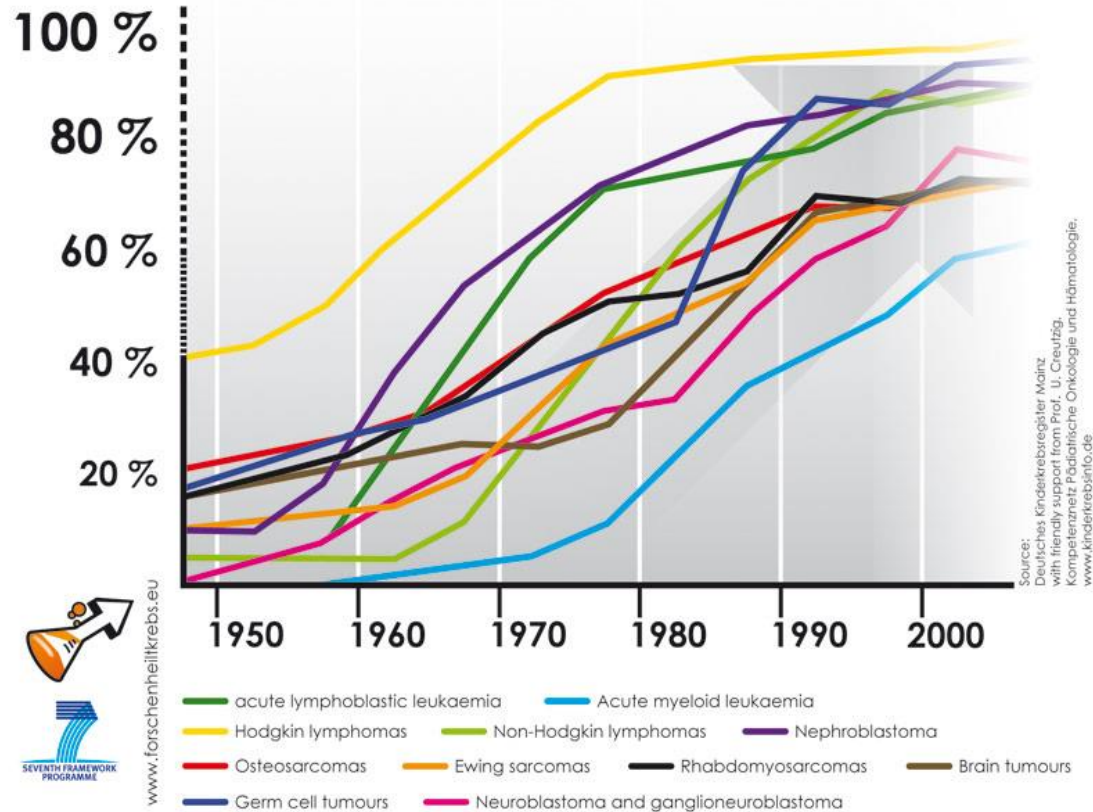




Managing the critically ill cancer patient: need for improvement?

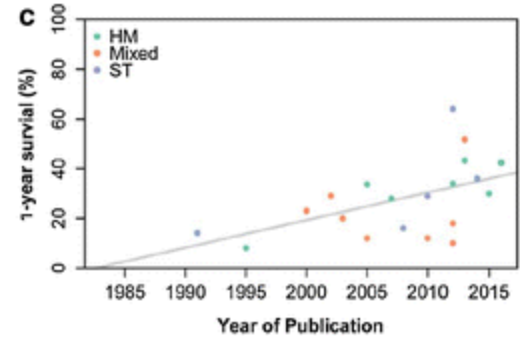
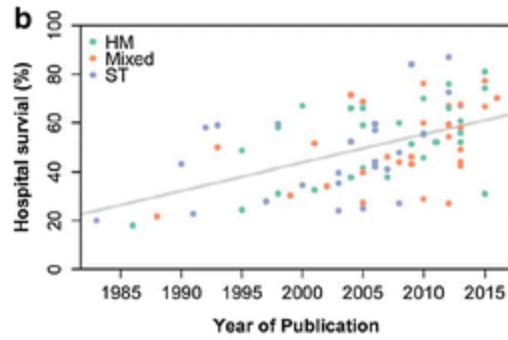
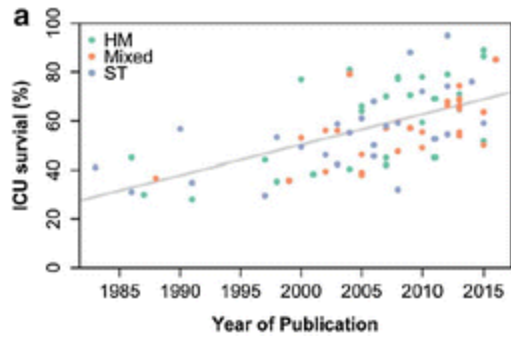
Roelie M. Wösten-van Asperen

Survival Rates of Children and Young Adults Suffering from Cancer





- About 40% of all pediatric cancer patients require PICU admission
- Lack of data on PICU outcome

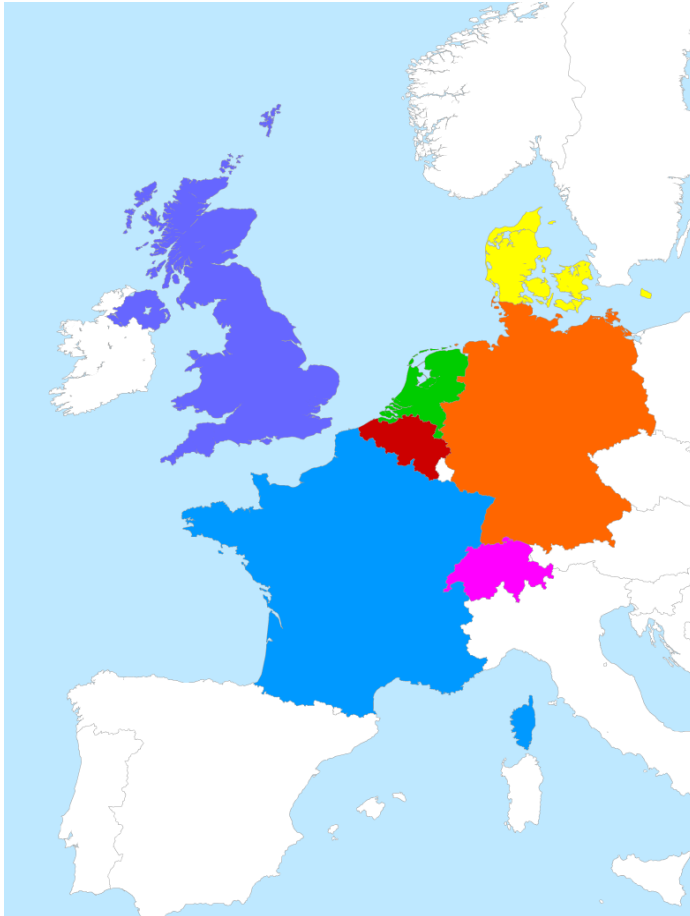




POKER

PICU ONCOLOGY KIDS IN EUROPE RESEARCH GROUP





- Denmark: Jeppe Sylvest Nielsen
- UK: Joe Brierley, Omer Aziz
- France: Frédéric Valla
- Switzerland: Patrick Marquis
- Germany: Eva Tschiedel, Christian Dohna-Schwake, Jenny Potratz, Martin Krause
- Belgium: Jef Willems
- The Netherlands: Sjef van Gestel, Martine van Grotel, Marry van den Heuvel-Eibrink, Roelie Wösten-van Asperen



Has the mortality of children with cancer admitted to pediatric intensive care unit changed over time?

A systematic review and meta-analysis by the POKER consortium.

