ASCO GUIDELINES

Data Supplement

American Society of Clinical Oncology Clinical Practice Guideline for Central Venous Catheter Care for the Oncology Patient

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Abdelkefi, J Support Oncolo, 2007	To evaluate whether Heparin-coated CVC are safe and effective approach to prevent CRBSI (80% power, two tailed Significant 5%)	246 patients with nontunnelled CVC (externalized, poly, double lumen Arrow International) with hemato-oncologic disease	Heparin-coated CVC with 50 mL/d of normal saline solution as a continuous infusion (Heparin-coated group)	Non-coated catheter with a continuous infusion of low-dose unfractionated Heparin with continuouse infusion of 100 U/kg/d	Y	Y	Y	Y	CRBSI rates in two groups; Secondary outcomes included an analysis of variables that may be significantfor the development of CRBSI eg. age, gender, therapy, side of puncture etc.	not stated	Catheter-related bloodstream infection occurred in 2.5% (3/120 catheters) in the Heparin-coated group (0.9 events per 1,000 days) and in 9.1% (11/120 catheters) in the control group (3.5 events per 1,000 days; P = 0.027).
Adlard, J Ped Onco Nurs, 2008 *not rct not in text	To test the limits of agreement between laboratory values obtained using the push–pull and standard methods of blood sampling from CVC devices in pediatric oncology patients.	30 pediatric oncology patients (8 mo - 17 years) with tunnelled Hickman or implanted CVC	Push–pull (mixing) method, limits both blood loss and potential exposure to pathogens. Blood is aspirated into a syringe and reinfused 3 times without disconnecting the syringe. After the third aspiration/ reinfusion cycle, the syringe is disconnected.	Discard method of blood draw	N	N	N	N	Agreement between lab values with push pull method and standard methods of blood sampling	not stated	The analyses suggest excellent agreement between assays using the 2 methods of blood sampling. There was no hemolysis observed in the paired samples as evidenced by the potassium levels (K cv 3.933 vs K rv 3.943), which are usually elevated in the presence of hemolysis. There was no evidence of hemodilution as evidenced by the HCT levels (HCT cv 29.323 vs HCT rv 29.317), which are lower in the presence of hemodilution. None of the 30 children developed a fever during the data collection period. Using the push–pull method of blood sampling did not appear to increase the risk of BSIs in these 30 pediatric oncology inpatients. The lab values between the paired blood samples were equivalent as evidenced by the highly similar means and SDs. At issues is blood loss resulting from discard contributing to volume depletion and that blood loss for diagnostic purposes may result in “nosocomial anemia” and the need for transfusions
Araujo, EJSO, 2007 not RCT	To compares two differenceerent venous accesses for totally implantable venous access devices (TIVAD) (Mini-Stitimplant, Vigon, FR) , the subclavian (SC) versus the internal jugular (IJ), in terms of early and late morbidity; without fluoroscopic control	1231 TIVADs were placed in 1201 patients	617/1231 inserted in SC vein in an ambulatory operating room, under vital Significantns and EKG monitoring, using local anaesthesia and without perioperative radiological control.	614/1231 inserted in IJ vein in an ambulatory operating room, under vital Significantns and EKG monitoring, using local anaesthesia and without perioperative radiological control.	N	N	N	N	Immediate complications; malposition; long term morbidity; VTE	not stated	Immediate complications were more frequent in the SC than in the IJ approach (respectively, 5.0% vs. 1.5%; p < 0.001); catheter malposition occurred in 2.3% when using the SC vein and in 0.2% for the IJ (p = 0.001). Long term morbidity was also more frequent in the SC than in the IJ group (respectively, 15.8%, 87/551, vs. 7.6%, 39/512; p < 0.001). Venous thrombosis developed in 2.0% of patients with an SC TIVAD as compared to 0.6% with an IJ TIVAD (p = 0.044). catheter malfunction was significantly dependent on the vein used: SC - 9.4% vs. IJ - 4.3% (p = 0.001). Results support the preferential use of the Internal Jugular vein for the insertion of TIVAD.

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Andrivet Clin Infec Dis 1994	To determine the incidence of bacteremic episodes in each group (tunneled vs non-tunneled), and assess the lifespan of the catheters in each group	Most patients with cancer (a few with AIDS) referred to the MICU for prolonged CVC (n=175; 169 evaluable; 212 catheters); 21 patients in non-tunneled group got polyurethane catheters, all others (both groups) got silicone catheters Randomization inappropriate: Size of study groups not planned.	Standard insertion, non tunnelled catheter (n=105 catheters)	Subcutaneous tunneled catheter (n=107 catheters)	N	N	Y	N	Episodes of bacteremia catheter lifespan	Not stated, but study period was 2 yrs 5 months, and mean life span of catheters was 116 +/- 6.5 days	Catheter life span: 112.5d in tunneled group, 119d in non-tunneled group (p>0.50) Bacteremia episodes: 26 (24.3%) in tunneled group, 25 (23.8%) in non-tunneled group (p>0.90) Observed rate of bacteremia of 25% in the tunneled group, detection of significantdifference of 5% in rate of bacteremia with a risk of <5% would have required inclusion of 300 patients in each group with a study period of 7 years. After true study period of 2 yrs and 5 months, difference between 2 groups in bacteremia was 0.%%. Findings suggest that routine SQ tunneling of CVCs is unnecessary in immunocompromised patients.
Aquino J Ped Hem Onc 2002	To determine if prophylactic urokinase flushes initiated at the time of CVC placement could reduce incidence of bacteremia associated with the use of CVCs	Newly diagnosed pediatric cancer patients receiving CVCs, catheter life expected to be >6 mos (n=103; 74 evaluable). Assuming 120 patients, bacteremia incidence 20%, study had power of 80% (5% significantlevel) to detect 75% reduction in Arm 1	Urokinase-Heparin monthly catheter flush (n=40)	Heparin alone monthly catheter flush (n=34)	D	N	Y	N	Bacteremia	Until CVC removal, patient required BMT, or port occluded and was infused with an antithrombolytic agent	Study closed prematurely (urokinase removed from market) Mean number of flushes: 9.5 in U-H group, 10.2 in Heparin group (p=0.62.) Bacteremia associated with + BC: 5 in U-H group, 7 in Heparin group (p=0.27). Overall rate of documented bacteremia: 0.4 and 0.6 events/1,000 catheter days in U-H and Heparin groups, respectively. No bleeding complications related to either flush noted. No difference in the incidence of bacteremia in patients who received monthly prophylactic doses of 5,000 IU of urokinase and Heparin compared with those who received Heparin alone.

