TABLE 1 - Summary of included studies

Author/country (year of publication)	Design	Follow-up	n age	Disease	Objetive	CLABSI frequency or incidence per 1.000 /catheter-days	Risk factors
Bergmann/Denmark (2016)	Multicentric, retrospective cohort	2008-2014	136 <4y: n = 60 4-9y: n = 50 >9y: n = 26	ALL	To assess the risk of first time BSI according to type of CVC during induction therapy in children with ALL.	BSI: 39 (29%). CLABSI: nt-CVC: 13/20 patients (65%) TEC: 10/19 patients (52.6%) nt-CVC: 8.4/1.000 catheter-days TEC: 7.6/1.000 catheter-days	Type of catheter - No difference between nt-CVC and TEC for 28-day cumulative incidence of BSI (p = 0.65), HR = 0.85 (95%CI 0.50-1.44) - Gram-negative blood isolates occurred more frequently in patients with a TEC (p = 0.009) - Multivariate analysis adjusting for age, sex, neutrophil count at CVC insertion, and risk group found no differences in incidences of BSIs according to CVC type (HR 0.90; 95%CI 0.51-1.58) Age - Lower risk in patients older than 9 years old.
Handrup/Denmark (2010)	Single-center, retrospective cohort	2000-2008	98 <4y: n = 40 4-9y: n = 32 >9y: n = 26	ALL	To evaluate the risk of CVC related complications in children with ALL in relation to time of catheter insertion and type of catheter.	Overall infection rate of 3.1/1,000 catheter days TEC: 5.4/1.000 catheter-days Port: 1.4/1.000 catheter-days	- Type of catheter (TEC x Port) (P = 0,0001), Incidence rate ratio 3.82 (95%CI 2.37–6.35) - Time of insertion: no difference between early and late placement (Port, p = 0.98, Incidence rate ratio 0.99, 95% CI 0.41–2.45; TEC, p = 0.54, Incidence rate ratio 0.81, 95%CI 0.40–1.86).

Hord/USA (2016)	Multicentric, retrospective cohort	2012-2015	1113 mean: 6.6y (SD: -) (range: -)	Hematological diseases and solid tumors	To determine the relative risk of CLABSI associated with different types of CVC; the characteristics of the patients who experienced CLABSI with different types of CVC; and the microbiology of CLABSI associated with different types of CVC.	Inpatients: TEC: 3.51/1.000 catheter-days Port: 1.48/1.000 catheter-days PICC: 3.07/1.000 catheter-days Ambulatory: TEC: 1.38/1.000 catheter-days Port: 0.16/1.000 catheter-days PICC: 1.38/1.000 catheter-days	CLABSI rates higher in inpatients for each catheter type. Risk factors for hospitalized patients: - Neutropenia (ANC <500) in patients with TEC (p = 0.029) - Mucositis in patients with TEC (p = 0.022) - Within 100 days post-SCT in patients with TEC (p < 0.001) - Diagnosis ALL Port (p < 0.001) - Organism type: Gram positive in patients with TEC and PICC (p = 0.003) No significant differences among CVC types considering age (p = 0.31), gender (p = 0.45) and diarrhea (p = 0.29) Ambulatory - Younger age in patients with TEC (p < 0.001) - Diarrhea (p = 0.021) - Within 100 days post-SCT in patients with TEC (p < 0.001) - Diagnosis os solid tumor in patients with PICC and ALL in Port (p < 0.001) - Diagnosis with diarrhea in patients with PICC (p = 0.021) - Organism type: gram negative in patients with TEC and PICC (p = 0.001) No significant differences among CVC types considering gender (p = 0.54); neutropenia (p=0.068) and mucositis (p = 0.128) Among inpatients and ambulatory patients CLABSI associated to TECs and PICC was higher than ports. CLABSI associated to TEC was higher than PICCs but with no statistical significance in ambulatory (P = 0.082 for inpatients).
Hoss/USA (2016)	Single-center, retrospective cohort	2007-2015	183 mean: 9.9y (SD: -) (range: 0.75-21y)	Hematological malignancies and solid tumors	To evaluate infectious complications of ports placed in pediatric oncologic patients who presented to a tertiary pediatric center and had severe neutropenia at the time of port placement.	Overall - ANC ≤ 500/mm3 0,33/1.000 catheter-days n=13 (18.1%) - ANC ≥ 500/mm3 0,40/1.000 catheter-days n=18 (16.2%) First 30 days - ANC ≤ 500/mm3 4,41/1.000 catheter-days n=9(12.5%) - ANC≥500/mm3 1,51/1.000 catheter-days n=5 (4.5%)	Overall - ANC ≤ 500/mm3; difference of incidence density p = 0.58 - ANC ≥ 500/mm3; difference of incidence p=0.84 First 30 days - ANC ≤ 500/mm3; difference of incidence density p=0.045 - ANC≥500/mm3; difference of incidence p=0.08