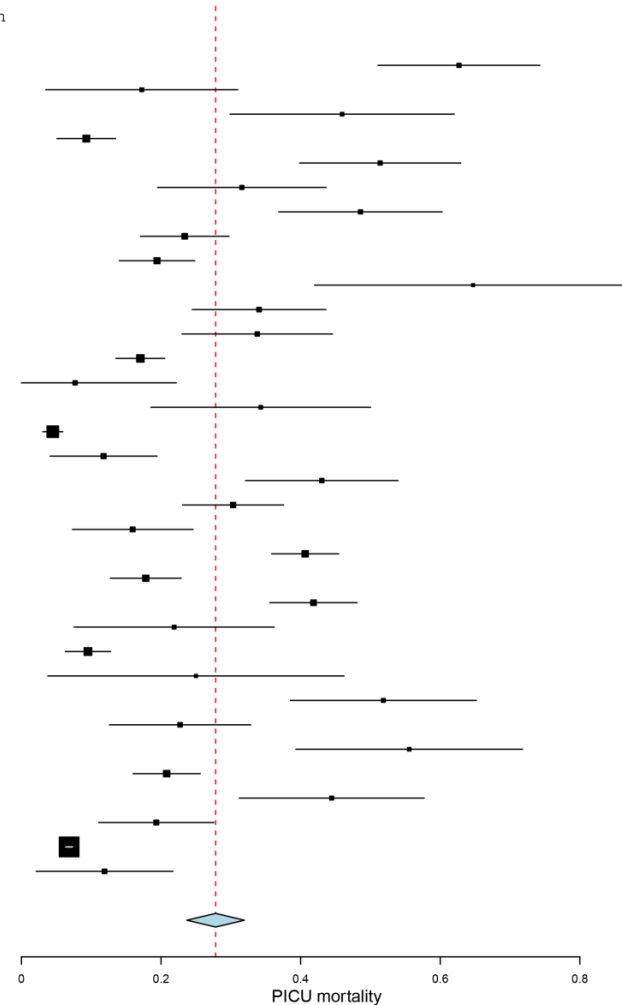
PICU mortality 27.8%

Studies [ref] – median year of conduct Estimate (95% CI) Died / PICU admission

Butt et al. a [15] 1981	0.627 (0.511, 0.743)	42/67
Butt et al. b [15] 1985	0.172 (0.035, 0.310)	5/29
Butt et al. c [15] 1984	0.459 (0.299, 0.620)	17/37
Meert et al. [23] 1986	0.093 (0.051, 0.135)	17/183
Sivan et al. [24] 1987	0.514 (0.398, 0.629)	37/72
van Veen et al. [25] 1988	0.316 (0.195, 0.436)	18/57
Heney et al. [26] 1988	0.486 (0.369, 0.603)	34/70
Parsons et al. [27] 1988	0.234 (0.170, 0.297)	40/171
Hallahan et al. [8] 1992	0.194 (0.140, 0.248)	40/206
Ben-Abraham et al. [28] 1992	0.647 (0.420, 0.874)	11/17
Abraham et al. [29] 1994	0.340 (0.245, 0.436)	32/94
Keengwe et al. [30] 1994	0.338 (0.230, 0.446)	25/74
Fiser et al. [31] 1996	0.170 (0.136, 0.205)	76/446
Heying et al. a [16] 1997	0.077 (0.000, 0.222)	1/13
Heying et al. b [16] 1997	0.343 (0.186, 0.500)	12/35
Dalton et al. [6] 1997	0.045 (0.031, 0.059)	36/802
Kutko et al. [32] 1998	0.118 (0.041, 0.194)	8/68
Khatab et al. [33] 1999	0.430 (0.321, 0.540)	34/79
da Silva et al. [34] 1999	0.303 (0.231, 0.376)	47/155
Pound et al. [35] 2000	0.159 (0.073, 0.246)	11/69
Tamburro et al. [7] 2000	0.406 (0.358, 0.455)	163/401
Tamburro et al. [36] 2000	0.178 (0.127, 0.229)	39/219
Pancera et al. [37] 2001	0.418 (0.356, 0.481)	100/239
Meyer et al. [38] 2002	0.219 (0.076, 0.362)	7/32
Haase et al. [39] 2003	0.095 (0.063, 0.128)	30/315
Schiller et al. [40] 2003	0.250 (0.038, 0.462)	4/16
Faraci et al. [41] 2005	0.519 (0.385, 0.652)	28/54
Owens et al. [42] 2005	0.227 (0.126, 0.328)	15/66
Dursun et al. [43] 2006	0.556 (0.393, 0.718)	20/36
Fausser et al. [44] 2007	0.208 (0.160, 0.256)	57/274
Ha et al. [45] 2007	0.444 (0.312, 0.577)	24/54
Garcia-Salido. [46] 2009	0.193 (0.111, 0.276)	17/88
Zinter et al. [47] 2011	0.068 (0.063, 0.073)	708/10365
Agulnik et al. [48] 2012	0.119 (0.021, 0.217)	5/42

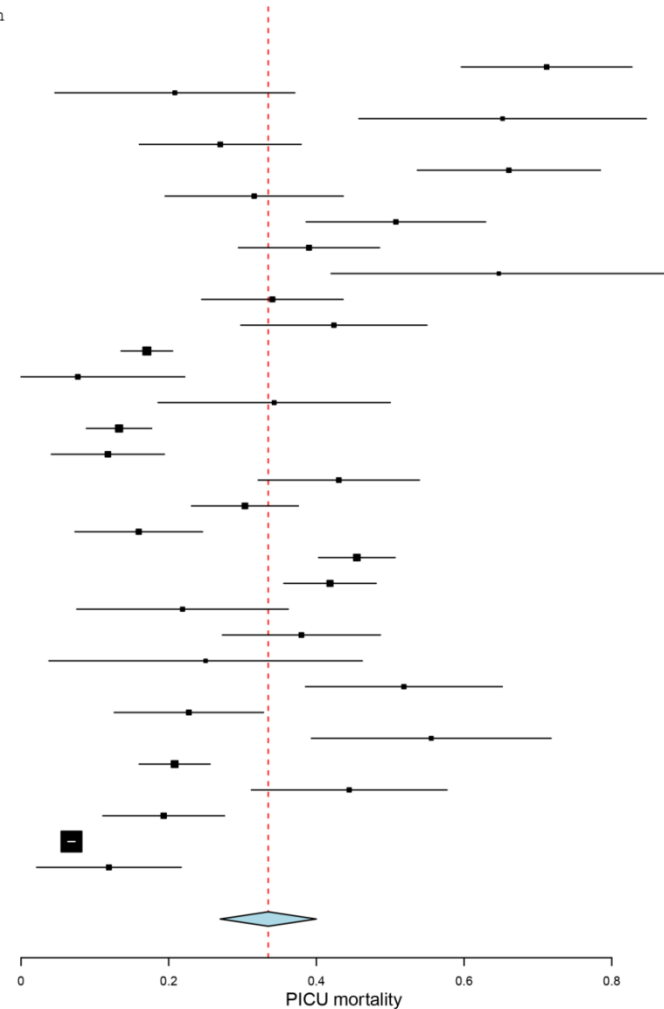
Overall ($I^2 = 96.54\%$, $P < 0.001$)

0.278 (0.237, 0.319) 1760/14945



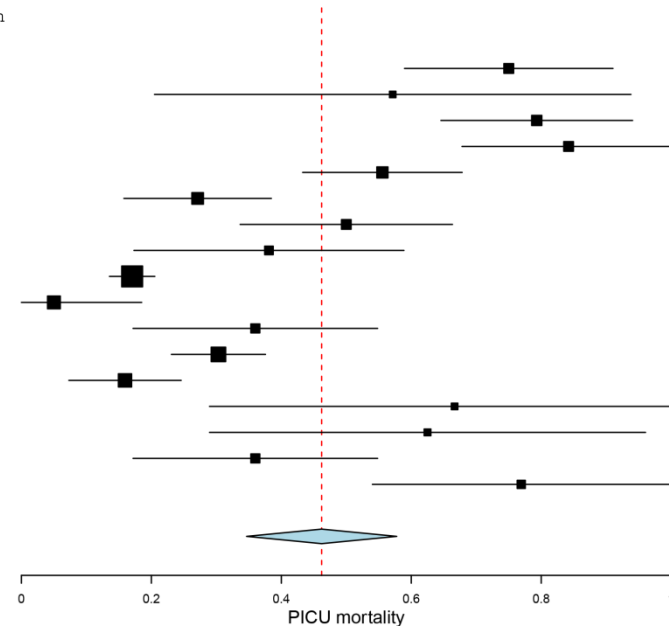
PICU mortality excl. post-operative patients 33.5%