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Atkinson J Ped Surg 1998	To determine if the addition of UK to standard antimicrobial treatment improves the clearance of established CVC sepsis	Pediatric cancer patients with a CVC, positive BCxs, and a dye study injection of the catheter that showed no evidence of gross thrombus or fibrin (n=63). Study excluded any patient with known thrombus on dye study	antibiotic + 2 boluses (5,000 U) UK given 12h apart via each lumen of the catheter (n=33)	antibiotic alone (n=30)	N	Y	N	N	Time from initiation of antibiotic treatment to patient becoming afebrile Time from initiation of antibiotic treatment to negative catheter culture Reduction in number of catheters requiring removal due to persistent clinical or culture-documented catheter sepsis	Until negative cultures were obtained and clinical Significantns resolved or when a failure was declared and the catheter removed	Clearance of infection: 21/30 (70%) antibiotic group, 24/33 UK+antibiotic group; clearance rate of 73% vs 70% (p=NS). 9 of 30 in antibiotic group required catheter removal, 9 of 33 in UK+antibiotic group required catheter removal. Study suggests that therapeutic addition of UK to the treatment of catheters with no clinical or radiological evidence of thrombus is of little benefit.
Barriga Med Ped Onc 1997	To test the hypothesis that intraluminal colonization of tunneled CVCs contributes to bacteremia only in non-neutropenic patients; to compare the efficacy ofvancomycin in preventing bactermia caused by vancomycin-sensitive organisms (VSO) in neutropenic and non-neutropenic patients; study had 80% power (significantlevel 0.05) to show reduction in VSO bacteremia in non-neutropenic patients from 15% to under 2%, assuming 60 febrile episodes in each group	Pediatric (majority) cancer patients (neutropenic & non-neutropenic) with tunneled CVCs (n=83)	Daily catheter flush with heparin+vanco (n=39)	Daily catheter flush with heparin (n=44)	D	N	N/A	N/A	Neutropenic and non-neutropenic febrile and bacteremic episodes	16,677 catheter days (8,666 heparin and 8,011 heparin+vanco)	Episodes of bacteremia: 44 total, 23 VSO, 16 in heparin group, 7 in heparin+vanco group (p=0.19). VSO bacteremia in neutropenic episodes: 7 in each group VSO bacteremia in non-neutropenic episodes: 9 in heparin group, 0 in heparin+vanco group (p=0.013). Vancomycin in the heparin flush sol'n can be used to prevent bacteremia by VSO in patients with CVCs, but this measure will be of modest benefit to cancer patients treatmented with intensive chemotherapy protocols.

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Benhamou BMT 2002	To compare the efficacy of 2 catheter dressing change frequencies in preventing skin toxicity at the catheter dressing site, in attenuating pain during and between dressing changes, without promoting local and systemic infection; estimated that minimum of 55 patients/arm needed to demonstrate a minimal difference of 30% in rate of grade >2 skin toxicity during hospitalization (2-tailed test, a=5%, B=10%, skin toxicity previously observed with 4-d rhythm 30%). Only 17% of dressing changes were performed per protocol in the 15-D group compared to 76% in the 4-D group (p<0.001)	Pediatric cancer patients undergoing high-dose chemotherapy and auto or allo BMT (n=113; 112 evaluable)	catheter dressing changed every 15 days (n=56)	catheter dressing changed every 4 days (n=56)	N	N	Y	Y	Skin toxicity at the catheter dressing site and its periphery. Bacteremia Local pain during and between dressing changes.	Through hospital discharge or catheter removal Mean duration of hospitalization was 48 d in the 15-D group and 47 d in the 4-D group	Cumulative proportions of patients with skin toxicity 2, 4, and 6 weeks after conditioning were 7%, 14%, and 16% in the 15-day group and 16%, 34%, and 44% in the 4-day group (logrank, p=0.001); patients in 4day group had 3.4-fold risk of developing grade >2 skin toxicity compared to 15-day group; adjusted for busulfan, Significant of test improved (logrank p<0.001). Pain during dressing change: 32% in 15-day group, 48% in 4-day group (p=0.09, when adjusted for busulfan); positive cutlture sample at catheter entry point: 15 (27%) in 15-dat group, 13 (23%) in 4 day group (p=NS). Although 13 cases of bacteremia were observed during follow-up period, only one infection in each group was catheter-related. The main result of this trial is a 70% relative reduction in the incidence of local skin toxicity in the group with less frequent dressing changes.
Bern Ann Int Med 1990	To determine whether very low doses of warfarin are useful in thrombosis prophylaxis in patients with CVCs; with 40 patients in each arm, study could detect with 95% CI drop from 30% to 15% incidence of thrombosis	patients receiving infusion chemotherapy via CVCs (n=121; 82 evaluable)	Warfarin 1mg po qd (n=42) patients in both arms got subclavian venograms after 90d or when sympatientoms/Significantns of thrombosis	No warfarin (n=40)	N	N	Y	N	Venogram-documented thrombosis	Patients on study for 90 days or until venogram-documented evidence of thrombosis	Venogram-documented thrombosis: 4 in warfarin arm, 15 in non-warfarin arm (p<0.001); Patients in non-warfarin arm with thrombosis had patientTs of 25.5 +/- 3.0 secs, patients without thrombosis had 28.0 +/- 3.7 secs (p<0.01); Patients in warfarin arm with thrombosis had patientTs of 23.6 +/- 2.2 secs; Patients without thrombosis had 27.2 +/- 3.9 secs (p<0.01); Patients in warfarin arm with thrombosis had patients of 12.3 +/- 0.9 secs; Patients without thrombosis had 14.7 +/- 2.5 secs (p<0.05) Findings strongly suggest that patients should receive very-low-dose warfarin therapy when they have indwelling catheters. [Note: text states that 13/15 in non-warfarin arm were sympatientomatic, whereas abstract states that 10/15 were sympatientomatic]
Biffi Cancer 2001	Compare complications between arms assuming a 5% removal rate of Groshongs due to infection, if 15% of control catheters were removed, study had 80% power (5% significantlevel, 2-sided test)	Patients with solid tumors, candidates for IV chemotherapy (n=304; 302 evaluable)	Silastic Groshong (valved) catheter tubing (n=152)	Silastic, open-ended catheter tubing (n=150)	N	Y	Y	Y	Percentage of patients with a complication within 6 mos of insertion (authors define multiple endpoints for complications; early = intraoperative and postimplant to first use; late = after the first chemotherapy course given through the catheter)	Minimum of 6 months; median 237 days	Early complications: NS (p=0.26); Late complications: NS (p=0.13) [excepatiention: withdrawl occlusion much greater in Groshong group, p<0.001]; Thrombosis: NS (p=0.22). Single center MSB used in both arms Cefazoline IV given 15 mins prior to implantation; Percentage of control patients requiring catheter removal (3.3%) much lower than anticipated during trial deSignificantn. Groshong connected to port not superior to traditional open-ended device in terms of early and late complications.

