Endocrine Dysfunction Criteria in Critically Ill Children:

The PODIUM Consensus Conference

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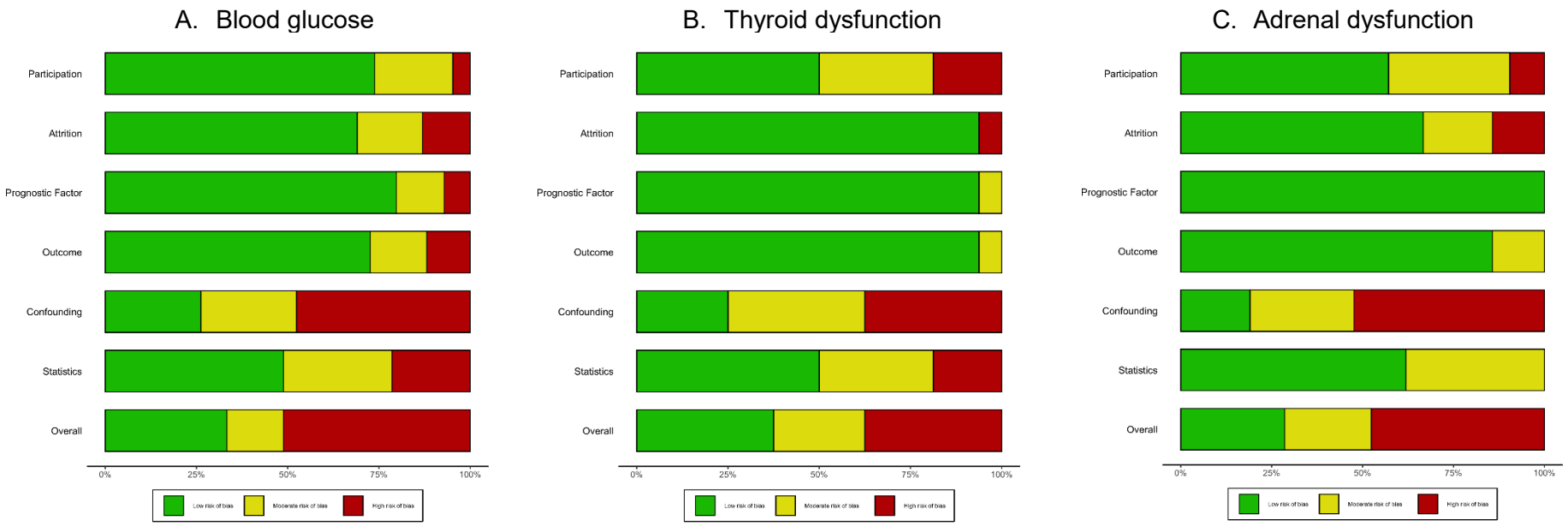
Data Supplement

Table of Contents

Content	Pages
Supplemental Figure 1. Risk of Bias Assessment Summary for Studies Included in the PODIUM Endocrine Dysfunction Systematic Review (n= 121 studies)	2
Supplemental Table 1. Studies Included in the PODIUM Endocrine Dysfunction Systematic Review (n=121 studies)	3-13
Supplemental Table 2. Performance Characteristics for Assessment Tools and Scores for Endocrine Dysfunction in Critically Ill Children (n=121 studies)	14-28
References	29-35
Research Priorities	36

Supplemental Figure 1. Risk of Bias Assessment Summary for Studies Included in the PODIUM Endocrine Dysfunction Systematic Review (n= 121 studies)



Supplemental Table 1. Studies Included in the PODIUM Endocrine Dysfunction Systematic Review (n=121 studies)

Author (yr)	Funding	Study design	Location	No. of sites	Study years	Setting	Data source(s)	Sample size	Recruitment	Age categories[a]	Age details[b]
A. Abnormal glucose homeostasis (n=84)											
Agbenyega (2000)	NGO	Non-randomized/quasi randomized controlled trial	Ghana	1	1995-1995	NR/Unable to determine	Prospective data collection	21	NR/Unable to determine	Children	Ages only provided for individual groups, not total cohort.
Alaei (2012)	NR	Prospective cohort, Observational/ descriptive study	Iran	1	2010-2010	PCICU (cardiac only)	Prospective data collection	379	Consecutive	Neonates Infants Children Adolescents	Mean patient age was 52.09 ± 45.91 months (range, 0.2-180 months)
Al-Moffada (2001)	NR	Retrospective cohort	Saudi Arabia	1	1988-1998	PICU of unknown composition	Chart review	28	Consecutive	Children Adolescents	Mean or median is not provided but state 79% were under 6 years of age
Asilioglu (2011)	NR	Retrospective cohort	Turkey	1	2005-2009	PICU of unknown composition	Chart review	65	Consecutive	Children Adolescents	Mean age 48 months (3 months-18 years)
Babbitt (2013)	NR	Case/control study (case matched), Retrospective cohort	United States	1	NR	PICU of unknown composition	Chart review	88	Consecutive	Infants Children	7.7 +/- 7.9 mths in the study group; 10.7 +/- 10.6 months in the control
Bahloul (2009)	NR	Retrospective cohort	Tunisia	1	1997-2004	Other (Medico-surgical PICU)	Chart review	222	Consecutive	Children Adolescents	Mean age of 7.54 3.8 years (range 0.3-15 years)
Ballweg (2007)	NR	Retrospective cohort	United States	1	NR	PCICU (cardiac only)	Prospective data collection, Other (Review of data base of previous prospective descriptive cohort study)	Of 247 who underwent surgery, neurodevel data availabl e on 188	Consecutive	Neonates Infants	1.01 +/- 0.03 yr; surgery during infancy; follow-up one year later
Ballweg (2009)	NR	Retrospective cohort	United States	1	1998-2003	PCICU (cardiac only)	Other (Database from previous prospective cohort study)	85 of 162 patients with complet	Consecutive	Neonates Infants	1.01 +/- 0.03 yr; surgery during infancy; follow-up one year later

								e data availabl e			
Bhutia (2013)	NR	Prospective cohort	India	1	2009-2010	PICU (non-cardiac only)	Prospective data collection	170	Consecutive	Infants Children Adolescents	NR
Branco (2005)	NR	Prospective cohort	Brazil	1	2001-2003	PICU of unknown composition	Prospective data collection	57	NR/Unable to determine	NR/Unable to determine	33.8 +/- 50.9 months
Burns (2008)	Govt., NGO	Prospective cohort, Retrospective cohort	England	2	1992-2006	NR/Unable to determine	Chart review, Prospective data collection	264 (35 with sympto matic hypogly cemia and 229 neurode velopm e -ntally normal infants)	NR/Unable to determine	Neonates	Median gestational age in the cases was 39.5 weeks and 39 weeks in the controls.
Chiaretti (2002)	NR	Retrospective cohort	Italy	1	1992-2000	PICU of unknown composition	Chart review	122	Consecutive	Infants Children Adolescents	Mean age at the time of head injury was 122.7±45.9 months
Chiaretti (1998)	NR	Retrospective cohort	Italy	1	1993-1996	PICU of unknown composition	Chart review	53	Consecutive	Infants Children Adolescents	Ranging in age between 2 months and 17 years (mean 6.04±4.98 years)
Chisti (2010)	NGO	Retrospective cohort	Bangladesh	1	2005-2006	Other (Special Care Ward)	Chart review	61	Consecutive	Neonates	The paper just refers to infants and babies but does not provide further details.
Chisti (2010)	Govt.	Case/control study (case matched), Retrospective cohort	Bangledesh	1	2005-2006	PICU (non-cariac only), Other (Special Care Ward (different terms used but described as patients requiring ICU support))	Chart review	90	Consecutive	Neonates	Not available
Chong (2015)	Other (Nil funding)	Retrospective cohort	Singapore	1	2003-2013	Mixed PICU (cardiac	Chart review	56	Consecutive	Infants Children	Median 8.6 (5, 11)

						and non-cardiac), ER				Adolescents	
Cochran (2003)	NR	Retrospective cohort	United States	1	2000-2000	PICU of unknown composition, Hospital floor outside the ICU	Chart review	123	Consecutive	Neonates Infants Children Adolescents	Median 4 years (IQR not described)
Day (2008)	NR	Retrospective cohort	England	1	2001-2004	Mixed PICU (cardiac and non-cardiac)	Chart review	97	Consecutive	Neonates Infants Children Adolescents	2.1 [7.2-4.7] IQR years
DeCampli (2010)	NGO	Retrospective cohort	United States	1	2006-2007	PCICU (cardiac only), Operating room (OR)	Chart review	144	Consecutive	Neonates Infants Children	Not available
deFerranti (2004)	NR	Secondary analysis of RCTs, Prospective cohort	United States	1	1988-1992	Operating room (OR)	Chart review	171	Consecutive	Neonates Infants	Median 6 (IGR 1-67) days
Egi (2008)	Govt.	Retrospective cohort	Japan	1	2003-2005	PCICU (cardiac only)	Chart review	40	Convenience	Neonates Infants Children	Not states
El-Sherbini (2018)	NR	Prospective cohort	Egypt	1	2014-2014	PICU of unknown composition	Prospective data collection	60	NR/Unable to determine	Infants Children Adolescents	Median 1.5 years [range 1.9 months to 11 years]
Falcao (2008)	NR	Retrospective cohort	United States	1	2006-2006	Mixed PICU (cardiac and non-cardiac)	Chart review	213	Consecutive	Neonates Infants Children	Median 3.62 months (IQR 0.69 - 27.79)
Faustino (2005)	NR	Retrospective cohort	United States	1	2000-2003	PICU of unknown composition	Chart review	942	Convenience	Neonates Infants Children Adolescents	Median 3.2 years (IQR 0.3 - 10.8 years)
Faustino (2019)	Govt.	Secondary analysis of RCTs	United States, Canada, United Kingdom, Australia	35	2012-2016	PICU (non-cardiac only)	Prospective data collection	698	Random	Infants Children Adolescents	Cases: median 3.6 yrs (IQR 0.9-10.4); Controls: median 4.4 yrs (IQR 1.3-11.7)
Filho (2016)	NR	Retrospective cohort	Brazil	1	2005-2010	NR/Unable to determine	Chart review	105	Consecutive	Children Adolescents	Age, yrs 8 (IQR:4-12)
Fu (2019)	Other (Authors reported receiving	Retrospective cohort, Observational/ descriptive study	China	1	2012-2018	PICU (non-cardiac only)	Chart review	213	Convenience	Children Adolescents	52.0 months (IQR: 20.5-86.5)