Studies [ref] – median year of conduct	Estimate (95% CI)	Died / PICU admission
Butt et al. a [15] 1981	0.712 (0.596, 0.827)	42/59
Butt et al. b [15] 1985	0.208 (0.046, 0.371)	5/24
Butt et al. c [15] 1984	0.652 (0.458, 0.847)	15/23
Meert et al. [23] 1986	0.270 (0.160, 0.379)	17/63
Sivan et al. [24] 1987	0.661 (0.537, 0.785)	37/56
van Veen et al. [25] 1988	0.316 (0.195, 0.436)	18/57
Heney et al. [26] 1988	0.508 (0.386, 0.629)	33/65
Parsons et al. [27] 1988	0.390 (0.294, 0.486)	39/100
Ben-Abraham et al. [28] 1992	0.647 (0.420, 0.874)	11/17
Abraham et al. [29] 1994	0.340 (0.245, 0.436)	32/94
Keengwe et al. [30] 1994	0.424 (0.298, 0.550)	25/59
Fiser et al. [31] 1996	0.170 (0.136, 0.205)	76/446
Heying et al. a [16] 1997	0.077 (0.000, 0.222)	1/13
Heying et al. b [16] 1997	0.343 (0.186, 0.500)	12/35
Dalton et al. [6] 1997	0.133 (0.089, 0.177)	30/226
Kutko et al. [32] 1998	0.118 (0.041, 0.194)	8/68
Khattab et al. [33] 1999	0.430 (0.321, 0.540)	34/79
da Silva et al. [34] 1999	0.303 (0.231, 0.376)	47/155
Pound et al. [35] 2000	0.159 (0.073, 0.246)	11/69
Tamburro et al. [7] 2000	0.455 (0.403, 0.507)	161/354
Pancera et al. [37] 2001	0.418 (0.356, 0.481)	100/239
Meyer et al. [38] 2002	0.219 (0.076, 0.362)	7/32
Haase et al. [39] 2003	0.380 (0.273, 0.487)	30/79
Schiller et al. [40] 2003	0.250 (0.038, 0.462)	4/16
Faraci et al. [41] 2005	0.519 (0.385, 0.652)	28/54
Owens et al. [42] 2005	0.227 (0.126, 0.328)	15/66
Dursun et al. [43] 2006	0.556 (0.393, 0.718)	20/36
Fausser et al. [44] 2007	0.208 (0.160, 0.256)	57/274
Ha et al. [45] 2007	0.444 (0.312, 0.577)	24/54
García-Salido et al. [46] 2009	0.193 (0.111, 0.276)	17/88
Zinter et al. [47] 2011	0.068 (0.063, 0.073)	708/10365
Agulnik et al. [48] 2012	0.119 (0.021, 0.217)	5/42
Overall ($I^2 = 97.07\%$, $P < 0.001$)	0.335 (0.270, 0.400)	1669/13407



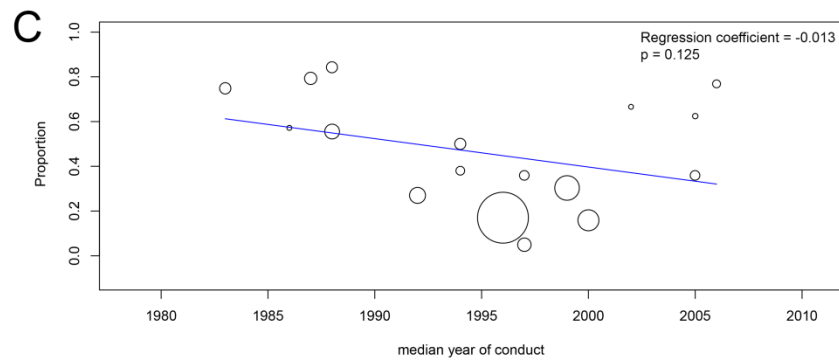
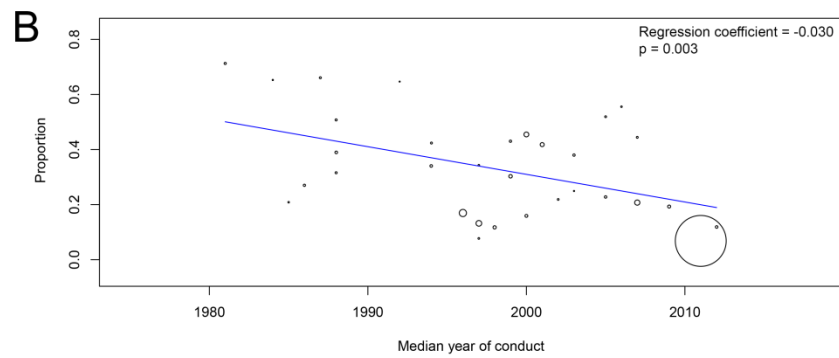
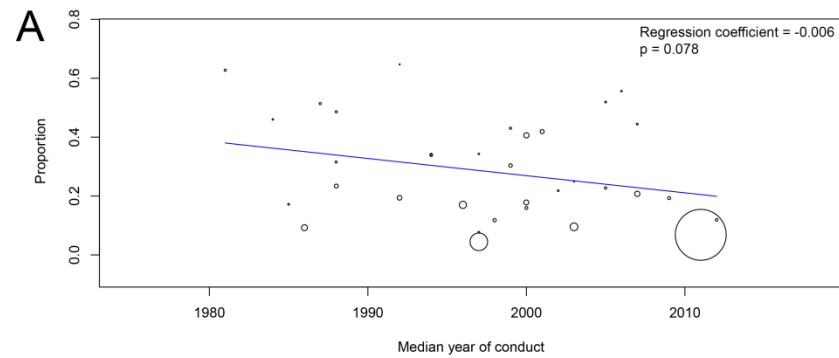
PICU mortality patients with sepsis 46.2%

Studies [ref] – median year of conduct	Estimate (95% CI)	Died / PICU admission
Butt et al. [15] 1983	0.750 (0.590, 0.910)	21/28
Meert et al. [23] 1986	0.571 (0.205, 0.938)	4/7
Sivan et al. [24] 1987	0.793 (0.646, 0.941)	23/29
Heney et al. [26] 1988	0.842 (0.678, 1.000)	16/19
Parsons et al. [27] 1988	0.556 (0.433, 0.678)	35/63
Hallahan et al. [8] 1992	0.271 (0.158, 0.385)	16/59
Abraham et al. [29] 1994	0.500 (0.337, 0.663)	18/36
Keengwe et al. [30] 1994	0.381 (0.173, 0.589)	8/21
Fiser et al. [31] 1996	0.170 (0.136, 0.205)	76/446
Heying et al. a [16] 1997	0.050 (0.000, 0.185)	0/9
Heying et al. b [16] 1997	0.360 (0.172, 0.548)	9/25
da Silva et al. [34] 1999	0.303 (0.231, 0.376)	47/155
Pound et al. [35] 2000	0.159 (0.073, 0.246)	11/69
Meyer et al. [38] 2002	0.667 (0.289, 1.000)	4/6
Faraci et al. [41] 2005	0.625 (0.290, 0.960)	5/8
Owens et al. [42] 2005	0.360 (0.172, 0.548)	9/25
Dursun et al. [43] 2006	0.769 (0.540, 0.998)	10/13
Overall ($I^2 = 93.29\%$, $P < 0.001$)	0.462 (0.347, 0.578)	312/1018



Use of PICU resources

Mortality				
PICU resource use	Studies	Odds ratio [CI 95%]	p-value	I ²
Mechanical ventilation	14	18.49 [13.79-24.78]	<0.001	6.09 %
Inotropic support	10	14.05 [9.16-21.57]	<0.001	0%
CRRT	4	3.24 [1.31-8.04]	0.01	20.3%





Conclusions

- PICU mortality of pediatric cancer patients is high (28%-46%)
- Mortality rates have remained static over time
- Need for PICU resources (mechanical ventilation, inotropic support and CRRT) significantly associated with PICU mortality.



POKER Delphi study: Research priorities on pediatric cancer patients admitted to PICU.