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Biffi Annal of Oncology, 2009	Comparison between 3 arms (landmark + IJ, ultrasound with subclavian, and cut down with deltoid pectoralis groove; with early and late complications recorded at the time of removal of the devices. Randomized.	Patients with solid tumors, candidates for IV chemotherapy (n=304; 302 evaluable)	Single port (Bard Port) using percutaneous landmark access to internal jugular (n=132)	Single port (Bard Port) using US guided access to subclavian (n=136) and third arm surgical cut-down access through the cepahalic vein at the deltoid-pectoralis grove (N=133)	N	U	Y	Y	Comparison of the three central venous insertion sites were the percentage of patients with a complication in the perioperative setting and within 6 months of insertion, i.e. during chemotherapy treatment.	Median followup was 265.5 days (range 0-1087)	No differences were found for early complication rate in the three groups {internal jugular: 0% [95% confidence interval (CI) 0.0% to 2.7%], subclavian: 0% (95% CI 0.0% to 2.7%), cephalic: 1.5% (95% CI 0.1% to 5.3%)}. US-guided subclavian insertion site had significantly lower failures (e.g. failed attempatients to place the catheter in agreement with the original arm of randomization, P = 0.001). Infections occurred in one, three and one patients (internal jugular, subclavian and cephalic access, respectively, P = 0.464), whereas venous thrombosis was observed in 15, 8 and 11 patients (P = 0.272). Central venous insertion modality and sites had no impact on either early or late complication rates, but US-guided subclavian insertion showed the lowest proportion of failures.
Bishai Peds 1999	To compare the relative efficacy and safety of amethocaine gel (requires 30 minute application time) and lidocaine-prilocaine cream (EMLA, requires 60 minute application time) in children with cancer undergoing Port-a-catheter puncture and to determine which patient factors influence judgments about pain; based on SD of pain scores (~2 u of 10) during previous port-a-catheter/EMLA study, and a difference of at least one face (1/5) on the faces scale, study needed at least 35 children (serving as own controls) for a power of 80% and an alpha of 5%	Pediatric patients (>5 y/o) with cancer (majority ALL) undergoing port-a-catheter puncture (n=42; 39 evaluable) Crossover study; patients served as own controls. Study accomplished blinding despite differences in timing of cream application;	Placebo gel x 30 mins then 1g of amethocaine gel x 30 mins (n=19 for first study drug application, then crossed over)	1g EMLA cream x 60 mins (n=20 for first study drug application, then crossed over)	D	N	Y	N	Patients had 2 port-a-catheter procedures performed at differenceerent times Pain (assessed by children on the faces scale [score of 0 to 5], and by parents and attending nurse operators on a continuous 10-cm visual analogue scale)	Not stated	Average length of time between applications of both creams was 18.3 days. No difference in pain assessments as rated by children, parents, or nurses (p=0.09, 0.54, and 0.78 respectively) Pain scores asSignificantned by children and parents were not influenced by age, gender, duration of dx, or anesthetic reg.imen (p>0.05. Nurses rated pain higher for younger children (p=0.003) and in males (p=0.004) with EMLA use. Transient erythema cocurred in 19 patients during amethocaine treatment, compared with 3 patients during EMLA (p<0.001.) Blanching occurred during 5 treatments with amethocaine and 24 with EMLA (p<0.001). Amethocaine gel was found to be clinically equivalent to EMLA cream for alleviation of pain during port-a-catheter puncture.
Bock JCO 1990	To find methods for decreasing the incidence of catheter-related sepsis in patients receiving immunotherapy	Cancer patients (all except 2 patients with solid tumors) undergoing immunotherapy (IL-2 +/- immune cells) requiring CVC insertion (n=92, 87 evaluable; 151 catheters for 129 randomized episodes; 125 episodes evaluable	IV oxacillin q4h (n=44 treatment episodes)	3-arm study, 2 control arms IV placebo (n=39 treatment episodes) catheter change to new site every 72 hours (n=42 treatment episodes)	D*	Y	Y	N	Catheter-related sepsis Positive peripheral BCxs positive drawback BCxs positive line tip Cxs	Until catheter removal	P values refer to oxacillin vs. both control arms Catheter-related sepsis: 0/44 in oxacillin group, 3/39 in IV; placebo group, 5/42 in catheter change group (p=0.50); positive peripheral BCxs (out of total # available Cxs): 14/77 in control groups, 1/37 in oxacillin group (p=0.035) positive drawback BCxs (out of total # available Cxs): 1/36 in oxacillin group, 27/74 in control groups (p=0.0001) positive line tip cxs (out of total #available Cxs): 4/38 in oxacillin group, 46/105 in control groups (p=0.0001)