	no funding for study)										
Fu (2017)	Other (Nil funding)	Retrospective cohort	China	1	2012-2014	Mixed PICU (cardiac and non-cardiac)	Chart review	109	Consecutive	Infants Children Adolescents	Median 54 (17-82) months
Ghafoori (2008)	NR	Case/control study, Retrospective cohort	United States	1	2001-2005	PCICU (cardiac only)	Chart review	24	Other (Infants and children with mediastinitis after CHD surgery)	Neonates Infants Children Adolescents	7.0 ± 10.9 in mediastinitis group
Gottschlich (2002)	NGO	Randomized controlled trial (RCT), Cross-over RCT, Pragmatic RCT	United States	1	1991-2001	PICU of unknown composition	Prospective data collection	72	Consecutive	Neonates Infants Children	Not stated
Graf (1995)	NR	Retrospective cohort	United States	1	1980-1991	PICU (non-cardiac only), Other (General wards)	Chart review	194	Consecutive	Neonates Infants Children Adolescents	Median 2.6 years (range 5 months - 18 years)
Hale (2018)	NR	Retrospective cohort, observational/ descriptive study	United States	1	2006-2013	NR/Unable to determine	Registry	1814	Other (Children with Trauma Registry data meeting inclusion/ exclusion criteria)	Neonates Infants Children Adolescents	6.17 ± 5.96, seizure group; (n=121) 7.67 ± 5.66, no seizure group (n=1693)
Hirshberg (2008)	NGO	Retrospective cohort	United States	1	2003-2003	Mixed PICU (cardiac and non-cardiac)	Chart review	863	Consecutive	Neonates Infants Children Adolescents	Median 2 years (IQR 0.4, 7.1 years)
Hu (2017)	Govt.	Case/control study (case matched)	China	1	2010-2016	NR/Unable to determine	NR/Unable to determine	296	NR/Unable to determine	Children Adolescents	Mean 8.11 yrs, SD 3.21
Hu (2018)	Govt.	Case/control study (case matched), Retrospective cohort	China	1	2013-2016	NR/Unable to determine	Chart review, EMR query, Registry	111 AKI patients with 111 matched controls	Consecutive	Infants Children	Not provided for whole cohort, only for those with and without AKI. Age at surgery (mo), median (IQR): no AKI, 36 (12,72); AKI 12 (4,45)
Huang (2012)	NR	Retrospective cohort	China	1	2010-2010	Mixed PICU (cardiac and non-cardiac)	Chart review, Other (Existing database)	233	NR/Unable to determine	Neonates Infants	Median 5 months (IQR 3-7)
Ichikawa (2017)	NR	Retrospective cohort	Japan	22	2004-2011	NR/Unable to determine	Registry	119	Consecutive	Neonates Infants Children Adolescents	Mean 8 years, SD 4.6 years
Jallow (2012)	Govt. NGO	Prospective cohort	The Gambia	1	1997-2009	Hospital floor	Prospective data collection	2901	NR/Unable to determine	Infants Children	Median 45 months [IQR 27-71]

						outside the ICU				Adolescents	
Jeschke (2014)	Govt. NGO	Prospective cohort	United States	1	NR	Other (Burns PICU)	Prospective data collection	230	NR/Unable to determine	NR/Unable to determine	Mean 7.3 years; SD 5.5
Jeschke (2010)	Govt. NGO	Secondary analysis of RCTs	United States	1	2002-2009	Other (Burns PICU)	Prospective data collection	208	Random	NR/Unable to determine	Mean 9 years, SD 6 yrs
Kan (2009)	NR	Cross-sectional study	Malaysia	1	2001-2006	Other (Neurosurgical ICU)	Chart review	146	NR/Unable to determine	Children Adolescents	Mean 11.7 years, SD 4.2 yrs
Khajavi (2018)	NR	Retrospective cohort	Iran	1	2012-2015	PICU (non-cardiac only)	Chart review, EMR query	201	Consecutive	Neonates Infants Children	Mean 3.16 months; SD 8.95
Khan (2015)	NR	Cross-sectional study	Pakistan	1	2011-2012	NR/Unable to determine	Chart review	150	Convenience	Infants Children Adolescents	Median 24 months (range: 1-147 months)
Klein (2008)	Other (No source of funding)	Retrospective cohort	United States	1	2001-2005	PICU (non-cardiac only)	Registry	1550	Consecutive	Neonates Infants Children Adolescents	Mean, 83.5 months; median, 49.7 months
Kraft (2014)	Govt. NGO	Secondary analysis of RCTs	United States	1	2002-2008	Other (Burns PICU)	Prospective data collection	106	Random	Neonates Infants Children Adolescents	Mean 9.3 years, SD 4.9 yrs
Krueger (2015)	NGO	Prospective cohort, Observational/ descriptive study	Switzerland	1	2007-2008	PICU of unknown composition	Prospective data collection	150	Consecutive	Neonates Infants	Mean age at surgery was 2.8 months (0.1-10.7 months). Then Children were examined at a mean age of 4.3 years (3.8- 4.7 years).
Kyle (2010)	NR	Retrospective cohort	United States	1	2005-2006	PICU of unknown composition	Chart review	110	NR/Unable to determine	Neonates Infants Children Adolescents	Median 11.2 years (Range 0.1 – 21.3)
Lee (2016)	Govt. NGO	Prospective cohort	China	1	2011-2012	PICU of unknown composition	Prospective data collection	295	Consecutive	Infants Children	Mean 2.06 years, SD 0.08 years
Leite (2013)	Govt.	Prospective cohort	Brazil	1	2006-2008	Mixed PICU (cardiac and non-cardiac)	Prospective data collection	221	Consecutive	Infants Children Adolescents	Median 2.3 years (IQR: 0.6-13.5)
Li (2015)	NR	Retrospective cohort	China	1	2008-2011	PICU (non-cardiac only)	Chart review	1349	Consecutive	Neonates Infants Children Adolescents	NR

Lodha (2009)	NR	Retrospective cohort	India	1	NR	PICU (non-cardiac only)	Chart review	209	NR/Unable to determine	Infants Children Adolescents	N/A
Lou (2010)	NR	Retrospective cohort	China	1	2009-2009	PCICU (cardiac only)	Chart review	100	Consecutive	Neonates Infants	
Maegaki (2015)	Govt.	Retrospective cohort	Japan	25	2005-2010	PICU of unknown composition, ER	Registry	201	Consecutive	Infants Children Adolescents	1-12m, 29/201; 13-24m, 48/201; 25-48m, 63/201; 49-188m, 61/201
Mahmoud (2018)	NR	Prospective cohort	Egypt	1	2015-2016	NR/Unable to determine	Chart review, Prospective data collection	105	NR/Unable to determine	Infants Children Adolescents	Mean 38.71 months; SD 48.6
Marsillio (2015)	NGO	Retrospective cohort	United States	1	2008-2012	Mixed PICU (cardiac and non-cardiac)	Chart review	116	Consecutive	Neonates Infants Children Adolescents	Median 0.8 years (0.1-3.8 years)
Marton (2007)	NR	Retrospective cohort	Italy	1	1986-2006	PICU (non-cardiac only)	Chart review	16	Consecutive	Neonates Infants	Mean 7 m, range 3-12 m
Melo (2010)	Govt.	Retrospective cohort	France	1	2000-2005	PICU (non-cardiac only)	Chart review	286	Consecutive	Neonates Infants Children Adolescents	Mean 7y (SD, 4.4y)
Melo (2009)	NGO	Cross-sectional study	France	1	2000-2005	PICU (non-cardiac only)	Chart review	58	Consecutive	Neonates Infants Children	Mean 2.8y (SD, 1.4y)
Moga (2011)	Other (Departme nt of Critical Care, Hospital for Sick Children)	Retrospective cohort, Observational/ descriptive study	Canada	1	2006-2007	PCICU (cardiac only)	Chart review	772	Consecutive	Neonates Infants Children Adolescents	NR
Nagao (2008)	Govt.	Retrospective cohort	Japan	>4	1998-2002	PICU of unknown composition, Hospital floor outside the ICU, ER, Other (Pediatric practice)	Other (Survery to sites)	184	Convenience	Neonates Children Adolescents	Unable to determine for the sample included in the multivariable logistic regression analysis
Narci (2009)	NR	Retrospective cohort	Turkey	1	2006-2008	ER	Chart review	74	Consecutive	Children Adolescents	Mean 7.0y (SD, 4.34)
Nayak (2013)	NGO	Retrospective cohort	United Kingdom	1	2003-2006	Mixed PICU (cardiac	Chart review, EMR query	1763	Consecutive	Neonates Infants Children	Median 1.1 years (IQR: 0.1-5.8)

						and non-cardiac)				Adolescents	
O'Brien (2010)	NR	Retrospective cohort	United States	1	2002-2007	PCICU (cardiac only)	Chart review	992	Consecutive	Neonates Infants Children Adolescents	Age (y) 2.7 +/- 4.2
Odek (2018)	NR	Retrospective cohort	Turkey	1	2008-2013	Mixed PICU (cardiac and non-cardiac)	Chart review	126	Consecutive	Neonates Infants Children Adolescents	Median 10 months, range 1.5-168 months
Ognibene (2011)	NR	Retrospective cohort	United States	1	2006-2006	Mixed PICU (cardiac and non-cardiac)	Chart review, EMR query	616	Consecutive	Neonates Infants Children Adolescents	NR
Paret (1999)	Other (Reported as none)	Retrospective cohort	Israel	1	1990-1993	PICU (non-cardiac only)	Chart review	61	Consecutive	Children Adolescents	Median 6y (range, 1-15)
Piastra (2017)	NGO, Other ("departmental resources")	Prospective cohort, Observational/ descriptive study	Italy	1	2009-2011	PICU (non-cardiac only), Operating room (OR)	Prospective data collection	352	Consecutive	Infants Children Adolescents	Mean age, 68 ± 66; median age 38 [9.0; 128.0]
Plubrukarn (2003)	NR	Retrospective cohort	Thailand	1	1993-2001	ER	Chart review	72	Consecutive	Infants Children Adolescents	Median 28m (range, 3m-14y)
Polito (2008)	NR	Retrospective cohort	United States	1	2003-2003	PCICU (cardiac only)	Other (Data gleaned from larger 2003 data set designed for a different investigation)	378	Other (Patients in primary data set with RACHS-1 >/=3)	Neonates Infants Children Adolescents	0.61 [0.01-14.41] [10%tile-90%tile]
Preissig (2009)	NR	Observational/ descriptive study	United States	1	2006-2007	PICU (non-cardiac only)	Chart review	155	Consecutive	Infants Children Adolescents	NR
Rake (2010)	NGO	Retrospective cohort	United States	1	2000-2005	PICU (non-cardiac only)	Chart review, EMR query, Registry	101	Consecutive	Neonates Infants Children Adolescents	Mean 8.4 years (SD 6.6)
Rhine (2012)	NR	Retrospective cohort	United States	1	NR	PICU of unknown composition	Chart review	35	NR/Unable to determine	Neonates Infants Children	NR
Seyed Sadaat (2012)	NR	Retrospective cohort	Iran	1	2007-2011	PICU of unknown composition	Chart review	122	Consecutive	Children Adolescents	
Srinivasan (2004)	NGO	Retrospective cohort	US	1	2001-2002	PICU (non-cardiac only)	Chart review, EMR query	152	Consecutive	Infants Children Adolescents	
Tala (2014)	Govt.	Retrospective cohort	United States	1	2007-2010	Mixed PICU (cardiac	Chart review	789	Consecutive	Neonates Infants	