Junqueira/Canada (2010)	Single-center, retrospective cohort	2005-2008	179 median: 4.1y (IQR: -) (range: 0.6-17.6y)	ALL	To determine whether severe neutropenia on the day of TIVAP insertion was a risk factor for catheter-associated infection (CAI) in children with acute lymphoblastic leukemia (ALL).	There were 43 CAIs (22%), and the infection rate was 0.35 per 1.000 catheter-days.	Severe neutropenia on the day of catheter placement (p = 0.137), RR: 0.61 (95%CI 0.33-1.09).
Kelly/USA (2013)	Single-center, retrospective case-control	2007-2009	123 median: 6.9y (IQR: -) (range: 0.33-22y)	Hematological malignancies and solid tumors	To define the microbiology and identify risk factors for CLABSI among outpatient children with cancer.	41 cases (33.3%) x 82 pared controls (66.6%)	Bivariate Risk Factors for Community-Onset CLABSI - Lower age (p = 0.02), OR 0.92 (95%CI 0.85-0.99) - Stem cell transplant recipiente (p = 0.02), OR 4.00 (95%CI 1.31-13.28) - ANC < 500 cells/µL within prior 1 wk (p < 0.001), OR 10.71 (95%CI 3.70-31.02) - Blood product transfusion red blood cell within prior 1wk (p < 0.001), OR=6.21 (95%CI 2.29-16.88) - Blood product transfusion: platelet (p < 0.001), OR 15.55 (95% CI 3.57-67.63) - TEC (p < 0.001), OR 4.36 (95%CI 1.54-12.36) - Duration since insertion (> 1 month) (p = 0.003), OR 9.95 (95% CI 2.21-44.81) Multivariate analyses: Independent predictors of community-onset CLABSI: - ANC < 500 cells/µL within prior 1 wk (p < 0.001), OR 17.46 (95%CI 4.71-64.67) - TEC (p = 0.002), OR 10.30 (95%CI 2.42-43.95)
Nam/South Korea (2010)	Single-center, retrospective cohort	2004-2005	225 mean: 7.06y (SD: 5.17y) (range: 0.25-18y)	Hematology malignancies, sarcomas, nervous system tumors, solid tumors	To investigate the incidence of complications, causes of Port removal, and risk factors for infection.	Early infections occurred in nine patients (4%) Late infections occurred in 26 patients (11,6%)	Univariate analysis For early infection: - Reimplantation (p = 0.022), OR 4.93 (95%CI 1.255-19.320) - Insertion in right jugular vein (p = 0.017), OR 5.800 (95%CI 1.375-24.457) - Long operation time (p = 0.045), OR 1.024 (95%CI 1.000-1.048). For late infection: - ANC < 500 (p = 0.001), OR 0.311 (95%CI 0.127-0.762) - Low platelet count < 50.000 mm3 (p < 0,011), OR 0.186 (95% CI 0.073-0.474) Multivariate analysis: For early infection: - Reimplantation (p = 0.033), OR 4.528 (95%CI 1.128-18.18). For late infection: - Low platelet count (p=0,005), OR 4.24 (95%CI 1.53-11.76).

