir if any age and unexplained seizures or unexplained CSF pleocytosis			<ul style="list-style-type: none">All infants if concern for HSV infection: 20 mg/kg/dose q8h

CSF Cerebrospinal fluid; ED Emergency department.

Table 3. Laboratory test availability and incorporation in febrile young infant CDTs among Canadian tertiary paediatric EDs

	Hospital sites																Units where available, n (%)
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	
Urinalysis																	
Available at Site	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	16 (100)
Present in CDT	✕	✕	✕	✕	✕	✕	✕	✕	●	●	●	●	●	●	●	●	8 (50)
Low-Risk values in CDT*	✕	✕	✕	✕	✕	✕	✕	✕	○	○	○	○	<10	<10	○	○	2 (13)
CBC white blood cell count																	
Available at Site	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	16 (100)
Present in CDT	✕	✕	✕	✕	✕	✕	✕	✕	●	●	●	●	●	●	●	●	8 (50)
Low-Risk values in CDT†	✕	✕	✕	✕	✕	✕	✕	✕	<20	○	5–15	○	○	5–15	5–15	○	4 (25)
CBC absolute neutrophil count																	
Available at Site	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	16 (100)
Present in CDT	✕	✕	✕	✕	✕	✕	✕	✕	●	●	●	●	●	●	●	●	8 (50)
Low-Risk values in CDT†	✕	✕	✕	✕	✕	✕	✕	✕	○	○	<10	○	○	<10	○	○	2 (13)
AST / ALT																	
Available at Site	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	16 (100)
Present in CDT	✕	✕	✕	✕	✕	✕	✕	✕	○	○	○	○	○	○	○	●	1 (6)
Low-Risk values in CDT	✕	✕	✕	✕	✕	✕	✕	✕	○	○	○	○	○	○	○	○	0 (0)
C-reactive protein																	
Available at Site	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	16 (100)
Present in CDT	✕	✕	✕	✕	✕	✕	✕	✕	○	●	○	○	●	●	○	○	3 (19)
Low-Risk values in CDT‡	✕	✕	✕	✕	✕	✕	✕	✕	○	○	○	○	<20	<20	○	○	2 (13)
Procalcitonin																	
Available at Site	○	○	○	●	○	○	○	○	○	○	○	○	○	○	○	○	1 (6)
Present in CDT	✕	✕	✕	✕	✕	✕	✕	✕	○	○	○	○	○	○	○	○	0 (0)
Low-Risk values in CDT	✕	✕	✕	✕	✕	✕	✕	✕	○	○	○	○	○	○	○	○	0 (0)
Stool cytology																	
Available at Site	○	○	●	●	○	○	●	●	○	○	○	○	●	○	●	○	6 (38)
Present in CDT	✕	✕	✕	✕	✕	✕	✕	✕	○	○	○	○	○	○	○	○	1 (6)
Low-Risk values in CDT§	✕	✕	✕	✕	✕	✕	✕	✕	○	○	○	○	○	○	<5	○	1 (6)

Table 3. Continued

	Hospital sites																Units where available, n (%)
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	
CSF white blood cell count																	
Available at Site	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	16 (100)
Present in CDT	✕	✕	✕	✕	✕	✕	✕	✕	●	●	●	●	●	●	●	●	8 (50)
1–28 days: Low-Risk values in CDT ^a	✕	✕	✕	✕	✕	✕	✕	✕	○	○	○	○	</= 18	</= 14	○	○	2 (13)
29–90 days: Low-Risk values in CDT ^a	✕	✕	✕	✕	✕	✕	✕	✕	○	○	○	○	</= 9	</= 5	○	○	2 (13)
Herpes simplex virus PCR in CSF																	
Available at Site	●	●	●	●	●	●	●	●	○	●	●	●	●	●	●	●	15 (94)
Present in CDT	✕	✕	✕	✕	✕	✕	✕	✕	○	●	○	●	●	●	○	●	5 (31)
Rapid respiratory syncytial virus test																	
Available at Site	○	●	●	○	○	●	○	○	○	●	●	●	●	○	●	●	9 (56)
Present in CDT	✕	✕	✕	✕	✕	✕	✕	✕	○	○	○	○	○	○	○	○	0 (0)
Rapid influenza test																	
Available at Site	○	●	●	○	○	●	○	○	●	●	●	●	●	○	●	●	10 (63)
Present in CDT	✕	✕	✕	✕	✕	✕	✕	✕	○	○	○	○	○	○	○	○	0 (0)
Multiplex respiratory viral test																	
Available at Site	●	○	●	●	●	●	●	●	○	●	●	●	●	●	●	●	14 (88)
Present in CDT	✕	✕	✕	✕	✕	✕	✕	✕	○	●	○	○	○	○	○	○	4 (25)

AST/ALT Aspartate transaminase/alanine transaminase; CBC Complete blood count; CSF Cerebrospinal fluid; CDT Clinical decision tool; HSV Herpes simplex virus; PCR Polymerase chain reaction.

● Available/Included; ○ Not available/Not included; ✕ Site does not have a CDT.

^aUrinalysis microscopy units in white blood cells per high power field.[†]CBC cell line units in 10³ cells/μL.[‡]C-reactive protein units in mg/L.[§]Stool cytology units in white blood cells per high power field.[¶]CSF white blood cell count units in cells/μL.

of interest were the prevalence and content of existing CDTs, and we did not assess adherence, nor clinical outcomes with the differing CDTs. We report on the CDTs in place in the ED and inpatient units of tertiary paediatric centres only, and CDTs presented may not be generalizable to nontertiary or nonpaediatric institutions.

CONCLUSIONS

CDTs designed to standardize the care of febrile young infants are not frequent among Canadian tertiary paediatric centres. Variation among existing CDTs highlights the need for the establishment of national practice guidelines. With data emerging from more recent studies using novel risk-stratification strategies, there is a significant need for updated evidence-based recommendations to inform institutional CDTs. A unified ED and inpatient CDT could help minimize practice variation, improve patient-centred outcomes, and inform future well designed prospective studies.

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