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Boland HTA 2003	To examine the clinical and cost-effectiveness of image-guided Hickman line insertions vs. blind Hickman line insertions by nurses in adult cancer patients; For blind vs. image-guided insertion, primary outcome measure was catheter misplacement rate; with 200 cases in each arm, a 1-tailed test at 5% significantlevel would have 80% power if true malposition rate were 0.5% under image-guidance and 5% under blind insertion.	Adult cancer patients (heme malignancies and solid tumors) (n=470)	Image-guided insertion of a Hickman (see Comments) (n=235)	Blind insertion of a Hickman (no image guidance at any point in the procedure) (n=235)	N	Y	Y	Y	Catheter tip misplacement (procedure mode, blind vs. image-guided insertion, primary analysis) Nurse skill (trainer vs. trainees, a priori subgroup analysis, assessed by pneumothorax rate) Cost-effectiveness		Misplaced catheter tips: 32 (14%) in blind arm, 1 (1%) in image-guided arm (p<0.001). No statistical significantdifferences in pneumothorax, arterial puncture, or hematoma between the 2 arms; Pneumothorax: 7 (3%) in blind arm, 2 (1%) in image-guide arm (p=0.175). No stat significantdifference between the mean cost per patient for image-guided vs blind procedure (464.57 pounds vs 440.40 pounds, respectively); Incremental cost-effectiveness analysis showed that incremental cost per misplaced catheter tip avoided was 183.22 pounds.
Bold Arch Surg 1998	To determine whether the use of real-time Doppler guidance ("Smart Needle") can decrease the failure or complication rate during routine, elective placement of a SC CVC, in patients considered at high risk for failure;	120 patients in each arm of trial to detect decrease in patients without a catheter after 2 passes from 28.7% to 10; 80% power (significantlevel of 0.01) patients at high risk of catheter placement failure (n=240)	Doppler-guided percutaneous SC vein catheterization ("Smart Needle") (n=119) After 2 failures of cannulation, patients in either arm crossed over to other arm	Standard Seldinger catheter insertion technique (n=121) If 2 failures after crossover, patient was declared a failure of SC vein cannulation	N	N	Y	Y	Successful cannulation of SC vein	Not stated	Initial success rate (1 or 2 attempts per patients): 81% for standard technique, 69.7% for Smart Needle (p=0.04); Initial technique failed in 59 patients overall, 55 patients crossed over to other arm (34 in Smart Needle group, 21 in standard group, 4 refused further attempatients); Crossover success rate: 18/21 in Smart Needle group (86%), 27/34 in standard group (79%) (p=0.56). Doppler guidance did not increase the success rate or decrease the complication rate of SC vein catheterization when compared with standard technique in high-risk patients.
Brandt ONF 1996	To determine the effect of 2 CVC dressing protocols on catheter-related infection in BMT recipients with tunneled, long-term CVCs; assuming infection rate of 50% with gauze and 18% with transparent dressings. Study had 80% power (significantlevel 0.05) with 35 patients/arm	Hospitalized, adult auto BMT recipients with newly inserted long-term silastic T-L tunneled Hickmans (n=105; 101 evaluable)	Opsite 3000 changed every 1 wk (n=48)	Dry, sterile gauze dressing changed q 24 h (n=53)	N	N	Y	N	catheter-related infections	Through catheter removal or hospital discharge	Mean duration of CVC use: 22.3 d (range, 4 to 63) for gauze group, 21 d (range, 3 to 68) for Opsite group. Prevalence of CVC sepsis: 2% in gauze, 10% in Opsite (p<0.05); When all categories of CVC-related infection were considered (definite CVC sepsis, suspected CVC sepsis, or tunnel infection) no stat significantdifference was found between groups over time in likelihood of remaining infection-free (p=0.76). Definite CVC-related sepsis occurred in 1 patient in gauze group and 5 in Opsite group; difference not stat Significant over time (p=0.067). Gauze patients required average of 7 dressing changes/wk, Opsite patients required average of 2.4 changes/wk (protocol specified 1/wk)

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Carde Eur J Can Clin Onco 1989	To compare external indwelling CVCs with totally implanted systems with regard to duration of use, complications, and convenience; estimated that 50 patients/group would be adequate to show a 35% difference between the success rate in each of the 2 groups, regardless of 6-mo success rate	Adult cancer patients requiring IV chemotherapy for >6 mos and had poor peripheral access or wanted a CVC from outset (n=106; 100 evaluable)	Totally implanted system (Port-a-catheter) (n=50)	External indwelling CVC (tunneled) (n=50)	N	N	Y	N	Ability to use device for at least 6 months. Removal of the device during 6-mo f/u.	Analysis performed 6 months after last patient entered trial; all patients follwed at least 6 months	Removal rates over 6-mo f/u: 50% in regular catheter, 10% in implanted catheter (p<0.001). Restrictions on patient activity: 18% in reg. catheter group, 0% in implanted group (p=0.02). Restrictions on hygiene: 49% in reg. catheter group, 5% in implanted group (p<0.001). Totally implanted access systems are more reliable, safer, and better tolerated than classical external catheters for solid tumor patients undergoing IV chemotherapy for >6 mos.
Carlo Am J Surg 2004	To evaluate whether a valved SQ port system (PASV) would have fewer associated complications as compared to a standard nonvalved port and whether the fewer complications demonstrated a cost-saving benefit.	Adult cancer patients requiring long-term venous access for chemotherapy, blood draws, or TPN (n=73). For the valved port group, catheters were flushed after each access with 10 mL normal saline, whereas the nonvalved group used 10 mL of Heparinized saline.	S-L PASV port catheter (n=37)	S-L same sized control nonvalved BardPort (n=36)	N	N	N/A	N/A	Adequacy of port function (difference in difficulty drawing blood or infusing, time spent accessing). Cost analysis	180 days or until port removal	Difference in difficulty withdrawing blood occurrences: 11 (3.0%) in valved group, 21 (6.1%) in nonvalved group (p=0.05); Inability to withdraw blood occurrences: 21 (5.8%) in valved group, 37 (11%) in nonvalved group (p=0.02) Total time (mins) to ensure port patency: 750 mins in valved group, 1545 mins in nonvalved group (p<0.03); No more than 2 patients from each group (range, 0 - 2) had port-site cellulitis, catheter sepsis, catheter leakage, or venous thrombosis (p for all NS). Demonstrated an advantage to using a totally implantable central venous port that employs a PASV valve system
Carratala Antimicrob Agents and chemotherapy 1999	Determine efficacy of antibiotic-lock technique in preventing endoluminal CRI with gram+ bacteria. Study had 80% power to detect 20% difference in rate of catheter hub colonization (5% significantlevel, 1-sided test).	Patients with heme malignancies and neutropenia (n=120; 117 evaluable)	Heparin +vancomycin (n=60)	Heparin alone (n=57) (both arms nontunneled multi-lumen, polyurethane; lock sol'n in catheter lumen for 1h q2d)	D	Y	Y	Y	significantcolonization of catheter hub; catheter-related bacteremia	Patients monitored until one of many pre-defined endpoints (including the 2 main outcomes assessed); catheters in place for 11d for heparin patients and 10d for heparin+vanco patients)	Significant colonization of catheter hub: 15.8% in control group, 0% of heparin+vanco group (p=0.001); catheter-related bacteremia: 7% of control group, 0% of heparin+vanco group (p=0.05). Heparin and vancomycin in antibiotic-lock technique effectively prevents catheter hub colonization with gram+ bacteria and subsequent bacteremia during chemotherapy-induced neutropenia in patients with heme malignancies