Park/South Korea (2020)	Single-center, retrospective cohort	2010-2016	470 mean: 6,67y (SD: -) (range: -)	Hematological malignancies and solid tumors	To identify controllable treatment-environment-related factors affecting the timing of a CLABSI onset.	0.28 per 1.000 catheter-days.	Univariate analysis: - Older age (p < 0.01), HR 1.09 (95%CI 1.05-1.14) - Hospital stay > 60 dias (p < 0.01), HR 8.40 (95%CI 5.14-13.73) - Hickman catheter (p < 0.01), HR 2.51 (95%CI 1.53-4.09) - Insertion at operation room (p < 0.01), HR 0.29 (95%CI 0.18, 0.46) - Use of antibiotic on insertion (p < 0.01), HR 2.93 (95%CI 1.79-4.80) - Abnormal catheter funtion (p < 0.01), HR 2.76 (95%CI 1.59-4.81) - Homecare nursing (p < 0.01), HR 2.04 (95%CI 1.28-3.25) - Increased number of transfusion (p < 0.01), HR 9.99 (95%CI 4.64-21.51) - Increased number of blood test (p < 0.01), HR 1.28 (95%CI 1.28-2.00) Multivariable analysis - Hospital stay > 60 dias (p < 0.01), HR 5.27 (95%IC 3.14-8.89) - Insertion at operation room (p < 0.01), HR 0.48 (95%IC 0.29-0.80) - Use of antibiotic on insertion (p < 0.01), HR 2.04 (95%IC 1.22-3.54) - Abnormal catheter function (p < 0.01), HR 2.02 (95%IC 1.15-3.54) - Increased number of transfusion (p < 0.01), HR 2.94 (95%CI 1.02-8.42) - Increased number of blood test (p < 0.01), HR 1.54 (95%CI 1.14-2.09)
Rogers/USA (2016)	Single-center retrospective case-control	2007-2011	40 median: 14y (IQR: 10-16) (range: -)	AML	To determine the rates and etiology of CLABSIs in patients with AML within our institution. Our secondary objectives were to determine the timing of and the associated risk factors for infection.	25 (62.5%).	Univariate analysis - Fever (p < 0.001) - Presence of diarrhea (p = 0.026) - Presence of echthyma (p = 0.019) - Number of line entries (p = 0.006) - Receipt of blood products (p = 0.003) - Not receiving antibiotics in the previous 4–7 days (p = 0.010) - Transfer to pediatric intensive care unit (p < 0.001) - Intensification cycles of chemotherapy (p = 0.003). Multivariable analysis - Diarrhea (p = 0.001) - Receipt of blood products in the preceding 4–7 days (p < 0.001) - Not receiving antibiotics (p < 0.001) - Intensification cycle of chemotherapy (p = 0.009)