Prestage

- Selection of panel of stakeholders
- Identification of preliminary research domains based on review of the literature and expert opinion
- Establishment of advisory group overseeing the design, execution and analysis of all phases of the study

Stage II: Delphi round 1

Collection of demographic information and gathering and quick prioritisation of topics with stakeholders

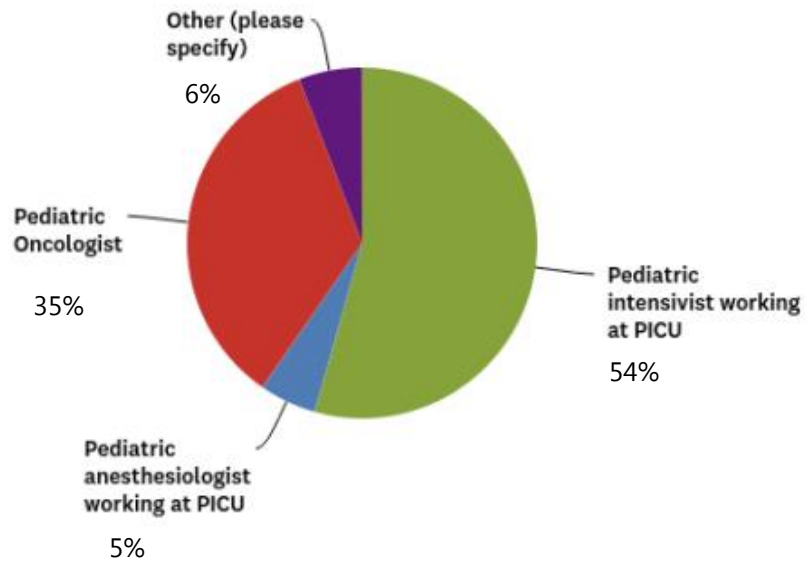
Stage III: Delphi round 2

Reflection on aggregated results from stage II and in-depth rating of topics

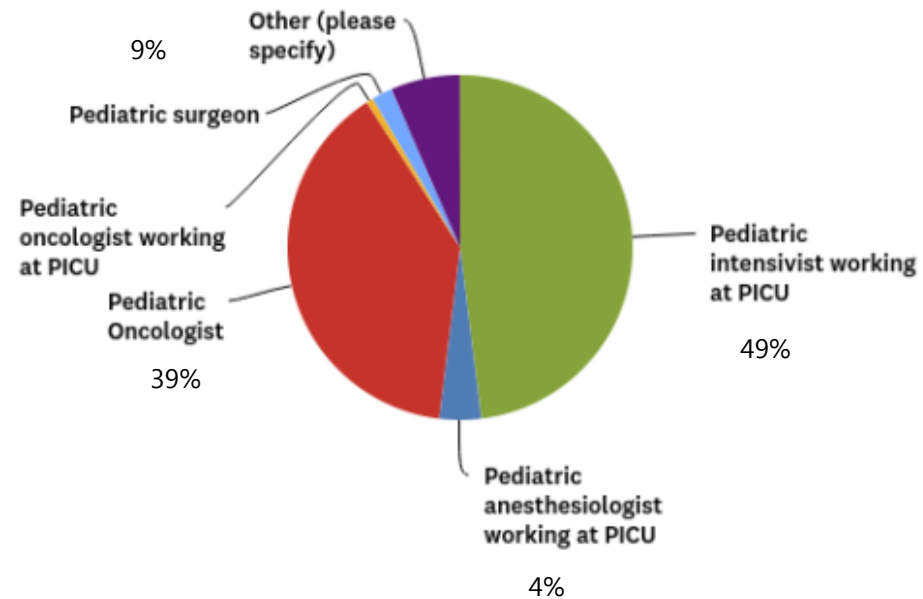
Stage IV: Delphi round 3

Final ranking of research topics

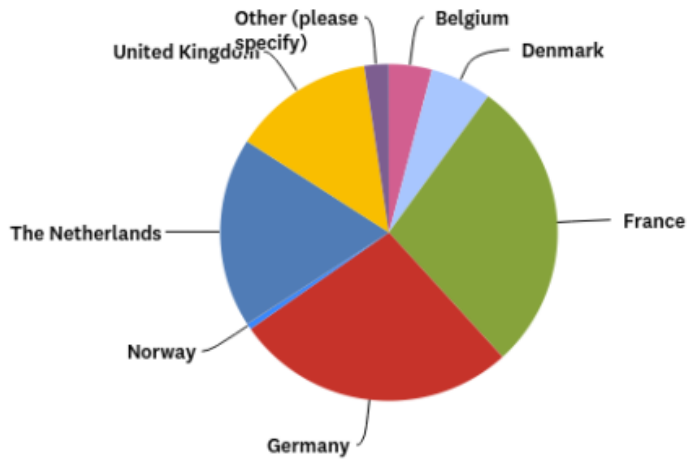
Round 1: 172 participants



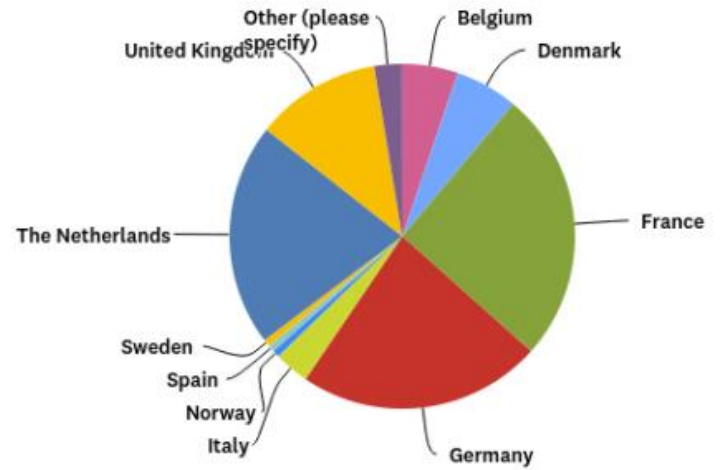
Round 2: 157 participants



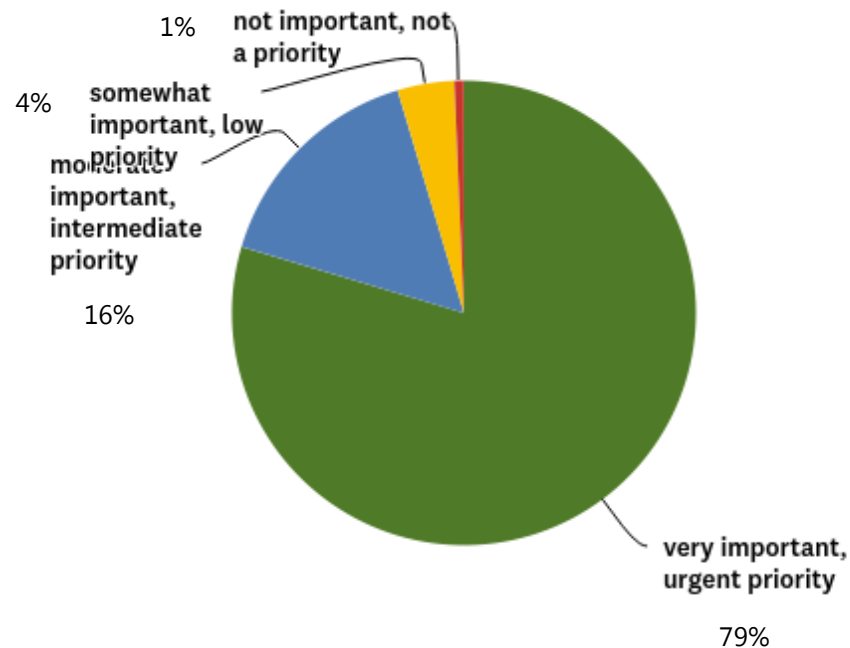
Round 1



Round 2



Determine the optimal timing of the use of life-sustaining therapies and identifying agreements and controversies between the different clinicians (intensivists, oncologists) and parents at the PICU on the futility and non-futility of these therapies in critically ill pediatric cancer patients.



Disproportionate care

Beneficial care





- Identifying patients who will benefit from ICU admission is often challenging.
- Lack of objective data on prognosis of pediatric cancer patients may make shared decision-making even more challenging.