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Ceasre, JCO, 2009	To evaluate two different modalities of flushing CVC (Broviac-Hickman) in pediatric patients with cancer in jugular and subclavian	n=101 patients received positive pressure cap, n=102 standard treatment	Experimental flushing with normal saline via a positive pressure cap (CLC 2000 device (ICU Medical Inc, San Clemente,CA) and weekly flushing	Standard flushing with Heparin solution twice a week	U	Y	U	U	Primary - CVC complication rates. Secondary - CVC survivial rates	Median 360 days	221 complications were recorded among 75,249 CVC-days (2.94 per 1,000 CVC-days). A higher incidence of CVC occlusion (83 v 41 episodes; P .0002) and bacteremia (24 v 9; P .01) were found in the experimental arm. The cumulative probability of developing at least one CVC complication was higher in the experimental arm than in the standard arm (65.1% [95% CI, 55% to 75%] v 43.8% [95% CI, 34% to 54%], respectively; P= .01). No difference was found in either the cause or the frequency of premature removal of CVCs between the two study arms. After a median follow-up of 360 days (range, 4 to 1,073), CVC survival was similar: 77% (95% CI, 66% to 84%) for the experimental arm and 69% (95% CI, 53% to 80%) for the standard arm (P = .7). The factors associated with the occurrence of CVC complication were a diagnosis of leukemia/lymphoma, double-lumen CVC, and experimental flushing. The only factor significantly associated with premature removal of a CVC was a diagnosis of leukemia/lymphoma (hazard rate,2.3; 95% CI, 1.1 to 4.7).
Chambers, J Hosp Infect, 2005	To establish the reduction of exit-site infections of tunnelled CVC in neutropenic patients with sustained release chlorhexidine dressings	112 tunnelled CVC in 95 patients undergoing chemotherapy or bone marrow transplant	sustained release chlorhexidine dressing	standard dressing	Y		Y		Development of exit-site and/or tunnel infection; secondary endpoint was the removal of the catheter for infection.	1 month and 3 months or at the time of catheter removal	Exit-site or combined exit-site/tunnel infections occurred in 23 (43%) of 54 catheters in the control group, and five (9%) of 58 catheters in the intervention group [odds ratio (OR) for intervention group compared with control groupZ0.13, 95% confidence intervals (CI) 0.04–0.37, P!0.001]. More tunnelled intravascular catheters were prematurely removed from the control group than the intervention group for documented infections [20/54 (37%) vs 6/58 (10%), ORZ0.20, 95%CI 0.53–0.07]. Chlorhexidine dressings reduced the incidence of exit-site/tunnel infections of indwelling tunnelled intravascular catheters without prolonging catheter survival in neutropenic patients
Chen, J of Clin Anesthesia, 2007	To compare percutaneous nonangiographic insertion of a venous access device with a standard surgical cutdown insertion technique.	100 patients with Arrow Implantable Vascular Access Systems devices	50/100 patients (in the percutaneous group (2 patient tunneled) received implantation through the internal jugular vein by experienced anesthesiologists	50/100 patients (surgical group with fluoroscopic guidance) received venous cutdown insertion through the cephalic or subclavian vein by surgeons	Y	Y	Y	Y	Failure rate; comfort, procedural complications, late complications	2 months after placement	Success rate 100%; more lidocaine is surgical group; 28 min insertion percutanious and 35 minutes in surgical group; premature removal 2/50 percutaneous and 7/50 for surgical group. The percutaneous technique was found to have several advantages, including reduced time for insertion and greater patient satisfaction with procedure. The percutaneously implanted devices also had fewer insertion-associated complications.

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Chu Anesth Analg 2004	To establish the accuracy of the IV-ECG technique (in placing catheters at the SVC-RA junction) by TEE and compare it with surface landmark technique.	Adult cancer patients scheduled for placement of CVC (port) at the time of major surgical procedure (n=60)	IV-ECG catheter tip guidance, placement evaluated by TEE	Surface landmark technique, placement evaluated by TEE	N	N	N	N	Correct placement of catheter tip	Not stated	Satisfactory placement: 30/30 IV-ECG patients, 16/30 standard technique patients (p<0.001) No difference between groups in total catheter tip placement time, initial catheter length, and TEE-corrected catheter length
Console, J chemotherapy, 2007 not RCT	The aim of this prospective study was to analyze the costs related to the use of polyurethane (PU) CVC ; subclavian placement.	44 patients with cancer	CVC was washed once a wk with Heparin but antibiotic prophylaxis was not given	NA	NA	NA	N A	NA	Complications/adverse events	6 months	3.9 adverse events for every 1000 days of catheterization (95% CI 2.5-6.7) Infection 15.9%; Thrombosis 6.8%; Intolerance reactions 2.3%; Phlebitis 2.3%; Other 2.3%; accidental removal 15.9%; 50% of events occurred within the first month
Couban JCO 2005	Whether warfarin 1mg every day reduces incidence of symptomatic CVC-associated thrombosis in cancer patients; Study planned to have 80% power (5% significant level, 2-sided) to detect 50% risk reduction in warfarin arm.	Patients with cancer requiring a CVC for >7d, >16 y/o (n=255)	Warfarin 1mg po qd (n=130)	Identical placebo qd (n=125) All study meds started after catheter insertion, up to 72h later	D	Y	Y	Y	Primary - symptomatic radiographically confirmed thrombosis of a CVC-associated vein Secondary - CVC lumen occlusion, CVC life span, premature CVC removal, bleeding, non-CVC-associated VTE, death	Patients followed until development of a symptomatic CVC-associated thrombosis, death, or for 3 months after CVC removal	Study closed early after futility analysis; study deSignificantn anticipated a rate of thrombosis in placebo arm of 32.5%, but actual rate (5%) in overall blinded population was much lower than projected. No statistically significant differences were found; also no Significant adverse events with warfarin.
Daghistani Med Ped Onc 1996	To evaluate the benefit of adding broad-spectrum antibiotic to the catheter flush solution. NO statistical analysis provided 3 patients considered "randomized" were put on a 3rd arm.	Cancer patients <22 y/o scheduled for or with an indwelling CVC (n=69; 61 evaluable)	Saline + Heparin +vancomycin + amikacin flush (n=28)	Saline + Heparin flush (n=33)	D	N	Y	N	catheter-related infections	Closing date of study (study lasted 17 mos)	catheter-related sepsis: 3 in control group, 2 in antibiotic group Cellulitis: 3 in control group, 2 in antibiotic group Overall rate of catheter-related sepsis in study extremely low With the low rate of catheter-related sepsis, the efficacy of antibiotic prophylaxis could not be statistically evaluated.
Darouiche, Ann Surg, 2005	To compare the impact of antimicrobial impregnation to tunneling of long-term CVC on rates of catheter colonization and CRBSI. 80% power, 95% CI	Adult patients (at 7 hospitals) who required a vascular access for 2 weeks; 351 inserted CVC subclavian (n=186 antimicromicrobial impregnated) and n=160 tunneled; 346 were evaluable for CRBSI	Silicone central venous catheter that was either impregnated with minocycline and rifampin	Tunneled CVC with no impregnation of minocycline or rifampin	Y	U	Y	Y	catheter colonization and CRBSI		Antimicrobial-impregnated catheters were as likely to be colonized as tunneled catheters (7.9 versus 6.3 per 1000 catheterdays). Bloodstream infection was 4 times less likely to originate from antimicrobial-impregnated than from tunneled catheters (0.36 versus 1.43 per 1000 catheter-days). Even when the catheter is no longer actively used, the mean duration of placement of tunneled catheters was longer than that of antimicrobial impregnated catheters (mean, 43.7 37.9 versus 30.2 21.1 day, P 0.001). Tunneled catheters were 3 times more likely than antimicrobial impregnated catheters to be removed because of positive blood cultures (19 of 160 11.9% versus 7 of 186 3.8% , P <0.008).