						and non-cardiac)				Children Adolescents	
Toro-Polo (2018)	NR	Retrospective cohort, Observational/ descriptive study	Peru	1	2012-2013	PICU (non-cardiac only)	Chart review	552	Convenience	Infants Children Adolescents	
Tude Melo (2010)	NGO	Retrospective cohort	France	1	2000-2005	ER	Chart review	315	Consecutive	Neonates Infants Children Adolescents	
Ulate (2008)	NR	Retrospective cohort	United States	1	2006-2007	Mixed PICU (cardiac and non-cardiac)	Chart review	177	Consecutive	Neonates Infants Children Adolescents	
Uleanya (2017)	NR	Prospective cohort	Nigeria	1	2014-2015	ER	Prospective data collection	300	Consecutive	Infants Children	
Wintergerst (2006)	NGO	Retrospective cohort	United States	1	2003-2004	Mixed PICU (cardiac and non-cardiac)	Chart review	1094	Consecutive	Neonates Children Adolescents	
Yates (2006)	NR	Retrospective cohort	United States	1	2002-2004	PCICU (cardiac only)	Chart review	184	Consecutive	Neonates Infants	
Yokochi (2016)	NR	Retrospective cohort	Japan	1	2004-2014	PICU	Chart review	213	Consecutive	Infants Children Adolescents	
Yung (2008)	NGO	Prospective cohort	Australia, New Zealand	9	2004-2004	Mixed PICU (cardiac and non-cardiac)	Prospective data collection	409	Consecutive	Neonates Infants Children Adolescents	
Zant (2016)	NR	Retrospective cohort	Germany	1	2008-2011	Other (Liver transplant patients)	Chart review	46	Consecutive	NR/Unable to determine	
B. Thyroid dysfunction (n=18)											
Aggarwal (2020)	NR	Retrospective cohort, Observational/ descriptive study	United States	1	2011-2016	ER	Registry	414	Consecutive	Neonates Infants Children Adolescents	14.7 +/-3.89, normal TSH ;15.1 +/- 3.00, abnormal TSH
Anand (1994)	NR	Case/control study (case matched)	India	1	NR	NR/Unable to determine	Prospective data collection	60	NR/Unable to determine	Infants	Mean 4.33 +/- 3.28 mos
Cantinotti (2013)	NR	Prospective cohort	Italy	1	2009-2011	PCICU (cardiac only)	Prospective data collection	162	NR/Unable to determine	Neonates Infants Children	NR
Dagan (2006)	NR	Prospective cohort	Israel	1	NR	NR/Unable to determine	Prospective data collection	20	NR/Unable to determine	Neonates	Not available

denBrinker (2005)	Industry	Prospective cohort	Netherlands	1	1997-2000	PICU of unknown composition	Prospective data collection	69	NR/Unable to determine	Neonates Infants Children Adolescents	Not available
El-Ella (2019)	NR	Prospective cohort, Observational/ descriptive study	Egypt	1	2017-2017	Mixed PICU (cardiac and non-cardiac)	Prospective data collection	70	NR/Unable to determine	Infants Children Adolescents	19.5 [1.3---180] months
Gielen (2012)	Govt.	Secondary analysis fo RCTs	Belgium	1	NR	PICU of unknown composition	Prospective data collection	588	Consecutive	Neonates Infants Children Adolescents	Not stated in the paper
Goldsmit (2011)	NR	Prospective cohort	Argentina	1	2007-2008	Mixed PICU (cardiac and non-cardiac)	Prospective data collection	94	Consecutive	Neonates	Enrolled at birth
Gottschlich (2002)	NGO	Randomized controlled trial (RCT), Cross-over RCT, Pragmatic RCT	United States	1	1991-2001	PICU of unknown composition	Prospective data collection	72	Consecutive	Neonates Infants Children	Not stated
Hebbar (2009)	NGO	Prospective cohort	United States	1	2005-2006	PICU (non-cardiac only)	Prospective data collection	73	NR/Unable to determine	Infants Children Adolescents	Median 72 months, range 3-228
Jacobs (2019)	Govt. NGO	Secondary analysis of RCTs	Belgium, Netherland	3	2012-2015	Mixed PICU (cardiac and non-cardiac)	Prospective data collection	982	Consecutive	Neonates Infants Children Adolescents	Median 1.92 years [0.35-7.57]
Marks (2009)	NGO	Prospective cohort	Canada	1	2003-2005	PCICU (cardiac only)	Prospective data collection	21	Consecutive	Children	Mean 57.7 (SD, 36.2)
Marwali (2019)	NR	Secondary analysis of RCTs	Indonesia	1	2013-2014	PCICU (cardiac only)	Other (Data base generated in the OTICC RCT)	203	Other (Data base generated in the OTICC RCT)	Neonates Infants Children	Median [IQR] provided for each of 4 groups
Merchant (2008)	NR	Prospective cohort	USA	1	2005-2005	PCICU (cardiac only)	Prospective data collection	20	Consecutive	Neonates Infants Children	Mean 9.0m (SD, 11.3)
Sayarifard (2018)	NGO	Prospective cohort, Observational/ descriptive study	Iran	1	2016-2017	PICU of unknown composition	Prospective data collection	35	Convenience	Infants Children Adolescents	2 years (SD: ± 3.8 years, range: 4 months - 15 years)
Suvarna (2009)	NR	Case/control study (case-matched)	India	1	NR	PICU of unknown composition	Chart review, Prospective data collection	30	Consecutive	Infants Children	
Talwar (2012)	NR	Prospective cohort	India	1	2008-2008	Mixed PICU (cardiac and non-cardiac)	Prospective data collection	100	Consecutive	Neonates Infants Children	

Yildizdas (2004)	NR	Case/control study (case matched)	Turkey	1	2000-2002	PICU of unknown composition	Prospective data collection	102	NR/Unable to determine	Infants Children	
C. Adrenal dysfunction (n=22)											
Amstadter (2011)	Govt., NGO	Prospective cohort	United States	1	2002-2004	NR/Unable to determine	Prospective data collection	103	Consecutive	Children Adolescents	14.63 +/- 6.18 years
Balbao (2014)	NGO	Prospective cohort	Brazil	1	2009-2011	PICU of unknown composition	Prospective data collection	34	Consecutive	Neonates Infants Children Adolescents	Median age was 34 months (range 0.7-201 months)
Bekhit (2019)	NR	Prospective cohort	Egypt	2	NR	PICU of unknown composition	Prospective data collection	81	NR/Unable to determine	Infants Children	Total cohort not summarized, but generally median 8.5-10 months (IQR 3-30 months)
Bone (2002)	NR	Prospective cohort	England	2	1997-1998	PICU of unknown composition	Prospective data collection	65	Consecutive	Infants Children Adolescents	Median age 2.5 years (range 0.2 - 15 years)
Garcia (2010)	NR	Prospective cohort	United States	1	2007-2008	PCICU (cardiac only)	Prospective data collection	21	Consecutive	Neonates	Median 7 days (IQR: 1 - 30 days)
Gottschlich (2002)	NGO	Randomized controlled trial (RCT), Cross-over RCT, Pragmatic RCT	United States	1	1991-2001	PICU of unknown composition	Prospective data collection	72	Consecutive	Neonates Infants Children	Not stated
Hatherill (1999)	NR	Prospective cohort	England	1	1996-1997	PICU of unknown composition	Prospective data collection	33	Consecutive	Infants Children Adolescents	Median 109 months (range 5 to 192 months)
Hebbar (2009)	NGO	Prospective cohort	United States	1	2005-2006	PICU (non-cardiac only)	Prospective data collection	73	NR/Unable to determine	Infants Children Adolescents	Median 72 months, range 3-228
Levy-Shraga (2016)	NR	Retrospective cohort	Israel	1	2006-2013	Mixed PICU (cardiac and non-cardiac)	Chart review	99	NR/Unable to determine	Neonates Infants Children Adolescents	Median 2 months, IQR 0.5-19
Lichtakowicz-Krynska (2004)	Govt.	Prospective cohort	United Kingdom	2	NR	PICU of unknown composition	Prospective data collection	60	NR/Unable to determine	NR/Unable to determine	Group A: mean 4.4 yrs (range 0.5-14.4); Group B mean 4.1 yrs (range 0.3 - 16.3)
Menon (2002)	NGO	Prospective cohort, Observational/ descriptive study	Canada	1	1997-1997	Mixed PICU (cardiac and non-cardiac)	Prospective data collection	13	Consecutive	Neonates Infants Children	1 day to 16 years
Menon (2010)	Govt.	Prospective cohort,	Canada	7	2005-2008	Mixed PICU (cardiac	Prospective data collection	381	Consecutive	Neonates Infants	4.01 years (IQR, 0.56-12.98),

		Observational/ Descriptive study				and non-cardiac)				Children Adolescents	
Menon (2018)	Govt.	Secondary analysis of RCTs	Canada	7	2014-2016	Mixed PICU (cardiac and non-cardiac)	Prospective data collection	30	Convenience	Neonates Infants Children Adolescents	Not stated
Nichols (2017)	Govt., NGO	Retrospective cohort	US	1	2013-2013	PICU (non-cardiac only)	Chart review	70	Consecutive	Infants Children Adolescents	No summary of entire cohort, but: median 74-77, IQR 19-174
Pizarro (2005)	Govt.	Prospective cohort	Brazil	1	2001-2003	PICU of unknown composition	Prospective data collection	57	Consecutive	Infants Children Adolescents	27 months (range: 1-213 months)
Samransamruajkit (2007)	Govt., NGO	Prospective cohort	Thailand	1	2005-2005	PICU of unknown composition	Prospective data collection	16	Consecutive	Infants Children Adolescents	Listed as 2 groups: median 3.5 mos (n=6), and 24 mos (n=10)
Sarthi (2007)	Govt., Other (Indian Council of Medical Research)	Prospective cohort	India	1	2004-2005	PICU of unknown composition	Prospective data collection	30	Consecutive	Infants Children	NR
Sasser (2012)	NR	Retrospective cohort	United States	1	2009-2010	PCICU (cardiac only)	Chart review, EMR query	41	Consecutive	Neonates	Median 6 Days (Range 1-38)
Singhi (2006)	NR	Prospective cohort	India	1	NR	ER	Prospective data collection	30	Consecutive	Infants Children	
van den Akker (2009)	Industry	Prospective cohort	Netherlands	1	NR	PICU of unknown composition	Prospective data collection	23	NR/Unable to determine	Infants Children Adolescents	
Verweij (2012)	NR	Retrospective cohort	Netherlands	1	2005-2008	Mixed PICU (cardiac and non-cardiac)	Chart review	62	Consecutive	Neonates Infants Children	
Yehya (2016)	Govt. NGO	Retrospective cohort	US	1	2011-2015	PICU (non-cardiac only)	Prospective data collection	155	Consecutive	Infants Children Adolescents	