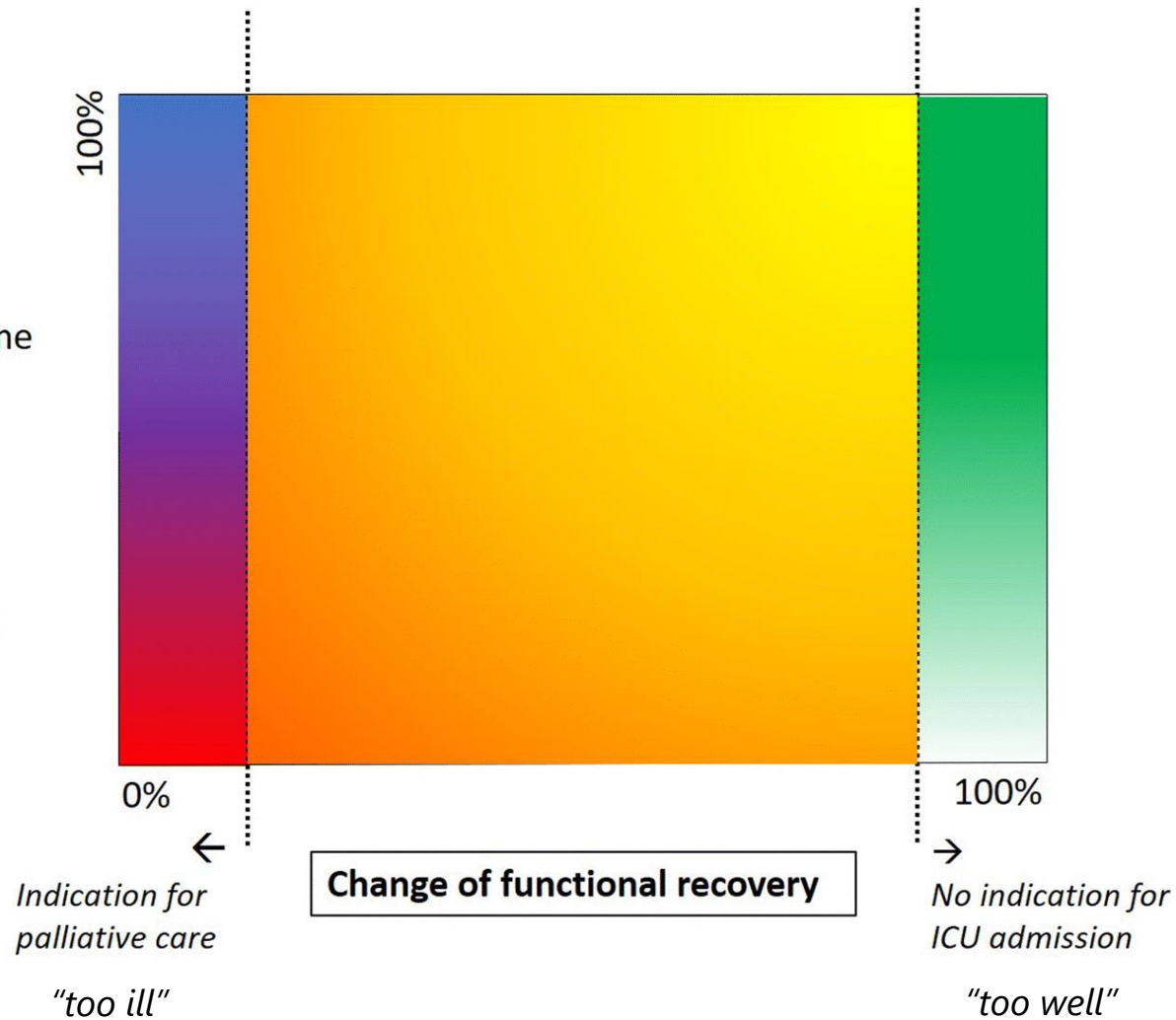


Time-limited trial

“An agreement between clinicians and a patient/family to use certain medical therapies over a defined period to see if the patient improves or deteriorates according to agreed-on clinical outcomes. If the patient improves, disease directed therapy continues. If the patient deteriorates, the therapies involved in the trial are withdrawn, and goals frequently shift more purely to palliation. If significant clinical uncertainty remains, another TLT might be renegotiated.”

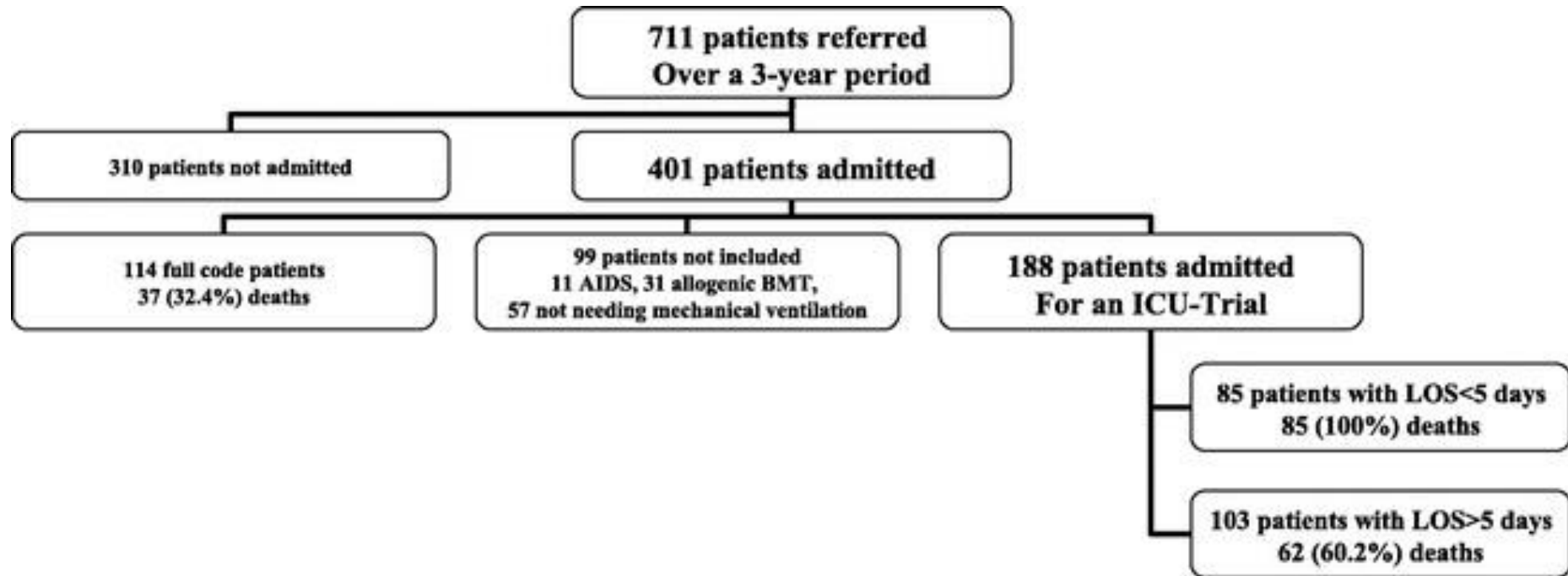
Context of situation, i.e.:

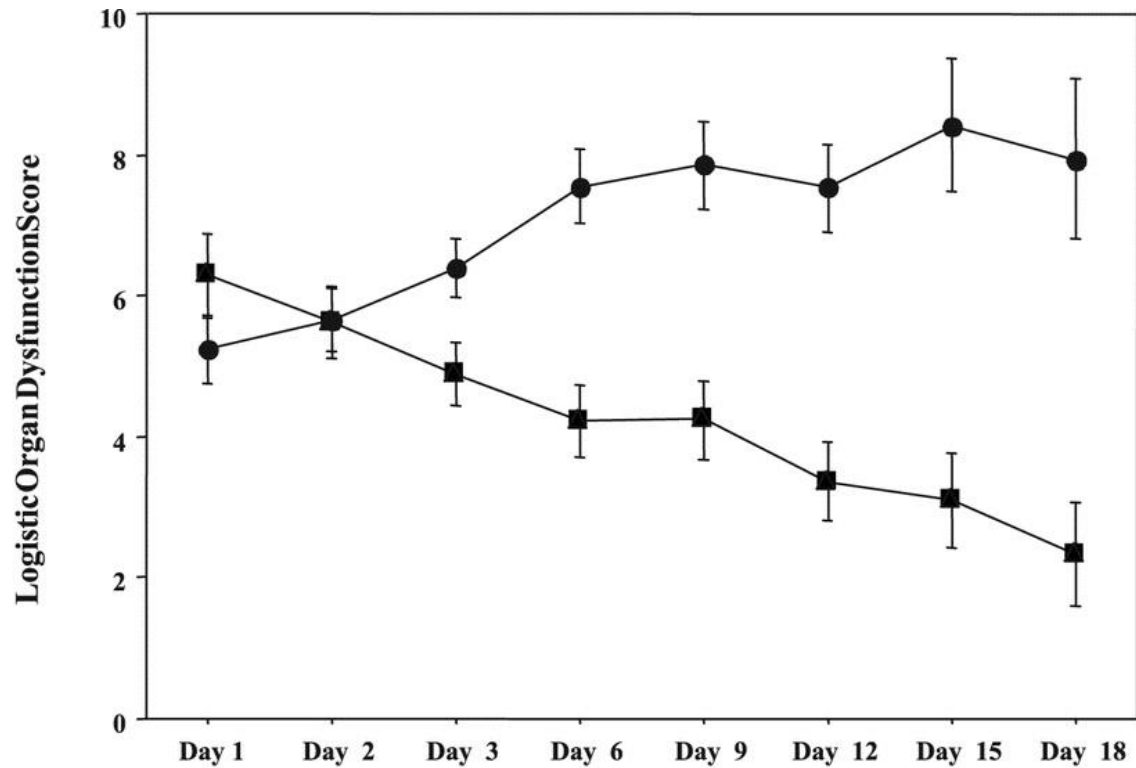
- Required time to adapt
- A patients personal wishes
- Resilience (abstract scale)