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de Cicco Lancet 1989	To assess the value of tunneling and to study the source of organisms and the routes by which microbial organisms colonize CVCs in patients with cancer on parenteral nutrition.	Cancer patients requiring a CVC for parenteral nutrition (n=109)	10-cm SQ tunneling of the CVC (SC vein) (n=51)	Direct insertion of CVC into the SC vein (n=58)	N	N	N	N	Microbial colonization (of catheter) Sepatienticemia	Time of removal of CVC	Sepatienticemia: 4 (7%) in control group, 2 (4%) of tunneled group (p=NS) Microbial colonization of the intravascular seg.ment of the CVC: 18 patients in control group, 4 in tunneled group (p<0.01)
de Cicco Ann of Onco, 2009	Evaluated efficacy and safety of early and short-term prophylaxis with acenocumarine or dalteparin in the prevention of non-occlusive or occlusive central vein catheter-related thrombosis (CVCrT); three arms; Randomized,. 90% power, two-sided test	Cancer patients scheduled for chemotherapy (n=450) n-=348 underwent at least two venography. All patients underwent venography on days 8 and 30, some of them on days 90, 150 and 210 after CVC.	Arm 1 - acenocumarine 1 mg/day for 3 days before and 8 days after central vein catheter (CVC) insertion;	Arm 3 - dalteparin 5000 IU 2 h before and daily for 8 days after CVC insertion; Arm 3 no anticoagulant treatment (NT).	U	Y	Y	Y	The primary efficacy end point of this study was CVCrT confirmed by venography. Secondary efficacy end points were clinically overt PE, confirmed by high probabilityventilation, perfusion lung scanning or by multislice computed tomography and death.	2 months after placement. Follow-up started after the second venography or on study withdrawal when this occurred.	Both acenocumarine and dalteparin reduced venography-detected CVCrT rate [21.9% acenocumarine versus 52.6% NT, odds ratio (OR) 0.3, P < 0.01; 40% dalteparin versus 52.6% NT, OR 0.6, P = 0.05]. Acenocumarine was more effective than dalteparin (OR 0.4, P = 0.01). The rate of occlusive CVCrT was not differenceerent in the three groups (0.9% acenocumarine, 3.3% dalteparin, 1.8% NT; P = 0.40). Most CVCrTs (95.6%) were observed on day 8 after CVC insertion and were nonocclusive.
Deitcher JVIR 2004	To compare the safety and efficacy of 1 or 2 instillations of 3 intraluminal concentrations of r-UK with placebo for reestablishment of total function to occluded CVCs.	Cancer patients with any semi-permanent or temporary CVC, D-L or S-L (T-L excl.) with withdrawal occlusion or total occlusion, >1 y/o, mean age 23 (n=108; 101 completed study)	Recombinant urokinase (r-UK) arms: 5,000 IU/mL 15,000 IU 25,000 IU	Matching placebo	D	N	N	Y	Reestablishment of a functional CVC after 1 or 2 instillations of study medications (functional catheter defined as ability to withdraw blood and infuse sol'ns through all treatment'd catheter lumens) Reestablishment of a functional CVC after 1 instillation of study meds	Until device removal or patient death; then 30 days	25,000 IU/mL r-UK vs placebo: 68% vs 28% (p=0.007) 15,000 IU/mL r-UK vs placebo: 69% vs 24% (p=0.004) 5,000 IU/mL r-UK vs placebo: 70% vs 28% (p=0.003) Comparisons of 3 concentrations showed no difference after 1 or 2 instillations with reg.ards to patency restoration Treatment-emergent hemorrhagic events occuring within 72 hrs after study drug exposure: 4 patients in 25,000 IU arm, 2 in the 15,000 IU arm, 0 in the 5,000 IU arm, 0 in the placebo arm (none of these considered by the investigator to be related to study drug)