Abbreviations: Govt., government; NGO, nongovernmental organization; NR, not reported; PICU, pediatric intensive care unit; PCICU, pediatric cardiac intensive care unit; IQR, interquartile range; SD, standard deviation; wks, weeks; mo, months; yr, years

[a]Neonates (0 to 30 days), Infants (31 days to < 1 year), Children (1 year to < 12 years), Adolescents (12 years to < 18 years)

[b]Data are presented as mean (SD) or median [interquartile range or range]

Supplemental Table 2. Performance Characteristics for Assessment Tools and Scores for Endocrine Dysfunction in Critically Ill Children (n=121 studies)

Author (yr)	Score/assessment tool	Is this a study of score/tool derivation or validation?	Inclusion criteria	Timing of score/tool assessment	Outcomes	Performance characteristics
A. Abnormal glucose homeostasis (n=84)						
Agbenyega (2000)	Glucose concentration	Derivation	Other (Severe malaria)	On admission to hospital	Other (Elevated lactate disposal)	Other: Pearson's correlation
Alaei (2012)	Glucose concentration	NR	PCICU population (only cardiac)	Measurements of blood glucose level was collected on postoperative days 1, 2, 3, and 7.	Mortality, Organ-specific outcomes/residual morbidity	aOR: Patients with severe hyperglycemia showed a significantly higher Mortality rate (16/64 deaths [25%] vs. 13/315 deaths [4.12%]; P<0.001]) and more morbidities (16/64 [25%] vs. 43/315 [13.65%]; P = 0.022).
Al-Moffada (2001)	Glucose concentration	Derivation	Other (Near drowning and drownings)	In the emergency room prior to PICU admission	Mortality, Functional outcomes /residual morbidity	Other: Chi squared test comparing proportions of bad neurologic outcomes in those with Glucose < 10 mmol/L versus > 10 mmol/L
Asilioglu (2011)	Glucose concentration	Derivation	Other (Traumatic brain injury patients)	On admission to PICU	Mortality, Functional outcomes /residual morbidity	Other: Comparison of means of glucose values in those with good versus bad outcomes
Babbitt (2013)	Glucose concentration	Derivation	Other (Intracranial injury)	Initial glucose (not clear ER versus PICU)	Other (Intracranial hemorrhage)	Se: Using a serum glucose level of greater than 120 mg/dL as the cutoff for hyperglycemia, yielded a sensitivity of 64% and specificity of 91% for intracranial injury
Bahloul (2009)	Glucose concentration	Derivation	Other (Traumatic Brain Injury)	On admission to PICU	Mortality	Other: Blood glucose level on admission was significantly higher among children who died (11.2 +/- 7 mmol /l vs. 8.7 +/- 4 mmol/L; p = 0.001)
Ballweg (2007)	Glucose concentration	Other (Description of glucose conc vs neurodevelopmental outcomes)	PCICU population (only cardiac)	All glucose measurements during PCICU stay	Other patient-centered outcomes, Other (Bayley Scales of Infant Development-II)	Other: No statistically significant correlations; glucose not important in univariable modeling
Ballweg (2009)	Glucose concentration	Other (Correlations of glucose conc with outcomes)	PCICU population (only cardiac), Other (Stage I palliation for various forms of single ventricle with arch obstruction.)	All glucose measurements during first 48 hrs	Other patient-centered outcomes, Other (Bayley Scales of Infant Development-II)	Other: Pearson's correlation. no statistically significant correlations for glucose during univariant modeling

Bhutia (2013)	Glucose concentration	Derivation	General PICU population (only non-cardiac)	At admission and daily for 7 days or till ICU discharge (whichever was earlier)	Mortality, Outcomes related to MODS, Other (Duration of stay in the PICU)	aOR: Of hyperglycemia >126 mg/dL and MODS: 2.96 (1.1-8.0); p= 0.033; aOR of hyperglycemia > 180 mg/dL and Mortality: 2.67 (1.1-6.5), p=0.031 and aOR of hyperglycemia > 200 mg/dL and Mortality: 3.4 (1.3-8.7); p=0.042
Branco (2005)	Glucose concentration	Derivation	Other (Septic shock)	Peak glucose level during the PICU admission	Mortality	Se: The best peak glucose level for predicting death in children with sepsis was 178 mg/dL (sensitivity, 0.714) Sp: The best peak glucose level for predicting death in children with sepsis was 178 mg/dL (specificity, 0.724) AUROC: The area under the receiver operator curve for peak glucose level and Mortality rate was 0.754 Other: The relative risk of death in patients with peak glucose levels of >178 mg/dL was 2.59 (range, 1.37-4.88).
Burns (2008)	Glucose concentration	Derivation	Other (Neonates)	Neonatal hypoglycemia	Functional outcomes /residual morbidity	Other: All except 1 of the infants with early transient hypoglycemia had outcomes within the reference range or mildly abnormal outcomes using a standardized neurologic assessment and Griffiths' Mental Developmental Scales
Chiaretii (2002)	Glucose concentration	NR	Other (Head injury)	Admission to PICU	Functional outcomes /residual morbidity	aOR: 1.55, 95% CI:1.01; 2.33, P value = 0.04
Chiaretti (1998)	Glucose concentration	Derivation	Other (Head injury)	On admission to PICU	Functional outcomes /residual morbidity	Other: Correlation but no R value provided. "There seemed to be a negative correlation between initial blood glucose level and outcome."
Chisti (2010)	Glucose concentration	Derivation	Other (Those with diarrheal illnesses)	On admission	Mortality	Se: Sensitivity of hypoglycemia to predict death with 95% confidence intervals was 40% (14-73%) Sp: Specificity of hypoglycemia to predict death with 95% confidence intervals was 88% (75- 95%) PPV: PPV of hypoglycemia to predict death with 95% confidence intervals was 40% (14-73%) aOR: 5.0, CI 1.1-23.0, P = 0.039
Chisti (2010)	Glucose concentration	Other (Identification of risk factors of poor outcomes)	General PICU population (only non-cardiac)	Not stated	Other (Bacteremia)	aOR: Hyperglycemia (> 11mmol/L): 5.0 (0.9-28.7)
Chong (2015)	Glucose concentration	Validation	General PICU population (mixed cardiac and non-cardiac)	ED glucose , glucose levels at 48 and 72 hours of PICU	Mortality, Other (Duration of mechanical ventilation)	Other: Using a cutoff glucose of 150mg/dL (8.3mmol/L), hyperglycemia was statistically significant for prolonged duration of mechanical ventilation and PICU stay. Persistent hyperglycemia up to 48 and 72 hours was also significantly associated with increased risk of death
Cochran (2003)	Glucose concentration	Derivation	Other (Did not specify - included all patients admitted to the hospital)	Hospital admission	Mortality, Organ-specific outcomes/residual morbidity, Other (Glasgow Outcome Scores)	aOR: Admission glucose (aOR 1.013 95% CI:1.003 - 10.23)
Day (2008)	Glucose concentration	Other (Association of hyperglycemia with risk of	General PICU population (mixed cardiac and non-cardiac)	All PICU glucose concentrations	Organ-specific outcomes/residual morbidity, Other (Risk of Mortality (PRISM))	Other: Pearson's correlation coefficients and p values. PRISM III: 0.545, p < 0.0001; MV Free Days: -0.44, p < 0.0001

		death (PRISM) and organ dysfunction)				
DeCampli (2010)	Glucose concentration	Derivation	PCICU population (only cardiac)	Glucose levels at multiple time points. There were 7 time points in the OR and PCICU.	Mortality, Other (Duration of Mechanical Ventilation, Length of Stay, infections (ETT, blood, urine, wound))	Other: Multivariate model for LOS found pre-CPB glucose as a significant factor (beta-coeff -0.002 95% CI not reported, p = 0.014)
deFerranti (2004)	Glucose concentration	Derivation	PCICU population (only cardiac),Other (OR)	Glucose levels at multiple time points intra-operatively. There were 7 time points but all were in OR and none in PCICU.	Functional outcomes /residual morbidity, Other (EEG findings, clinical seizures)	AUROC: Reported for only one time point (90 min after circ arrest or low flow CPB): 0.764, 95% CI not reported
Egi (2008)	Glucose concentration	Derivation	PCICU population (only cardiac)	Glucose levels for the whole PCICU admission	Mortality	AUROC: 6 AUCs were given depending on whether mean glucose or max glucose levels were used as well as the period that these measurements were taken. For overall PCICI stay, AUROC of mean glucose was 0.76.; AUROC for max glucose was 0.71. No 95% CI was given for all AUROCs aOR: For mean glucose for Mortality: 1.07 (95% CIL 1.01 - 1.13)
El-Sherbini (2018)	Glucose concentration	Derivation	General PICU population (only non-cardiac)	Day 1 of PICU admission	Mortality, Outcomes related to MODS	Other: Correlations of hyperglycemia (BG > 126 mg/dL) with PRISM and MODS; beta cell dysfunction in 43% and low insulin sensitivity in 30%; severe hyperglycemia (G > 180 mg/dL) associated with Mortality
Falcao (2008)	Glucose concentration	Derivation	PCICU population (only cardiac)	Glucose levels on first 10 days after cardiac surgery	Mortality, Other (Duration of Mechanical Ventilation, Length of Stay, renal and hepatic dysfunction, new infection and CNS events)	AUROC: For morbidity against duration of hyperglycemia: 0.813; AUROC for Mortality and duration of hyperglycemia: 0.795 aOR: For peak glucose for Mortality: 1.002 (95% CI: 0.996 - 1.008); aOR for duration of hyperglycemia (<126mg/dL): 1.406 (95% CI 1.033 - 1.914). AOR for peaj glucose for morbidities: 0.997 (95% CI: 0.992 - 1.041); aOR duration of hyperglycemia for morbidities: 1.952 (1.522 - 2.503)
Faustino (2005)	Glucose concentration	Derivation	General PICU population (mixed cardiac and non-cardiac)	Any glucose measurement within PICU stay	Mortality, Other (Length of PICU stay)	Other: Correlation between max glucose level within 10 days of initial glucose measurement and PICU LOS. Also higher glucose level, higher Mortality.
Faustino (2019)	Glucose concentration	Derivation	General PICU population (only non-cardiac)	BG levels through ICU admission	Mortality, Outcomes related to MODS	Other: Comparisons: Hypoglycemia group ICU free days 15.3 (0-22.3) vs No hypoglycemia group ICU free days 20.2 (IQR 5.3-24.1), p 0.04
Filho (2016)	Glucose concentration	Other (Study of association)	Other (Children who underwent elective resection for brain tumor)	On admission to PICU	Mortality, Organ-specific outcomes/residual morbidity, Other (PICU and hospital length of stay)	aOR: Multivariate analysis showed that peak blood glucose levels on postoperative Day 1 were independently associated with a higher odds ratio for postoperative complication (OR 1.05). Other: The occurrence of hyperglycemia (>150 mg/dl) upon admission to the ICU was associated with longer ICU (p = 0.003) and hospital (p = 0.001) stays.