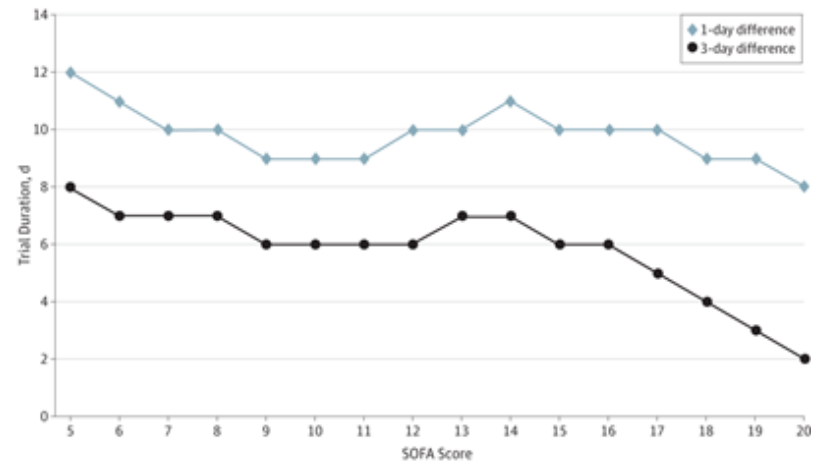
What is the optimal duration for a
TLT?



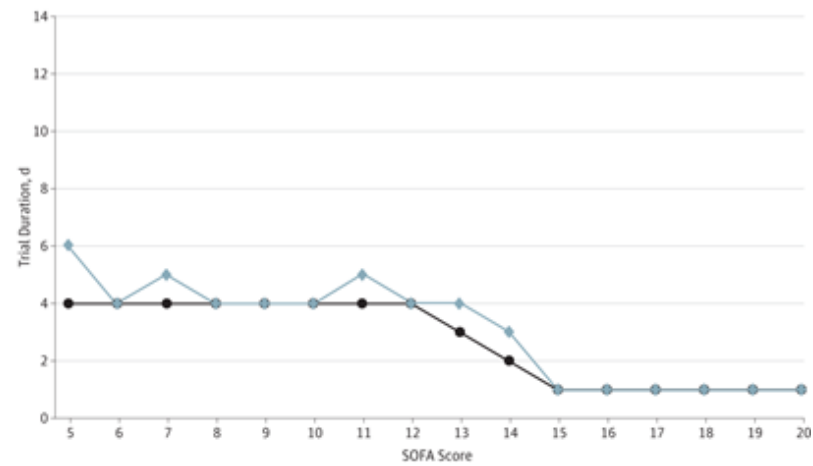


■ Survivors	n = 41	n = 41	n = 41	n = 40	n = 30	n = 27	n = 19	n = 15
● Non survivors	n = 62	n = 62	n = 62	n = 62	n = 45	n = 34	n = 22	n = 16
Total	n = 103	n = 103	n = 103	n = 102	n = 75	n = 61	n = 41	n = 31

A All patients



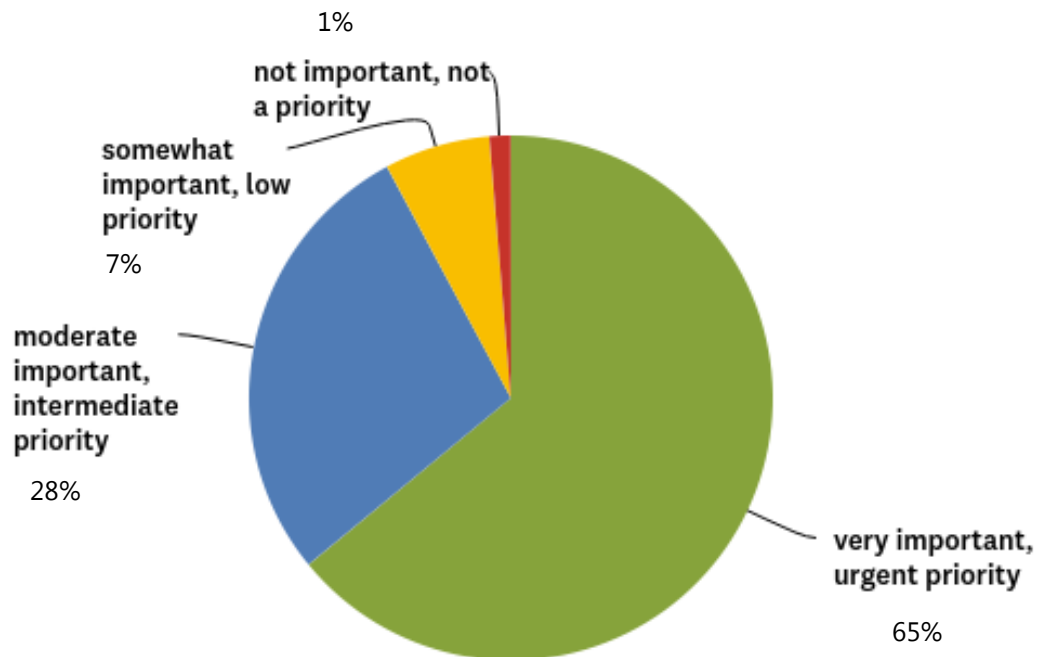
B Patients with nonhematologic malignant neoplasms