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deMoissac ONF 1998	To examine the effects of changing IV administration sets every 48 hours vs every 24 hours on the incidence of infusion-related sepatienticemia in neutropenic patients with cancer, using rates of infusate colonization as an indicator of risk.	Adult cancer in-patients (majority heme malignancies) or stem cell transplant recipients, possessing a surgically tunneled CVC and neutropenic for a minimum of 2 d (n=50; 413 administration sets examined)	IV administration sets changed q 48 h (n=25; 177 sets)	IV administration sets changed q 24 h (n=25; 236 sets)	N	N	N/A	N/A	Rates of infusate colonization Microorganisms identified Incidence of infusion-related sepatienticemia	Subjects continued in study for a maximum of 5 measures (repeated measures study), until they were no longer neutropenic, or were transferred or discharged from hospital	62% of subjects completed the five proposed infusate measurements. Data on 423 IV sets were examined, 10 of which were inadvertently discarded prior to sampling and therefore excluded from further analysis. Number of entries into IV sets to deliver treatment: 7.2 +/- 5.5 in 24 h group, 14.2 +/- 11.7 in 48 h group (p<0.01). Colonized IV sets: 9 (5%) in 48 h group, 9 (4%) in 24 h group (p=NS); 18 (4%) of 413 IV sets had microorganisms >15 CFU/mL; no corresponding BCxs were positive for the same organisms, and no subject developed infusion-related sepatienticemia at any point during study; 78% of colonized infusate specimens were coag-neg.ative staph
Dillon JCO 2004	Compare the efficacy of every 2 weeks urokinase with standard Heparin flushes for reducing the incidence of CRIs and occlusions; study power not given.	Pediatric cancer patients undergoing active chemotherapy, expected to require catheter for >6mos (n=577, 568 evaluable; 51% external tunneled catheters, 49% ports)	Urokinase flush every 2 week (n=284)y	Heparin flush every 2 week (n=284) Both drugs remained in lumen for minimum of 1h but up to 2 weeks; authors originally refer to sol'n as a flush, but later refer to it as a lock	N	N	N	N	Time to first occlusion Time to first device-related infection	Until catheter removal for occlusion, infection, completion of therapy, or voluntary withdrawal (Due to early closure of study, most patients treated for 4mos or less)	Study closed without complete accrual (due to new FDA restrictions on urokinase). Early closure affected long-term followup, but did not significantly compromise the primary study end points Occlusive events (partial+total): urokinase 23%, Heparin 31% (p=0.02) - but then states later in study that no difference in the number of total occlusive events were noted in either the urokinase or Heparin treatment groups as a whole. Time to first occlusive event: Significant longer with urokinase (p=0.006). Rate of occlusive events: urokinase, 1.7/1,000 days; Heparin, 2.8/1,000 days (p=0.003); Rate of infection: urokinase, 1.6/1,000 days; Heparin, 2.2/1,000 days (p=0.05) Time to first infection: NS (p=0.07) (Stratifying by catheter type led to Significant results)
Douard, Support Cancer Care, 2006	To assess the efficacy of equimolar mixture of nitrous oxide/oxygen (EMNO) toprevent pain induced by venous access ports (VAPs) implantation in cancer patients. Power of 95% and type I error rate 0f 5%.	42/83 EMNO and 41/83 placebo; Preliminary study 25 patients to show 20% decline in VAS pain score ; internal jugular access in 96% of patients	Breath via a facial mask, EMNO	Breath via a facial mask, with placebo mixture comprising 50% oxygen and 50% nitrogen.	Y	Y	Y	Y	Primary end-point patients' assessment of the severity of pain (VAS, 0 to 100) and the proportion of patients suffering pain in each group. The secondary criteria were side effects, tolerability of EMNO, and the level of satisfaction of both the patients and the medical team.	Post surgical unit measure of patient satisfaction and pain	Eighty-three adults (42 in the EMNO group and 41 in the placebo group) were included. VAPs were implanted in the jugular vein in 95% of patients. In the placebo group, 78% of the patients declared that they found VAP implantation painful vs. 34% in the EMNO group (p=0.001). The severity of the pain was reduced by 50% in the EMNO group in comparison with placebo (p=0.0125). Although the median time to perform implantation was strictly identical in both groups (20 min), the estimated duration of surgery seemed longer to patients in the control group. Patient and investigator satisfaction indexes were >90% in both groups

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Engervall J Hosp Infec 1995	To determine whether a reduction of dressings from twice to once a week could be performed safely in neutropenic patients.	Patients with heme malignancies (1 with aplastic anemia) requring permanent CVC (n=32, 39 catheters)	Tegaderm changed once a week (n=16, 20 catheters)	Tegaderm changed twice a week (n=16, 19 catheters)	N	N	N/A	N/A	Number of catheters removed due to complications. Overall catheter survival time		Study stopped after interim analysis. Catheter usage time: 39.5 daysr once a week, 46 days twice a week No difference in catheter survival time; No difference in suspected CVC-related infections requiring catheter removal All clinical variables tended to favor the twice weekly group with less CVCs removed due to suspected CVC-related infection and fewer days of fever, antibiotic treatment, erythema at exit site, and extra dressings (none of these differences reached statistical significance)
Fortun, J Antibac chemotherapy, 2006	To evaluate the outcome of the episodes of catheter-related bacteraemia (CRB) associated with long-term intravascular devices used for chemotherapy or parenteral nutrition and that were managed with ALT during a 44 month period; Hickman or totally implantable catheters.	801 devices placed in 105 patients during a 44 mo period. 127 episodes of bacteraemia, with 92 being catheter related. Of these 48/92 were included in analysis. 19/42 were treated with ALT and 29/42 were treated with systemic antibiotics	Patients with CVC managed with Antibiotic-lock solution (ALT) consisted of a Heparin solution of 20 IU/mL including vancomycin (for Gram-positive microorganisms) or ciprofloxacin or gentamicin (for Gram-neg.ative bacilli), all at a concentration of 2 mg/mL. ALT was used for a minimum of 8–12 h/day, during 5–14 days.ALT was used in conjunction with systemic therapy.	Patients with CVC managed with systemic antibiotics only	N	N	Y	N	Effectiveness was assessed by clinical and microbiological criteria: # episodes of catheter-related bacteraemia epidosodes that failed to be cured	During treatment phase	Isolated microorganisms were similar in the two groups. The catheter had to be removed during therapy in one episode in the antibiotic-lock group and in seven episodes in the control group. Relapse of the bacteraemia with the same microorganism after stopping therapy was observed in two and three patients in the study group and the control group, respectively; Successful treatment was achieved in 84% and 65% of the episodes in the antibiotic-lock group and the control group, respectively (P = 0.27).
Fraenkel, Crit Care Med, 2006	To compare the infection rate of silver-platinum-carbon (SPC)-impregnated catheters with rifampicin-minocycline (RM)-coated catheters.subclavian insertion.	25/319 RM and 22/327 patients had cancer	SPC silver platinum carbon impregnated CVC	RM rifampicin minocyline coated CVC	Y	Y	Y	Y	Cultures results; colonization rates and catheter in situ and time to colonization - secondary outcomes	life of catheter	646 central venous catheters (RM 319, SPC 327) were inserted, and 574 (89%) were microbiologically evaluable. Colonization rates were lower for the RM catheters than SPC catheters (25 of 280, 8.9%; 43 of 294,14.6%; p .039). A Kaplan-Meier analysis that included catheter time in situ did not quite achieve statistical Significantnificance (p =.055). catheter-related bloodstream infection was infrequent for both catheter-types (RM 4, 1.4%; SPC 5, 1.7%).