Fu (2019)	Glucose concentration	Derivation	Other (PICU traumatic brain injury patients with GCS < 13)	Probably at PICU admission but not completely clear	Mortality, Other (MV, PICU and hospital free days)	aOR: 1.077 (0.978 to 1.186), p = 0..133
Fu (2017)	Glucose concentration	Validation	General PICU population (mixed cardiac and non-cardiac)	ED glucose and PICU glucose	Mortality, Other (PICU-, hospital-free days and ventilatory-free days)	Se: 76.5% fdor ED glucose > 10.2 mmok/L forMortality as outcome Sp: 85.9% for ED glucose > 10.2 mmol/L forMortality as outcome AUROC: 0.871 (95% CI 0.795 - 0.928) for ED glucose andMortality
Ghafoori (2008)	Glucose concentration	Other (Associations with development of mediastinitis)	PCICU population (only cardiac), Other (Occurrence of mediastinitis)	24 h glucose peak >7.2 mM	Other (Occurrence of mediastinitis)	aOR: 3.86 (1.07-14.02) p= 0.039
Gottschlich (2002)	Glucose concentration, Adrenal axis evaluation, Thyroid function evaluation, Other (Glucagon, gastrin, epinephrine, insulin, dopmaine)	Other (Descriptive levels of all the hormones of interest)	General PICU population (only non-cardiac)	PICU admission and weekly after that	Other (Levels of the hormones)	Other: Description of the weekly values of hormones of interest depending on the group assigned to (early or late enteral feeding)
Graf (1995)	Glucose concentration	Derivation	General PICU population (only non-cardiac), Other (General wards)	ED glucose	Mortality, Other (Glasgow Outcome Scores)	Other: Multiple sensitivities and specificities noted in the article. However, because these levels are measures in ED, this article should be excluded.
Hale (2018)	Glucose concentration	Derivation	Other (Pediatric trauma patients requiring hospital admission)	Hospital admission glucose concentrations.	Outcomes related to MODS, Other (Seizures requiring medication following TBI and continuing following hospital discharge)	aOR: Moderate hyperglycemia (141-199 mg/dL) 2.8 [1.8-4.3)]; Severe hyperglycemia (> 200 mg/dL), 3.3 [1.9-6.0]
Hirshberg (2008)	Glucose concentration	Derivation	General PICU population (mixed cardiac and non-cardiac)	All glucose levels within PICU stay	Mortality, Other (Hospital LOS, nosocomial infections)	aOR: For hyperglycemia (< 150mg/dL) for mortality: 9.6 (95% CI: 1.2 - 77.2); aOR for glucose variability: 40.5 (95% CI: 4.6 - 358.7); Hyperglycemia also higher odds for nosocomial infection (aOR: 2.0 95% CI: 1.0-4.2); Hyperglycemia associated with Hospital LOS (beta coefficient not reported)
Hu (2017)	Glucose concentration	Derivation	Other (Isolated head trauma with specific CT findings)	Within 24 hours of admission	Mortality, Functional outcomes /residual	aOR: Progressive hemorrhagic brain injury - low risk, medium risk and high risk Goodness of fit (calibration): C-statistic (HL method) for derivation model 0.87 (95% CI 0.81-0.9); validation model 0.88 (0.78-0.95)

					morbidity, Organ-specific outcomes/residual morbidity	
Hu (2018)	Glucose concentration	Other (Study of association)	PCICU population (only cardiac)	NR	Organ-specific outcomes/residual morbidity, Outcomes related to MODS	Other: Logistic regression showed intraoperative glycemic fluctuation was one of the risk factors for AKI (p¼.033) and degree of AKI severity stage increased when the glycemic fluctuation increased (p<.01)
Huang (2012)	Glucose concentration	Derivation	PCICU population (only cardiac)	Pre-operative BG, intraoperative BG and post-operative BG for 2 days	Mortality, Organ-specific outcomes/residual morbidity, Other (Length of stay)	AUROC: Weight at surgery and operating time aOR: Weight at surgery and operating time Goodness of fit (Calibration): Weight at surgery and operating time by H-L method
Ichikawa (2017)	Glucose concentration	Derivation	Other (Children with severe TBI from a large registry)	Unsure - some values at admission	Mortality, Functional outcomes /residual morbidity	AUROC: Serum glucose >/= 200 mg/dL, GCS =/< 5 at admission, subarachnoid hemorrhage, dilated pupils aOR: Serum glucose >/= 200 mg/dL, GCS =/< 5 at admission, subarachnoid hemorrhage, dilated pupils
Jallow (2012)	Glucose concentration	Derivation	Other (Blood smear positive for asexual P. falciparum parasites and met WHO criteria for severe malaria)	At and during admission	Mortality, Functional outcomes /residual morbidity	Se: Hypoglycemia 33.7 Sp: Hypoglycemia 79.7 AUROC: Hypoglycemia 0.56 (95% CI 0.53 - 0.59) aOR: Hypoglycemia aOR 1.7 (95% CI 1.2-2.3)
Jeschke (2014)	Glucose concentration	Other (Comparison between survivors and non-survivors)	Other (Burns PICU population)	Up to 90 days following PICU admission	Mortality	Other: Non-survivors had higher BG levels than survivors from Day 2-7 and lasted 61-90 days after burn injury
Jeschke (2010)	Glucose concentration	Derivation	Other (Burns PICU population)	During ICU admission	Mortality	LR: Daily average glucose levels < 140 mg/dL and mortality - LR test statistic 66.074; 6:00 am glucose levels < 130 mg/dL and mortality likelihood ratio test statistic - 50.877 AUROC: Daily average glucose levels < 140 mg/dL and mortality - 0.96; 6:00 am glucose levels < 130 mg/dL and mortality - 0.92
Kan (2009)	Glucose concentration	Derivation	Other (Neurosurgical ICU)	At admission to ICU and during ICU stay	Functional outcomes /residual morbidity	aOR: Admission glucose level and poor outcome - aOR for every mg/dL 1.19 (95% CI 1.00 - 1.42)
Khajavi (2018)	Glucose concentration	Derivation	General PICU population (only non-cardiac)	BG during ICU admission	Mortality	aOR: Of hyperglycemia (BG > 150 mg/dL) 2.14 (95% CI 1.00 - 4.6; aOR of glucose variability (both BG > 150 mg/dL and < 60 mg/dL) 3.08 (95% CI 1.13-8.43))
Khan (2015)	Glucose concentration	Derivation	Other (PICU – unable to determine composition)	First 48 hours of PICU admission	Mortality	Other: Univariate analysis only using cut-off of 126mg/dL. Higher mortality in group with hyperglycemia.
Klein (2008)	Glucose concentration	Other (Study of association)	General PICU population (only non-cardiac)	Maximum glucose level in the first day of PICU admission	Mortality, Other (PICU LOS and mechanical ventilation days)	Other: Controlling for PRISM in survivors, GLFD was not associated with PLOS (P = .75) or with MVD (P = .06). GLFD was not significantly associated with survival (P = .76).

Kraft (2014)	Glucose concentration	Derivation	Other (Burns PICU population)	At and during ICU admission	Organ-specific outcomes/residual morbidity	Other: Incidence of pneumonia: 30% in group with BG > 150 mg/dL and 19% in group with BG < 150 mg/dL, p < 0.05
Krueger (2015)	Glucose concentration	Other (Study of association)	PCICU population (only cardiac)	Glucose measurement immediately after admission to the ICU and then in hourly intervals for 4 hours.	Functional outcomes /residual morbidity, Other patient-centered outcomes	Other: Higher postoperative glucose levels were related to better cognitive performance in the univariate analysis (P < .03), but not when other risk factors were taken into account.
Kyle (2010)	Glucose concentration	Derivation	General PICU population (only non-cardiac), Other (Received continuous infusion of insulin)	During the first 5 days of insulin infusion in the PICU	Mortality, Outcomes related to MODS, Other (Length of stay)	aOR: Trend towards association between hyperglycemia for more than 24 hrs and mortality (aOR 3.2, 95% CI 0.9-11.6), p = 0.079
Lee (2016)	Glucose concentration	Derivation	Other (Children with severe HFMD)	At and during hospital admission	Mortality	aOR: BG > 120 mg/dL and short-term 3 day mortality aOR 2.12 (95% CI 0.33-13.58); BG > 120 mg/dL and hospital mortality aOR 1.01 (95% CI 0.21-4.74)
Leite (2013)	Glucose concentration	Derivation	General PICU population (mixed cardiac and non-cardiac)	Blood glucose levels with first 72 hrs of admission to PICU	Mortality, Organ-specific outcomes/residual morbidity, Outcomes related to MODS, Other (Length of stay)	aOR: For hyperglycemia in first 24 hrs and mortality: 4.5 (95% CI 1.3-14.5); aOR for hyperglycemia for first 48 hrs and mortality: 7.4 (95% CI 2.0-27.4); aOR for hypoglycemia and prolonged LOS: 3.5 (95% CI 12.-10.1); aOR for hypoglycemia and mortality in malnourished: 6.9 (95% CI 1.2-40.8)
Li (2015)	Glucose concentration	Derivation	General PICU population (only non-cardiac)	Initial admission glucose and mean glucose within first 24 hours of PICU admission	Mortality	aOR: Hyperglycemia associated with mortality (aOR: 2.06 95%CI: 1.07-3.96). Hypoglycemia associated with mortality (aOR =12.68; 95 % CI, 4.48- 35.88)
Lodha (2009)	Glucose concentration	Derivation	General PICU population (only non-cardiac)	Day 1 of ICU admission	Mortality	Other: Hypoglycemia (BG< 60 mg/dL) is associated with ICU mortality (p=0.003)
Lou (2010)	Glucose concentration	Validation	PCICU population (only cardiac)	NR	Mortality, Organ-specific outcomes/residual morbidity	aOR: Patients with hyperglycemia >150 had decreased OR to reach the composite (death, morbidity) endpoint (OR 0.22 95CI: 0.065-0.740, P=0.014)
Maegaki (2015)	Glucose concentration	Other (Investigational)	Other (Children presenting with status epilepticus)	At onset of status epilepticus	Mortality, Functional outcomes /residual morbidity	aOR: For poor outcome (defined as neurological sequelae or in-hospital death), blood glucose <61 or >250 mg/dL, 7.101 (95%CI, 1.114-45.266), p=0.038
Mahmoud (2018)	Glucose concentration	Derivation	General PICU population (only non-cardiac)	Random blood glucose	Other (Critical illness polyneuropathy, critical illness myopathy)	Other: Comparison: CIP/CIM patients with BG 230 mg/L vs non-CIP/CIM patients with BG 165 mg/dL, p < 0.001
Marsillio (2015)	Glucose concentration	Derivation	General PICU population (only non-cardiac), PCICU population (only cardiac)	4 days prior to first at of positive blood culture from central line.	Mortality, Other (Ventilator-free days; ICU LOS)	aOR: Hyperlgycemia (>126mg/dL) associated with mortality in chidlren with CLABSI (aOR 1.9, 95% CI: 1.1 -6.4). No association in linear regression analysis for VFD and ICU LOS with glucose levels.