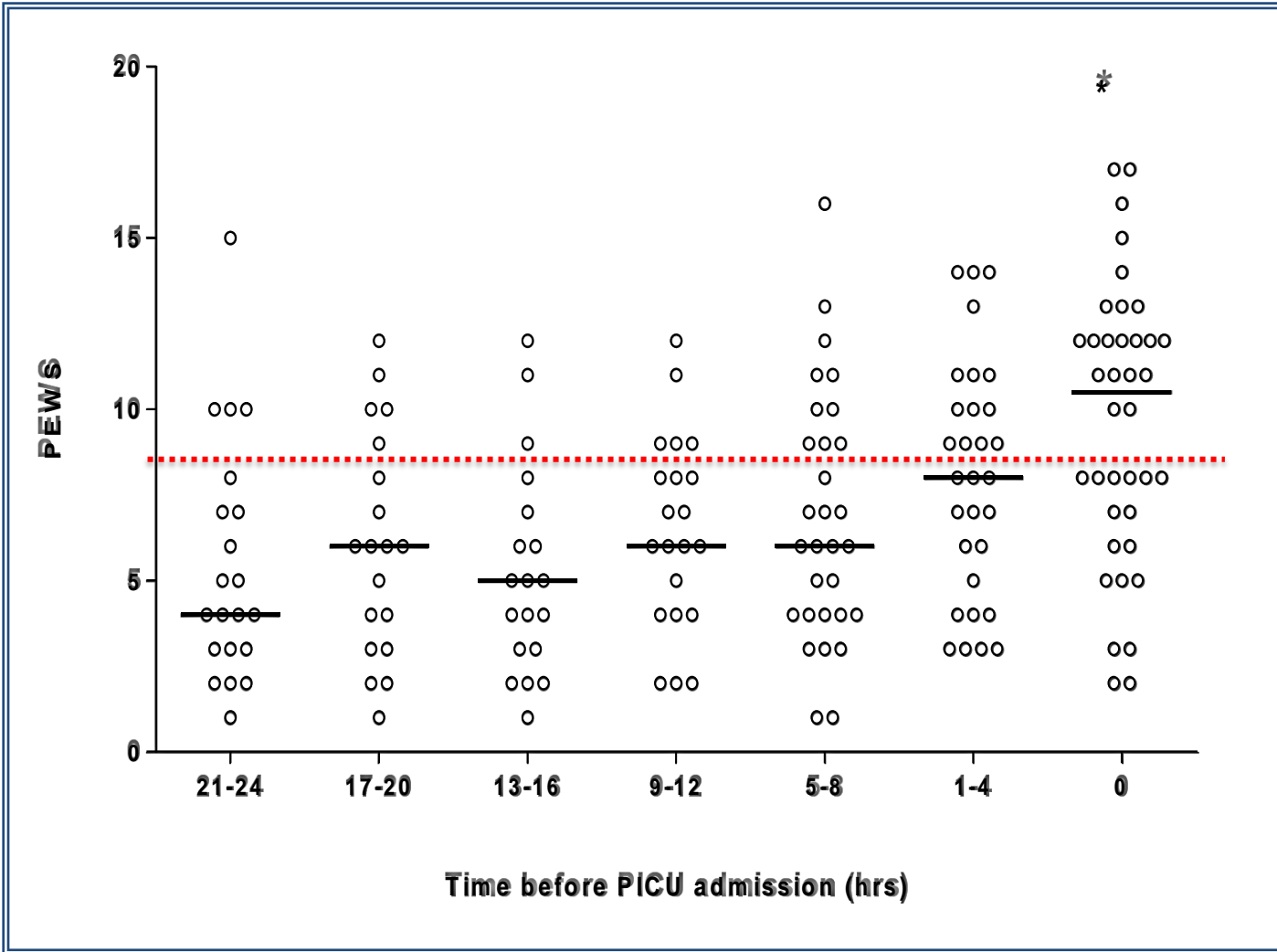


Time-limited trials at the PICU



Development of specific early warning scores to timely recognize critically ill pediatric cancer patients on the non-ICU ward requiring intensive care support.







**Princess
MÁXIMA**
center for pediatric oncology



Wilhelmina Kinderziekenhuis

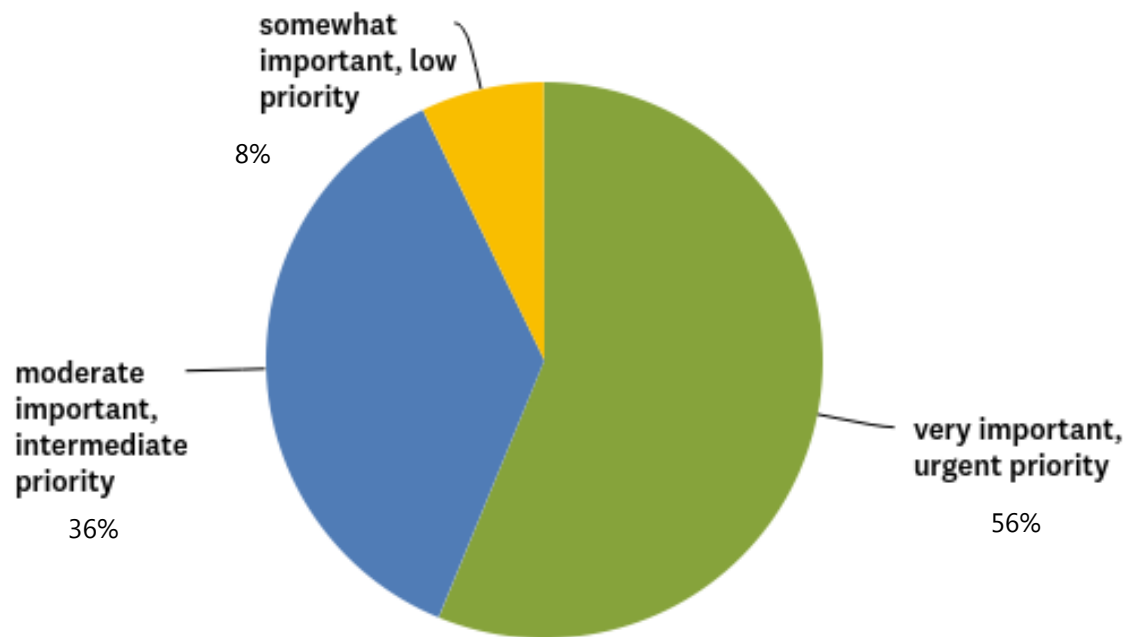
Identifying the critically ill pediatric cancer patient: need for specific oncological pediatric early warning score?

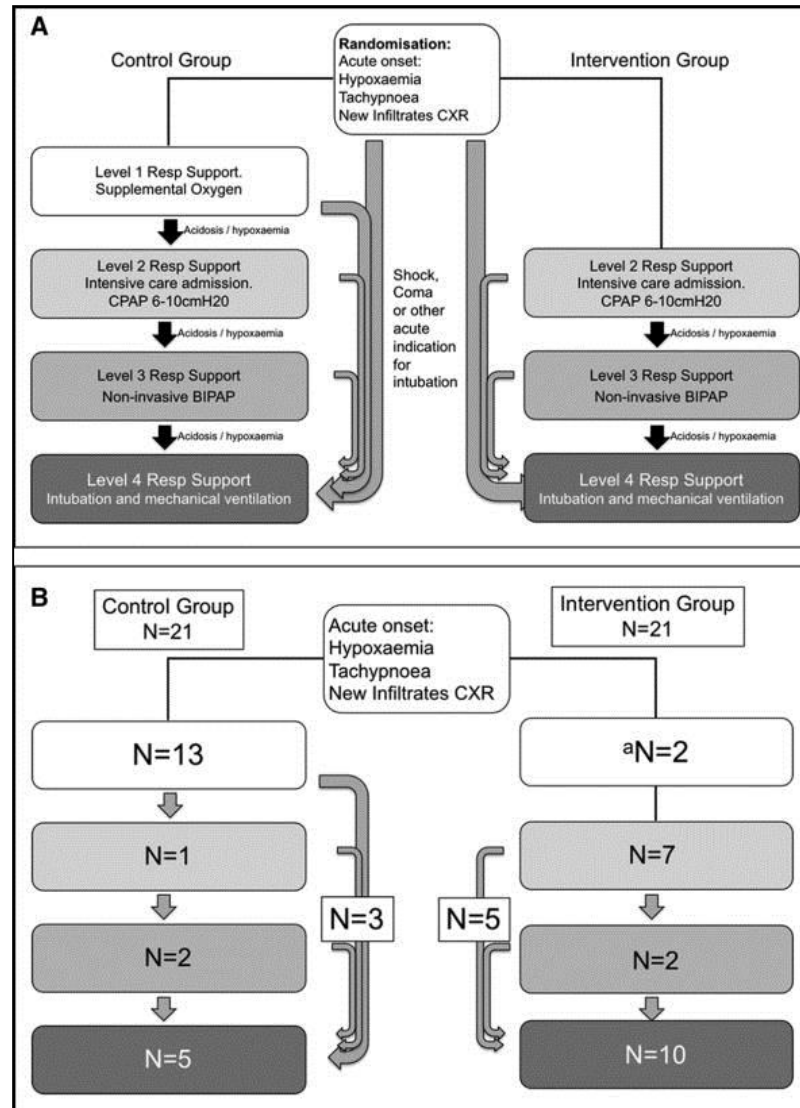


SO-PEWS

Marijn Soetman

Determine the role of non-invasive ventilation in acute respiratory insufficiency in critically ill pediatric cancer patients.





Clinical Management		Early CPAP, <i>n</i> = 21	Standard Care, <i>n</i> = 21
PICU admission, <i>n</i> (%)	Yes	19 (90.5)	9 (42.9)
	No	2 (9.5)	12 (57.1)
Length of stay in PICU (d) ^a	Mean (sd)	7.3 (7.3)	3.8 (8.2)
	Median (IQR)	5 (4–8)	0 (0–3)
CPAP (level 2 respiratory support) received, <i>n</i> (%)	Yes	18 ^c (85.7)	4 (19.0)
	No ^b	3 (14.3)	17 (81.0)
Maximum CPAP pressures (cm H ₂ O)	Median (IQR)	6.0 (6.0–8.0)	6.0 (6.0–7.3)
BiPAP (level 3 respiratory support) received at any time, <i>n</i> (%)	Yes	7 (33.3)	4 (19.0)
Maximum BiPAP pressures (cm H ₂ O)	Positive end-expiratory pressure, median (IQR)	8.0 (7.0–8.0)	8.0 (6.5–8.0)
	Peak inspiratory pressure, median (IQR)	20 (18.0–22.0)	20 (14.4–22.0)
Direct indication for intubation, <i>n</i> (%) ^d		5 (23.8)	3 (14.3)
High flow nasal cannula received, <i>n</i> (%)		4 (19.0)	3 (14.3)
Length of stay in acute hospital (d)	Mean (sd)	61.8 (98.2)	72.8 (83.4)
	Median (IQR)	41 (11–57)	51 (18–86)

BiPAP = bilevel positive airway pressure, CPAP = continuous positive airways pressure, IQR = interquartile range.
^aOne patient in the standard care group was missing length of stay in PICU.
^bIn two cases, a PICU bed was not available in 24 hr, and in one CPAP was not tolerated.
^cIncludes eight cases who did not complete the full intervention of CPAP for > 12 hr/d for 4 d.
^dIntubated without stepping up through levels (1)–2–3 respiratory support.