Taveira/Brazil (2016)	Single-center, retrospective cohort	2010-2012	188 median: 4.6y (IQR: -) (range: -)	Hematological malignancies and solid tumors	To determine the incidence of CLABSIs in pediatric cancer patients with Port and the risk factors for these infections in a developing country setting.	Cumulative incidence n = 94 (50%). Incidence density 1.21/1.000 catheter-days.	Bivariate anaysis - Chemotherapy prior to insertion (p = 0.002), RR 1.00 (CI95% 0.53-0.87) - Fever up to 7 days preceding Port insertion (p = 0.13), RR 1.00 (95%CI 0.56-1.08) - Antibiotic therapy up to 7 days preceding Port insertion (p = 0.20), RR 1.00 (95% CI=0.62-1.10) - WBC count <1000/mm³ on day of insertion (p = 0.003), RR 1.54 (CI95% 1.16-2.06) - ANC on day of Port insertion (p = 0.055), RR 1.25 (CI95% 1.0-1.56) Multivariate analysis - Chronic malnutrition (p < 0.05), RR 1.41 (95%CI 1.03-1.93) - White blood cell count less than 1,000 mm³ on the day of implantation (p < 0.01), RR 1.64 (95%CI 1.22-2.20) - Port insertion prior to chemotherapy (p < 0.01), RR 1.56 (95% CI 1.21-2.02) - Days of Port, RR 0.997 (95%CI 0.997-0.998)
Van den Bosch/The Netherlands (2018)	Single-center, retrospective cohort	2015-2017	201 median: 4y (IQR: -) (range: 0-18y)	Hematological malignancies and solid tumors	To describe incidence, severity, and outcome of early and late CVC-related complications in order to identify risk factors for CVC-related complications	1.51/1000 catheter-days. TEC: 3,92/1000 catheter-days. Port: 0.70 /1000 catheter-days.	- CVC type (TEC): significant risk factor for CLABSI in univariated (p = 0.005), OR 2.78 (95%CI 1.41–5.47), and multivariate analysis (p=0.002), OR 3.05 (95%CI 1.49–6.32) - CLABSIs during neutropenia associated to CVC type – non significant (0.79) - Number of lumens (double lumen): p = 0.001, OR: 3.31, (95% CI: 1.68–6.54) - Lumen diameter (≥ 7Fr): p < 0.001, OR: 4.31 (95%CI 2.16–8.64)
VanHouwelinge/ USA (2018)	Single-center, retrospective cohort	2013-2016	542 mean: 7.9y (SD: -) (range: -)	Hematological malignancies and solid tumors	To describe the association of neutropenia and development early post-operative infection in pediatric oncology patients	14 CLABSI (12 bacteremia + 2 bacteremia and port). Incidence: 3,3%. 4 Port site infecions.	Early postoperative infection (considering CLABSI and Port site infections) Univariate analysis - Severe neutropenia x non severe neutropenia (> 500/mm3): p < 0.001 / Ajusted for fever and underlying disease (p = 0.11), OR 2.42 (95%CI 0.82-7.18) - Pre-operative fever within two weeks of procedure (p = 0.001), OR: 4.72 (95%CI 1.55-14.37) - Disease (Leukemia and Lymphoma > Solid tumor) (p = 0.032), OR: 2.33 (95%CI 0.61-8.86) - Lower hemoglobin: 25% decrease in odds of infection for every one unit (g/dL) increase in hemoglobin (p = 0.025), OR 0.75 (95%CI 0.58–0.96). Multivariate analysis - Disease: leukemia and Lymphoma (p = 0.0564), OR 4.37 (95% CI 0.96–19.86) - Presence of preoperative fever within two weeks of procedure (p = 0.0010), OR 6.09 (95%CI 2.08–17.81)

Yacobovich/Israel (2015)	Multicentric, retrospective cohort	2006-2008	262 median: 7.4y (IQR: -) (range: 0.08-28.3 y)	Hematological malignancies and solid tumors	To describe the host, underlying disease and CVC-related risk factors for symptomatic BSI in pediatric patients with CVC.	Incidence of BSIs was 1.95 per 1.000 patient-days. Incidence of CLABSI 2.84/1.000 catheter-days.	Younger age (p = 0.022), HR 1.05 (95%CI 1.01–1.1) Type of catheter - Higher risk for BSI in TEC versus Port (p<0.0001), HR 2.16 (1.5–3.14) - Higher risk for BSI in PICC versus Port (p<0.0001), HR 1.43 (1.07–2.16) - Lower risk for coagulase negative *Staphylococcus* in PICC (8.5%, 95%CI 4.9-13.5%) versus Ports (15.3%, 95%CI 9.5-22.9%) and TECs (18.5%, 95%CI 11.5–27.3%) Insertion site - Higher risk for BSI when inserted in the right side versus the left side (p = 0.038), HR 1.39 (95%CI 1.02–1.89) Disease: Group A (ALL and solid tumor) – higher HR for BSI in TEC (1.85, 95%CI 1.15–2.97) and PICC (1.42, 95%CI 0.94–2.17) versus TEC (p = 0.003). Group B (AML and SCT) – no differences in BSI incidence according to catheter type (p=0,65).

ALL acute lymphocytic leukemia; *AML* acute myeloid leukemia; *ANC* absolute neutrophil count; *BSI* bloodstream infections; *CI* confidence interval; *CLABSI* central line-associated bloodstream infection; *CVC* central venous catheter; *HR* hazard ratio; *IQR* interquartile range; *nt-CVC* non-tunneled central venous catheter; *OR* odds ratio; *PICC* peripherally inserted central catheter; *Port* totally implantable venous access port; *RR* relative risk; *SCT* stem cell transplant; *SD* standard deviation; *TEC* tunneled externalized catheter; *WBC* white blood count