Marton (2007)	Glucose concentration	Other (Investigational)	Other (Infants <12m with severe TBI)	Within the first 24 h post-admission	Functional outcomes /residual morbidity	Other: Correlation: for the outcome of GOS at discharge and at 12m after discharge (GOS<5), blood glucose >200mg/dL at 24h: Pearson correlation coefficient, -0.90 (p<0.0001)
Melo (2010)	Glucose concentration	Validation	Other (Children with severe TBI)	With 48h from admission	Mortality	aOR: For mortality, blood glucose >200mg/dL: 6.14 (95%CI, 2.25-16.73), p=0.0003
Melo (2009)	Glucose concentration	Other (Investigational)	Other (Children <6y with severe TBI (GCS<=8) due to fall from windows)	At admission	Mortality	aOR: For in-hospital mortality, blood glucose >200mg/dL: 12.77 (95%CI, 1.21-134.68), p=0.034
Moga (2011)	Glucose concentration	Other (Study of association)	PCICU population (only cardiac)	Postoperative glucose values were analyzed for 72 hrs and divided into 6-hr intervals.	Mortality, Organ-specific outcomes/residual morbidity, Other (Composite morbidity-mortality outcome, stroke, seizures, hospital/intensive care unit stay. Longer durations of moderate or severe hyperglycemia were associated with increased odds of the composite morbidity-mortality outcome, lactic acidosis, cardiac arrest, vasopressin use, ventilation time, longer intensive care unit/hospital stays.)	aOR: Composite outcome, 2.25 (1.51-3.35), P <.001 ICU stay 0.266 (0.064), P <.001 Hospital stay, 0.184 (0.063), P < .004 Seizure 2.60 (1.10-6.14), P = .03 Lactic acidosis 3.18 (1.64-6.12), P =.001
Nagao (2008)	Glucose concentration	Validation	Other (Influenza-associated encephalopathy)	Unable to determine	Mortality	aOR: For the outcome of mortality, blood glucose >=150 mg/dL (P=0.04) for multivariable regression analysis, but aOR (95%CI) not reported
Narci (2009)	Glucose concentration	Other (Investigational)	Other (Pediatric trauma patients)	At admission	Other (Liver trauma)	aOR: For morbidity (definition not provided), blood glucose (cutoff not provided): 3.01, p=0.03 (95%CI not provided) Other: Correlation: for hospital LOS, ICU LOS, blood glucose (cutoff not provided), r=0.08, p=0.93; r=0.87, p=0.39 respectively
Nayak (2013)	Glucose concentration	Derivation	General PICU population (mixed cardiac and non-cardiac)	Admission to PICU (0-3 hrs); Day 1 of PICU (3-24 hrs), Day 2, Day 3 and so forth during PICU stay	Mortality	Other: Hazard ratio for day 1 delta glucose per mg/dL and 100-day mortality: 1.07 (1.03-1.10)

O'Brien (2010)	Glucose concentration	Other (Study of association)	PCICU population (only cardiac)	The highest glucose while on CPB was recorded.	Other (Bacteremia)	Other: Unadjusted odds ratio: each intraoperative increase of 1 mg/dL in glucose level was related to a patient having a 1.0% increased risk of postoperative bacteremia (odds ratio, 1.01; 95% confidence interval, 1.004 to 1.019; p < 0.004).
Odek (2018)	Glucose concentration	Other (Study of association)	General PICU population (mixed cardiac and non-cardiac)	Day 1 of PICU admission at 1, 2, 4, 8, and 24 hours	Outcomes related to MODS, Other (Higher Wernovsky inotropic score and vasoactive-inotropic score)	Other: Multivariate model, we found higher PRISM III-24 score (OR, 1.1; 95% CI 1.02-1.18; p= 0.004) was significantly associated with postoperative hyperglycemia. Postoperative hyperglycemia was not associated with duration of MV (p=0.840), length of PICU stay (p=0.299), healthcare associated infections (p=0.569), or mortality (p=0.690).
Ognibene (2011)	Glucose concentration	Derivation	General PICU population (mixed cardiac and non-cardiac)	NR	Mortality, Other (Length of stay, days of mechanical ventilation)	Other: Spontaneous hypoglycemia (BG < 60 mg/dL) and greater length of stay (p<0.001) and more days of mechanical ventilation (p<0.001); hyperglycemia (BG > 150 mg/dL) associated with longer lengths of stay (p<0.001), and more days of mechanical ventilation (p=0.01)
Paret (1999)	Glucose concentration	Other (Investigational)	Other (Trauma from fall of at least 1m)	At admission to the ED	Mortality	Other: Correlation: univariate correlation of higher blood glucose at presentation with mortality (p<0.001, but r-value not provided). No adjustment for confounders was done.
Piastra (2017)	Glucose concentration	Validation	Other (Patients undergoing craniotomy)	During surgery for craniotomy	Other patient-centered outcomes, Other (PICU duration of stay as a function of the Glycemic Stress Index)	Se: For PICU LOS > 200 hrs, 86% Sp: For PICU LOS > 200 hrs, 69% PPV: For PICU LOS > 200 hrs, 5.4% NPV: For PICU LOS > 200 hrs, 99.6% LR: For PICU LOS > 200 hrs, + LR, 2.8; -LR, 0.2 AUROC: 0.74 (p = 0.03) for GSI to predict PICU stay >200 h and 0.67 (p = 0.01) to predict PICU stay >100 h
Plubrukarn (2003)	Glucose concentration	Other (Investigational)	Other (children presenting to the ED with near drowning)	At presentation to the ED	Mortality, Functional outcomes /residual morbidity	PPV: for poor outcome (death or vegetative state), high blood glucose (unclear cutoff): 66.7%
Polito (2008)	Glucose concentration	Other (Association of intraoperative glucose conc and hospital LOS)	PCICU population (only cardiac), Other (Cardiac surgery patients with RACHS-1 >/=3)	Intraoperative glucose concentrations	Other (Primary: hospital LOS; secondary: death or severe in-hospital morbidity)	Other: No association of intraop glucose and hospital LOS on multivariable analysis
Preissig (2009)	Glucose concentration	Validation	General PICU population (only non-cardiac)	No specific timeframe	Other (Outcome was hyperglycemia)	Other: Pts with PELOD >12 had higher BGs, higher insulin requirements, and longer period on insulin therapy
Rake (2010)	Glucose concentration	Derivation	General PICU population (only non-cardiac)	First 72 hrs of PICU stay	Mortality	aOR: Mean BG and PICU mortality (aOR: 1.02, 95% CI 1.00-1.05); BG variability and PICU mortality (aOR: 1.03, 95% CI 1.01-1.05)
Rhine (2012)	Glucose concentration	Validation	Other (Trauma)	Admission	Functional outcomes /residual morbidity, Organ-specific	aOR: GLASGOW OUTCOME SCALE: OR for poor GOS 5.20 (95CI: 1.15-23.54, X2 2.14, P0.03 if BG>150 on admission

					outcomes/residual morbidity	
Seyed Sadaat (2012)	Glucose concentration	NR	General PICU population (only non-cardiac)	NR	Mortality, Other (LOS)	aOR: Persistent hyperglycemia over first 2 days OR 2.84 (0.89-9.1), P=0.08; Persistent hyperglycemia over first 3 days OR 11.1 (2.95-41.7), P=0.001 Other: Mean BG survivors vs nonsurvivors on day 1: 244 +/- 121 vs 184 +/- 62; P=0.003, similar on days 2 and 3 (212 v 146, 183 v 111)
Srinivasan (2004)	Glucose concentration	Validation	General PICU population (only non-cardiac)	Entire PICU stay	Mortality	aOR: Median BG >150 mg/dL had OR 2.96 (95CI 1.06-8.33; p<0.05) for mortality Other: Correlation of BG level at 24h with mortality, p<0.001, R2=0.18, BG<100 - 8.3% mortality, BG 100-140 12.5%, BG 141-180 20%, BG>180 28.5%
Tala (2014)	Glucose concentration	Validation	General PICU population (mixed cardiac and non-cardiac)	Highest blood glucose measured during the admission	Mortality, Functional outcomes /residual morbidity	Se: Of BG>150 for predicting VTE: 91% Sp: 38% AUROC: 0.72, p=0.02 aOR: 4.1, 95CI: 1.2-14.1, p=0.02
Toro-Polo (2018)	Glucose concentration	Derivation	General PICU population (only non-cardiac)	First blood glucose level at PICU admission	Mortality	Se: For glucose < 65 mg/dL, 17.4%; for glucose > 200 mg/dL, 19.6% Sp: 91.7% for glucose values of < 65mg/dL (3.61mmol/L) and for > 200mg/dL (> 11.1mmol/L) , 93.9%) PPV: For glucose < 65 mg/dL, 29.6%; for glucose > 200 mg/dL, 39.1% NPV: For glucose < 65 mg/dL, 84.7%; for glucose > 200mg/dL, 85.4% AUROC: 0.53 (95%CI 0.45 to 0.60) aOR: < 65mg/dL (3.61mmol/L) (RR: 2.01; 95%CI 1.14 - 3.53), glucose > 200mg/ dL (> 11.1mmol/L) (RR: 2.91; 95%CI 1.71 - 4.55)
Tude Melo (2010)	Glucose concentration	Validation	Other (Neurotrauma)	Admission	Mortality	aOR: >=180 mg/dL OR for mortality 6.14 (95CI: 2.25-16.73)
Ulate (2008)	Glucose concentration	Derivation	PCICU population (only cardiac)	Day 1 of ICU admission; first 5 days of ICU admission	Mortality, Other (Length of stay)	Other: No association of hyperglycemia with mortality in first 24 hrs; Higher mortality with hyperglycemia (different definitions cut-offs) in day 2-5 span
Uleanya (2017)	Glucose concentration	Derivation	General PICU population (only non-cardiac)	NR	Mortality	aOR: Hypoglycemia (<60mg/dL) with survival: 0.2, 95CI: 0.09-0.47; hyperglycemia (>200mg/dL) with survival: 0.12, 95CI: 0.03-0.51
Wintergerst (2006)	Glucose concentration	Derivation	General PICU population (mixed cardiac and non-cardiac)	All glucose levels within PICU stay	Mortality, Other (PICU and Hospital LOS)	Other: Maximal glucose > 110mg/dL was associated with longer PICU LOS and hospital LOS. Max glucose also associated increased mortality. Glucose variablity also associated with increased mortality.
Yates (2006)	Glucose concentration	Other (Associations of various glucose measures and adverse outcomes)	General PICU population (only non-cardiac)	All glucose measurements during PCICU stay	Mortality, Organ-specific outcomes/residual morbidity, Other (Composite morbidity related to organ dysfunction; durations of stay)	aOR: 1.48, p=0.002 for duration of hyperglycemia > 126 mg/dL
Yokochi (2016)	Glucose concentration	Other (Prediction of acute encephalopathy with biphasic	General PICU population (only non-cardiac)	All glucose levels during PICU stay	Functional outcomes /residual morbidity	Blood glucose (mg/dl) was higher in AESD group: 244.5 (IQR 14–392, n=18) vs non-AESD group 159 (IQR 13–381, n=193) p <0.01. BG cut-off > 228 mg/dL was a predictor of AESD in the multivariable model with sensitivity of 93% and specificity of 91%.