Outcomes	Early Continuous Positive Airways Pressure, <i>n</i> = 21	Standard Care, <i>n</i> = 21	Effect Estimate (95% CI)	<i>p</i>
Primary outcome				
Requirement for intubation and invasive mechanical ventilation (level 4 respiratory support) within 30 d post randomization, <i>n</i> (%)	10 (47.6)	5 (23.8)	2.00 (0.82–4.86) ^a	0.11
			23.8 (–4.3 to 51.9) ^b	0.12
			2.91 (0.78–10.89) ^c	
			3.07 (0.73–12.83) ^d	
Secondary outcomes				
Maximum PELOD score at 30 d post randomization, mean (sd)	34.4 (25.9)	22.4 (17.6)	12.0 (–1.8 to 25.8) ^e	0.087
			15.9 (0.8–30.9) ^f	0.040
Aggregate PELOD score at 30 d post randomization, mean (sd)	593.4 (713.4)	285 (321.9)	308.4 (–36.8 to 653.6) ^e	0.079
			387.9 (5.7–770.1) ^f	0.047
Mortality at 30 d post randomization, <i>n</i> (%)	7 (33.3)	1 (4.8)	10.00 (1.10–90.59) ^c	0.041
			35.29 (1.82–685.61) ^d	0.019
Days alive and free from any ventilatory support at 30 d post randomization, mean (sd)	18.5 (13.9)	24.5 (10.2)	–6.0 (–13.7–1.6) ^e	0.12
			–7.6 (–15.9–0.8) ^f	0.073
Days alive and free from supplemental O ₂ at 30 d post randomization, mean (sd)	12.0 (11.7)	13.6 (10.0)	–1.6 (–8.4–5.2) ^e	0.63
			–1.7 (–9.1–5.7) ^f	0.64
Hospital mortality, <i>n</i> (%)	11 (52.4)	5 (23.8)	3.52 (0.94–13.17) ^c	0.062
			5.77 (1.15–28.88) ^d	0.033
Mortality at 90 d post randomization, <i>n</i> (%)	11 (52.4)	4 (19.1)	4.68 (1.17–18.69) ^c	0.029
			11.39 (1.60–81.21) ^d	0.015
Mortality at 1 yr post randomization, <i>n</i> (%)	13 (61.9)	9 (42.7)	2.17 (0.63–7.44) ^c	0.22
			2.49 (0.58–10.62) ^d	0.22

PELOD = Pediatric Logistic Organ Dysfunction.

^aRelative risk.

^bAbsolute risk difference (%).

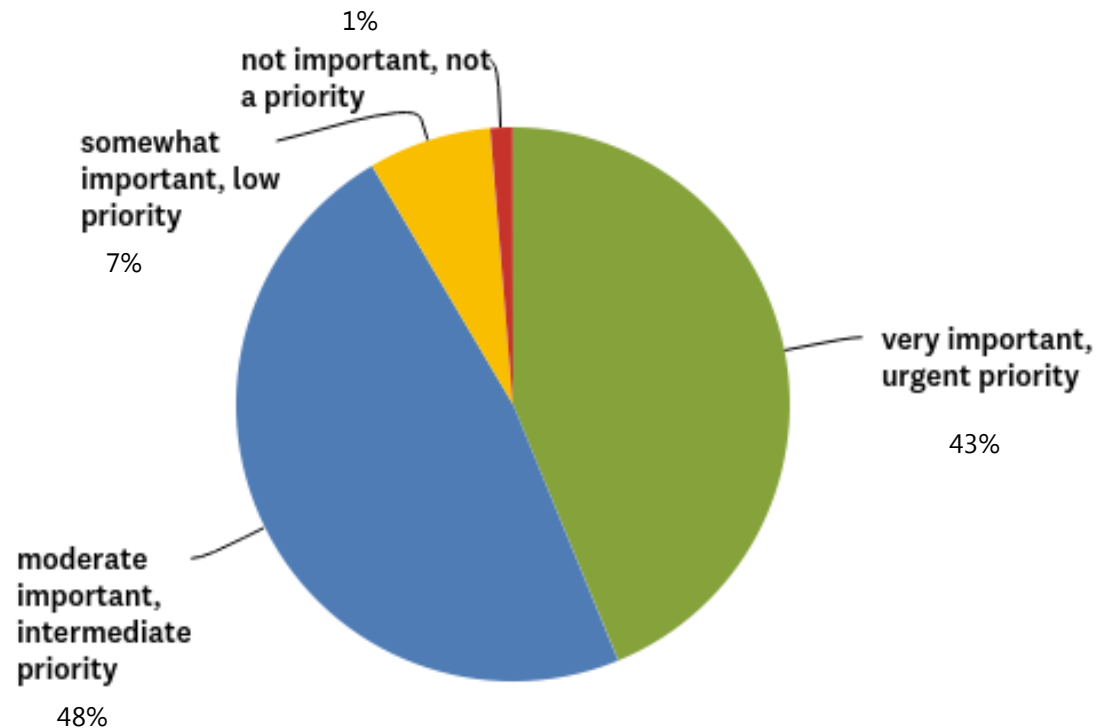
^cOdds ratio.

^dAdjusted odds ratio (adjusted for age, weight for age z score, bone marrow transplant, and Pediatric Index of Mortality 2, 2016 Recalibration [PIM2r (2016)] score).

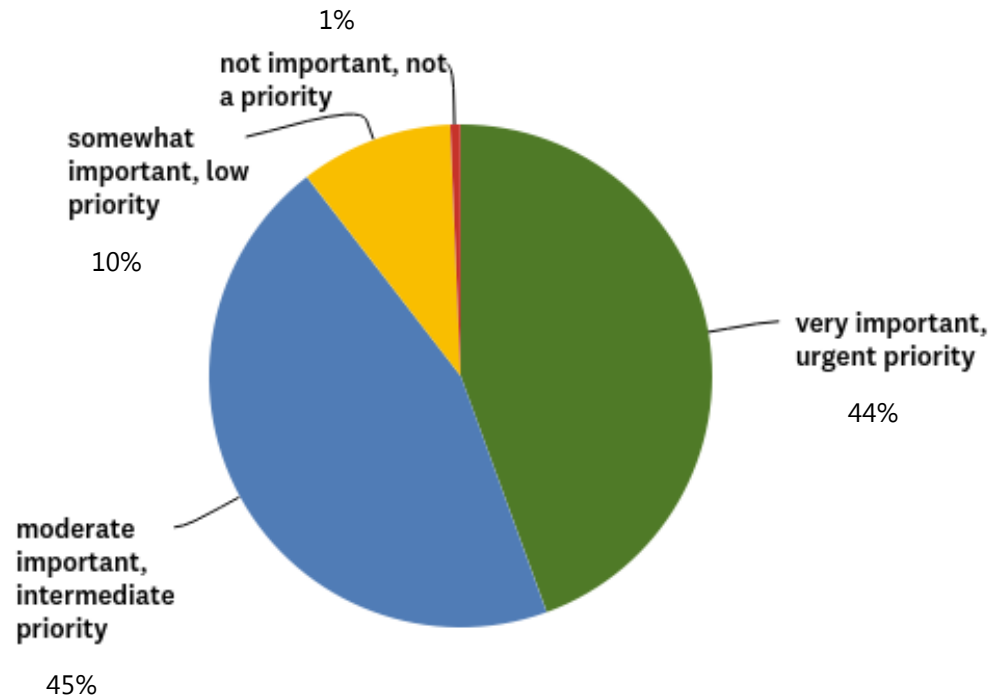
^eMean difference.

^fAdjusted mean difference (adjusted for age, weight for age z score, bone marrow transplant, and PIM2r [2016] score).

Exploring end-of-life care and ethical issues: i.e. change to end-of-life care, ethical considerations regarding decision making, communication with patients and parents, 'suffering' in pediatric cancer patients and their families on PICU, young people decision making in oncology.



Sepsis in critically ill pediatric cancer patients at the PICU: management, outcomes, and costs.





There is a lot of hard work
that needs to be done.

Martti Ahtisaari