		seizures and late reduced diffusion (AESD))				
Yung (2008)	Glucose concentration	Other (Association of hyperglycemia with PELOD >10 and death)	General PICU population (mixed cardiac and non-cardiac)	All glucose values during first 14 days or PICU stay	Mortality, Outcomes related to MODS, Other (Specifically PELOD >10)	aOR: PELOD >10: 3.41 [1.91-6.10]; death: 3.12 [1.26-7.70] [95% CI]
Zant (2016)	Glucose concentration	Derivation	Other (Liver transplant patients only)	Perioperative liver transplant period (Day -1 to Post-op Day 7)	Mortality, Other (rejection, Infection and re-transplantation)	Other: Univariate analysis for outcomes based on cut-off glucose of 200mg/dL. No difference in all 4 outcomes.
B. Thyroid dysfunction (n=18)						
Aggarwal (2020)	Thyroid function evaluation	Other (TSH concentrations in relation to trauma patient characteristics)	Other (Pediatric trauma patients evaluated in ED)	At time of ED evaluation	Other (Outcome was TSH concentrations. Relevant predictors were gender and traumatic brain injury)	aOR: Abnormal TSH: females (odds ratio (OR): 4.95, 95% confidence interval (CI): 2.01, 12.21, p<0.01; moderate to severe TBI, (OR: 8.11, 95% CI: 2.51, 26.16, p<0.001)
Anand (1994)	Thyroid function evaluation	Derivation	General PICU population (only non-cardiac)	At admission	Mortality	Other: Statistical test is unclear, but mean T3 on admission was 0.62 +/- 0.63 ng/mL, dropped to 0.13 +/- 0.28 before death, or up to 1.67 +/- 0.75 at discharge (similar to control of 1.90 +/- 0.62. No significant differences with total T4.
Cantinotti (2013)	Thyroid function evaluation	Other (Exploration of trends of TSH, fT4, fT3 over the perioperative period)	PCICU population (only cardiac)	Perioperative period	Other (Time to extubation)	Other: Patients followed with serial measurements of TSH, fT4, fT3 over the perioperative period. Importantly, all patients received dexamethasone 1 mg/kg, which suppresses TSH, rendering the relevance to sepsis very minimal. Also, the use of these rarely measured fT4 and fT3 are not generalizable.
Dagan (2006)	Thyroid function evaluation	Other (Descriptive)	PCICU population (only cardiac)	Preoperative, Days 1,3,5,7 and 14 post-op	Other (Inotrope requirement)	Other: T test: Higher fT4 levels on Day 5 and 7 post-op in patients with minimal inotrope requirement compared to those with high inotrope requirement.
denBrinker (2005)	Thyroid function evaluation	Derivation	General PICU population (mixed cardiac and non-cardiac)	Day 1 of PICU admission	Mortality	aOR: For Mortality: 3.7 for every doubling of the Total T3/reverse T3 ratio and 1.4 for every 10 nmol/ liter lower Total T4 level on admission. No 95% CI given
El-Ella (2019)	Thyroid function evaluation	Derivation	General PICU population (mixed cardiac and non-cardiac)	Single blood sample obtained within 24 h of PICU admission for thyroid assessment: non-thyroidal illness syndrome (NTIS)	Mortality	aOR: NTIS independently predicted Mortality (OR = 3.91; 95% CI = 1.006---15.19; P = .0491)

Gielen (2012)	Thyroid function evaluation	Derivation	General PICU population (mixed cardiac and non-cardiac)	From day of randomization to Day 3 of PICU admission or PICU discharge if earlier than 3 days	Mortality	aOR: Increase from baseline in T3/rT3 was significantly associated with a lower likelihood for earlier live discharge (HR per unit increase, 0.863; 95% CI, 0.806-0.927; P =0.0001)
Goldsmit (2011)	Thyroid function evaluation	Derivation	Other (Neonates)	At admission	Mortality	Other: RR (risk ratio): risk of death for pts with low (≤2SD below nl) T3 & T4 & TSH 10.75 (95CI 3.9-29)
Gottschlich (2002)	Glucose concentration, Adrenal axis evaluation, Thyroid function evaluation, Other (Glucagon, gastrin, epinephrine, insulin, dopamine)	Other (Descriptive levels of all the hormones of interest)	General PICU population (only non-cardiac)	PICU admission and weekly after that	Other (Levels of the hormones)	Other: Description of the weekly values of hormones of interest depending on the group assigned to (early or late enteral feeding)
Hebbar (2009)	Adrenal axis evaluation, Thyroid function evaluation, Other (Other)	Other (Incidence of neuroendocrine dysfunction; correlation with severity of illness and presence of sepsis)	General PICU population (only non-cardiac)	Within 12 hours of PICU admission	Mortality, Other (ICU length of stay, ventilator days)	Other: Comparisons between septic and non-septic groups
Jacobs (2019)	Thyroid function evaluation	Other (Analysis of correlation of thyroid levels with outcomes)	General PICU population (mixed cardiac and non-cardiac)	NR	Mortality, Other (PICU LOS, acquisition of new infection)	aOR: Admission T4 OR for 90d mortality 0.968 [0.953-0.983], p<0.0001; with PICU LOS: Beta estimate -0.049 [-6.995-1.032] p=0.008; OR with new infection 1.725 [1.095-2.717], p=0.01
Marks (2009)	Thyroid function evaluation	Other (Investigational)	PCICU population (only cardiac)	Preoperatively within 1 wk of surgery, postoperatively upon arrival to the pediatric intensive care unit (PICU), twice daily at 0800 and 2400 h up to and including postoperative day (POD) 3, and at 0800 h from POD 4-7 inclusive if the patient remained in the PICU	Outcomes related to MODS	Other: Correlation: Mixed-effect modeling showed a significant relation between the PELOD scores and the night samples of TSH (P=0.002), TT3 (P=0.0001 and 0.002), FT3I (P=0.047 and 0.151), T3U (P= 0.007),FT4 (P=0.014), and rT3 (P=0.016)

Marwali (2019)	Thyroid function evaluation	Other (Occurrence of LCOS in relation to T3 supplementation or not)	PCICU population (only cardiac)	Anytime 6-40 hours post Ao cross clamp release; at6 hr post Ao cross-clamp release;	Outcomes related to MODS, Other (LCOS, low cardiac output syndrome, time to tracheal extubation, measures of cardiac output)	aOR: Total number of patients exhibiting LCOS at anytime 6 -48 h after Ao cross-clamp removal: significantly higher in placebo group [n = 86 vs. 66, respectively, p < 0.001; OR (95% CI) 0.43 (0.36-0.52)]
Merchant (2008)	Thyroid function evaluation	Other (Investigational)	PCICU population (only cardiac)	Preoperative, and 2, 12, 24, and 48 h after CPB	Other (PICU LOS, IS)	Other: Correlation: for the outcome of PICU LOS, FT4: r=-0.504, p-0.023; for the outcome of IS on POD1 and POD2, FT4: r=-0.523, p=0.018, and r=-0.495, p=0.027, respectively. No significant correlation between FT4 an ventilation days, FiO2 at 2h, or TISS on POD2
Sayarifard (2018)	Thyroid function evaluation	Derivation	Other (PICU of unknown composition)	Day 1 and 3 of PICU admission	Mortality	Other: p values comparing thyroid function tests of survivors and non-survivors
Suvarna (2009)	Thyroid function evaluation	NR	General PICU population (only non-cardiac)	Admission and pre-discharge	Mortality	Se: ADMISSION: T3 <=46, 88%. T4 <=4.5 63% Sp: ADMISSION: T3 <=46 41%, T4 <=4.5 86% AUROC: Best performing AUROC (0.91) was T3 at @ discharge, Sn 88, Sp 86, with cutoff value <=56.5 ng/dL. T3 on admission AUROC 0.68, cutoff <=46, Sn 88, Sp 41
Talwar (2012)	Thyroid function evaluation	Other (Search for associations between thyroid levels and AUCs with complications.)	PCICU population (only cardiac)	Perioperative period	Mortality, Other (Inotropic score, duration of ventilation)	Other: Demonstrated no cutoffs per se, but showed a significant association between AUC for TT4, FT3, TT3 and inotrope score and duration of ventilation (R2: 3-6%). And significant association between TT4 AUC and survivors vs nonsurvivors. No discussion of steroid exposure.
Yildizdas (2004)	Thyroid function evaluation	NR	General PICU population (only non-cardiac)	Not specified, but before dopamine was started, early in course	Mortality	Other: Anova, Mann-Whitney comparisons b/n sepsis/septic shock, and controls. Sepsis TT3 0.91 +/- 0.22 nmol/L, septic shock 0.64 +/- 0.23, control 2.11 +/- 0.59 P<0.001; survivors 1.00 +/- 0.16, non-survivors 0.58 +/- 0.16, P <0.001
C. Adrenal dysfunction (n=22)						
Amstadter (2011)	Adrenal axis evaluation	Derivation	Other (Trauma patients)	Once patient was stable. Exact timing unknown.	Functional outcomes /residual morbidity	aOR: Multiple variants for the CRHRI gene were analyzed regarding the risk of PTSD. Therefore, there is no one OR to provide.
Balbao (2014)	Adrenal axis evaluation	Derivation	General PICU population (mixed cardiac and non-cardiac)	First 48 hours after admission	Other (Vasotropic inotropic score)	Se: A salivary cortisol concentration post-ACTH of ≤226 nM (8.2 ug/dl) had a sensitivity of 79% to discriminate need for vasoactive or inotropic support. Sp: A salivary cortisol concentration post-ACTH of ≤226 nM (8.2 ug/dl) had a specificity of 62% to discriminate need for vasoactive or inotropic support. AUROC: A salivary cortisol concentration post-ACTH of ≤226 nM (8.2 ug/dl) had a sensitivity of 79% and a specificity of 62% to discriminate need for vasoactive or inotropic support (area under receiver operating characteristic (ROC) curve 0.74).
Bekhit (2019)	Adrenal axis evaluation	Derivation	NR	Early morning fasting, within 24h of admission	Mortality, Other (PRISM III, MV	Se: At cortisol cutoff of 30.05 mcg/dL, 89.5% Sp: At cortisol cutoff of 30.05 mcg/dL, 64.5%

					duration, inotropic support, PICU LOS, PICU Mortality)	PPV: at cortisol cutoff of 30.05 mcg/dL, 43.6% NPV: At cortisol cutoff of 30.05 mcg/dL, 95.2% AUROC: 0.783, 95CI: 0.673-0.893
Bone (2002)	Adrenal axis evaluation	Derivation	Other (Meningococcal disease)	On admission	Other (Glasgow Meningococcal Septicemic Prognostic Score)	Other: AI was defined as a peak cortisol value on the LDST of < 500 nmol/L or an 8 am cortisol value of <140 nmol/L. Children with a GMSPS of 9 or greater had a significantly higher mean 8 am cortisol value (685 +/- 330 nmol/L) compared with those with a GMSPS of <9, who had a mean 8 am cortisol value of (388 +/- 282 nmol/L; P < .01)
Garcia (2010)	Adrenal axis evaluation	Other (Descriptive levels of cortisol after ACTH simulation)	PCICU population (only cardiac)	Not clearly described	Other (Cortisol levels)	Other: Cortisol levels after low dose ACTH tests in hemodynamic unstable neonate after cardiac surgery
Gottschlich (2002)	Glucose concentration, Adrenal axis evaluation, Thyroid function evaluation, Other (Glucagon, gastrin, epinephrine, insulin, dopmaine)	Other (Descriptive levels of all the hormones of interest)	General PICU population (only non-cardiac)	PICU admission and weekly after that	Other (Levels of the hormones)	Other: Description of the weekly values of hormones of interest depending on the group assigned to (early or late enteral feeding)
Hatherill (1999)	Adrenal axis evaluation	Derivation	Other (Septic shock)	Immediately after admission	Mortality, Outcomes related to MODS	Other: Insufficiency was defined as a post-Synacthen cortisol increment < 200 nmol/l. Median calculated risk of mortality corrected for age was 17% (range, 7-29%) in adrenal insufficiency compared with 7% (range, 3-22%) in those with adequate adrenal function (p = 0.128). Children with adrenal insufficiency were more likely to require adrenaline or noradrenaline for hemodynamic support (p = 0.032; odds ratio 6.1; 95% confidence interval, 1.2 to 30.1). Application of the vasopressor score (table 4) showed a significant linear trend for them to require a greater vasopressor dose (p = 0.0025; Chi-squared test for trend).
Hebbar (2009)	Adrenal axis evaluation, Thyroid function evaluation, Other (Other)	Other (Incidence of neuroendocrine dysfunction; correlation with severity of illness and presence of sepsis)	General PICU population (only non-cardiac)	Within 12 hours of PICU admission	Mortality, Other (ICU length of stay, ventilator days)	Other: Comparisons between septic and non-septic groups
Levy-Shraga (2016)	Adrenal axis evaluation	Derivation	General PICU population (mixed	During PICU admission	Mortality	Se: Baseline cortisol >/= 600 nmol/L and risk of mortality: 0.54 Sp: Baseline cortisol >/= 600 nmol/L and risk of mortality: 0.70 AUROC: Baseline cortisol >/= 600 nmol/L and risk of mortality: 0.63

			cardiac and non-cardiac)			
Lichtakowicz-Krynska (2004)	Adrenal axis evaluation, Other (Aldosterone and plasma renin)	Other (Comparison of aldosterone levels between children with meningococcal sepsis and children without sepsis)	General PICU population (only non-cardiac)	At and during admission at 8 hrly intervals	Other (Correlation between aldosterone, plasma renin and cortisol levels between groups as well as correlations with severity of illness and vasopressor score)	Other: Children with meningococcal sepsis had lower aldosterone levels compared to children without sepsis (423.1 +/- 88.5 pg/ml vs 1489.2 +/- 244 pg/ml, p<0.0001); no correlation between aldosterone and plasma renin;
Menon (2002)	Adrenal axis evaluation	Other (assessment of adrenal insufficiency (AI) by various criteria)	General PICU population (mixed cardiac and non-cardiac)	Uncertain; at the ~time of defined hemodynamic instability	Mortality, Other (Occurrence of AI in patients with hemodynamic instability)	Other: % of patients with AI per various definitions
Menon (2010)	Adrenal axis evaluation	Other (Sort of a validation of the low dose cosyntropin stimulation test)	General PICU population (mixed cardiac and non-cardiac)	Day 1 of PICU admission	Other (Prevalence of adrenal insufficiency on admission to the PICU)	Other: At admission, 115 patients (30.2%; 95% CI, 25.9-35.1)
Menon (2018)	Adrenal axis evaluation	Derivation	General PICU population (mixed cardiac and non-cardiac)	Admission to PICU	Other (Correlation between cortisol levels and severity of illness and vasoactive inotrope scores)	Other: Baseline free cortisol and total cortisol levels were strongly correlated with baseline PRISM score and moderately correlated with admission VIS. Serum TC levels were highly correlated with FC levels
Nichols (2017)	Adrenal axis evaluation	Validation	General PICU population (only non-cardiac)	At consideration of treatment with stress dose hydrocortisone	Mortality, Other (PICU LOS, Hos LOS, Vent-free days, vasopressor-free, Hosp acquired infection, PRISM-III)	Other: No differences in LOSs, VFDs, VasoFDs, mortality, between rSTC <18 vs ≥18. Log-transformed rSTC modestly positively correlated with PRISM III @ 12h: r=0.3932; r2 = 0.16, p<0.001
Pizarro (2005)	Adrenal axis evaluation	Derivation	General PICU population (only non-cardiac)	First 24 hrs after diagnosis of septic shock	Mortality, Other (Shock states - fluid responsive, fluid refractory and catecholamine refractory)	Other: All children with fluid responsive shock had corticotropin response > 9 mcg/dL(p < 0.05); corticotropin response < 9 mcg/dL was independent predictor of septic shock (p<0.05); no association of adrenal responsiveness with mortality

Samransamruajkit (2007)	Adrenal axis evaluation	Validation	General PICU population (only non-cardiac)	Within 24h of ICU admission	Mortality, Other (PRISM III)	Other: According to definition of of basal cortisol < 15,2 mcg/dL (415 nmol/L) n=4; or increment ≤9 mcg/dL (250 nmol/L) n=6. No difference in mortality. AI group had higher PRISM III 8.3 v 5.6 (p<0.05).
Sarthi (2007)	Adrenal axis evaluation	Derivation	General PICU population (only non-cardiac)	"Soon after a dx of fluid refractory septic shock was made"	Mortality	Se: Ranged 50-88% depending on increment of cortisol, with 1 mcg stim Sp: Ranged 59-95% depending on increment of cortisol, with 1 mcg stim AUROC: Good performance of 60 min stim: <8 sn 75, sp 82. Peak cort increase <7 sn 63, sp 100 Other: Basal cortisols were 48 mcg/dL (39-67) in rel AI pts, and 115 (62-157) in nl adrenal reserve, P=0.015. Basal was 69 (49-82) in survivors, 73 (40-122) in nonsurvivors, P=0.52
Sasser (2012)	Adrenal axis evaluation	Validation	PCICU population (only cardiac)	"Immediate postoperative period"	Mortality, Organ-specific outcomes/residual morbidity	Other: Correlation analysis was performed between immediate postop cortisol and numerous outcomes. Significant correlations were HIGHER cortisol with HIGHER lactate and SaO2-SvO2 difference, max inotrope score, therefore higher cortisol correlates with SOI. Low cortisol was not associated with worse outcomes in this postop cardiac cohort.
Singhi (2006)	Adrenal axis evaluation	Derivation	Other (ED meningitis patients)	At presentation	Outcomes related to MODS	aOR: Cortisol > 42 had OR 9.8 (95CI: 1.7-55; P=0.01 for hearing or neurologic sequelae Other: Median cortisol in those with neuro sequelae 45 (90CI: 11-89), compared to those without 30 (4-62); P=0.43.
van den Akker (2009)	Adrenal axis evaluation	NR	NR	NR	NR	NR
Verweij (2012)	Adrenal axis evaluation	Validation	PCICU population (only cardiac)	Not specified - prior to hydrocortisone therapy, which was median 36h (16-156 hrs)	Other (Response to hydrocortisone therapy for low cardiac output syndrome)	Other: Analysis using mixed models ANOVA showed no difference between groups (cortisol <3.6 mcg/dL vs >3.6 mcg/dL) in response to hydrocortisone therapy for LCOS as measured by lactate, BP changes, glucose changes, renal failure, time to extubation or ICU LOS.
Yehya (2016)	Adrenal axis evaluation	Validation	General PICU population (only non-cardiac)	Measurement of random cortisol before starting hydrocortisone therapy	Mortality, Other (VFD)	Other: Correlation of cortisol with PRISM-III: r2 0.11, P=0.001; correlation cortisol with vasopressor score: r2 = 0.07, p=0.001; Pts with cort ≥18 treated with hydrocortisone had higher PRISM-III (P=0.006) and higher vasopressor scores (P<0.001)

Abbreviations: aOR, adjusted odds ratio; AUROC, area under the receiver operating characteristics curve; LR, likelihood ratio; NPV, negative predictive value; PPV, positive predictive value; Se, sensitivity; Sp, specificity; PICU, pediatric intensive care unit; PCICU, pediatric cardiac intensive care unit

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Research Priorities

1. We recommend directing future research into utility of glycosylated hemoglobin (HgbA1c), plasma fructosamine or glycated albumin as potential biomarkers of abnormal glucose homeostasis in critically ill children.
2. We recommend future research priorities into markers of adrenal axis function at the cellular level to further define the axis in critically ill children.
3. Future studies of copeptin as an index of ADH production may enable improved characterization of posterior pituitary function as part of a clinically relevant scoring system.