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Frank Surg 2001	To determine the infection rate of silver-platinum-carbon (SPC)-impregnated	Cancer patients referred for venous access for chemotherapy (n=106; 100 evaluable)	Ion-implanted catheter (n=51)	Untreated catheter (n=49)	D	N	N	N	Incidence of catheter malfunction (evidenced by lack of flow on withdrawal or infusion); DVT; length of time to first thrombotic episode	Median f/u intervals: 7.4 mos for ion catheters, 5 mos for untreated catheters	Inability to aspirate: 47% in ion group, 39% in control (p=NS). Inability to infuse: 6% in ion group, 2% in control group (p=NS). No difference in 1-year clot-free survival No patient had a DVT Study failed to detect any substantially beneficial effect of ion implantation on the external surface of silicone CVCs with respect to incidence of thrombosis-related catheter dysfunction.
Freiberger J Ped Onc Nurs 1992	To evaluate rifampicin-minocycline (RM)-coated catheters.	Pediatric oncology patients (oncology & bone marrow units) with newly placed CVCs (n=60) Study does not state how many allocated to each arm.	Four arms: Betadine + Teg.aderm Betadine + gauze	Hibiclens + Teg.aderm Hibiclens + gauze	N	N	N	N	Amount of microbial growth at catheter exit site Cx of exit site wound done at insertion, then again at 5th dressing change	Study concluded at end of 5th dressing change	Bacterial growth between groups: p=NS. Betadine groups more likely to have redness at site (p=0.037). A sample of 271 subjects would be needed to provide sufficient power to detect true differences in the 4 dressing groups
Gabrial J Vasc Interv Radiol, 2010	To evalute the efficacy and safety of the thrombolytic tenecteplase, a fibrin-specific recombinant tissue plasinogen activator, for restoring function to a dysfunctional CVC	Adult oatients with dysfunctional CVC (n= 97)	Patients received an initial dose of intraluminal tenecteplase (TNK) (up to 2 mg), a second dose of tenecteplase if indicated, and a third placebo (PBO) dose (n=50)	PBO-TNK-TNK arm, placebo was instilled first followed by up to two doses of tenecteplase, if needed, for restoration of catheter function (n=47)	Y	Y	Y	Y	Catheter function: blood could be withdrawn and solution infused.	120 minutes	Within 120 minutes of initial study drug instillation, catheter function was restored to 30 patients (60%) in the TNK-TNK-PBO arm and 11 patients (23%) in the PBO-TNK-TNK arm, for a treatment difference of 37 percentage points (95% confidence interval 18-55; P = .0002). Cumulative restoration rates for CVC function increased to 87% after the second dose of tenecteplase in both study arms combined. Two patients developed a deep vein thrombosis (DVT) after exposure to tenecteplase; one DVT was considered to be drug related. No cases of intracranial hemorrhage, major bleeding, embolic events, catheter-related bloodstream infections, or catheter-related complications were reported.
Giles Aeta Ehir Belg 2002	To investigate the effect of the frequency of catheter insertion site care and the type of dressing applied on the incidence of CVC infections	Adult patients undergoing surgical procedures (majority cancer) (n=74; 76 catheters, 72 catheters evaluable)		Sterile gauze + dressing changed every 1 day (n=39)	N	N	Y	N	Insertion site infections catheter tip infections	Until catheter removal	Mean duration of CVC was 8.0 +/- 4 d. No episodes of catheter-related sepsis. Positive site cxs: 1 in occlusive dressing group, 2 in gauze group (p=0.3); Positive tip cxs: 3 in occlusive dressing group, 7 in gauze group (p=0.2)

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Groeg.er Ann Surg 1993	To evaluate the effect of a silver-impregnated cuff on the incidence of catheter-related bacteremia/fungemia or tunnel tract infection in cancer patients with chronic dual-lumen tunneled catheters; assuming incidence of infections with standard catheters approx 25% and a 15% decrease to 10% using catheter with silver cuff is clinically meaningful. With 192 patients study had power of 80% (p<0.05, 2-sided).	Cancer patients requiring long-term Hickman-type catheters (n=200)	D-L tunneled cuffed silastic CVC, with a second more proximal SQ silver-impregnated cuff (n=92)	D-L tunneled cuffed silastic CVC, without a second cuff (n=108)	N	N	Y	N/A	Clinically documented first catheter-related infection (bacteremia / fungemia / tunnel tract infection); subsequent infections not included in analysis	Until device removal or patient death; written and telephone f/u conducted if patient not seen by PI for 3 mos	Hazard rate for infection/day: 0.0022 (95% CI, 0.0015 to 0.0030) for standard catheters, 0.0027 (95% CI, 0.0019 to 0.0037) for catheters with silver-impregnated cuffs (p=NS) Infection-free interval of both catheters: no difference over lifetime of catheter, or over first 48 days post-insertion.
Haire BMT 1991	To determine the true rate of SC vein thrombosis after catheter placement in autologous marrow transplant patients, and to determine if Groshongs offer a clinically significant advantage over Hickmans.	Patients requiring SC vein catheterization before autologous marrow or peripheral stem cell transplant (n=45; 23 evaluable)	Groshong catheters (S-L and D-L) (n=11)	Hickman catheters (S-L and D-L) (n=12)	N	N	Y	N	Thrombosis as assessed by arm vein venography (done if clinical suspicion or if there was reconstitution of marrow function before hospital discharge)	Catheters in place a mean of 38.8 days prior to venography (range 5-69 days)	Total obstruction: 5 in Groshong group, 5 in Hickman group (no p value given). Partial obstruction: 3 in Groshong group, 9 in Hickman group (no p value given). Groshong catheters had a thrombosis rate similar to that seen with Hickman catheters All patients received bilateral catheters Only 30% of all catheters remained free of thrombosis
Haire Throm and Hemo 1994	To investigate the theoretical superiority of t-PA over standard bolus urokinase therapy in the treatment of thrombotically obstructed catheters	Cancer patients with radiographically-proven thrombus occlusion of catheter, >19 y/o (n=48; 50 catheters)	2 mg recom t-PA (dwell time 2h) (n=28 catheters) For both arms, 2nd dose allowed if necessary; repeat contrast injection done when catheter function restored or after 2 doses of study drug)	10,000 U UK (dwell time 2h) (n=22 catheters)	D	N	N/A	N/A	Catheter function: blood could be withdrawn and solution infused. Anatomic: Thrombus radiographically determined to have full or partial resolution	Data on long-term outcomes after initial resoration of function were not collected	Restoration of function: 13/22 catheters with UK, 25/28 catheters with t-PA (p=0.013). Total clot resolution after 1 dose: 4/22 in UK arm, 13/28 t-PA arm (p=0.036). Total clot resolution (ultimate): 7/22 in UK arm, 17/28 in t-PA arm (p=0.042). No complications (incl. bleeding) observed in ether group
Hanna JCO 2004	Long-term silicone catheters impregnated with M-R are ore efficacious than control catheters. Assuming the rate of infection in controls to be 14%, a total of 330 patients detects a significantdifference between study arms with 80% power (one-tailed significantlevel, 5%).	Adult cancer patients (n=355; 356 catheters)	Minocycline-rifampin impregnated silicone catheters (catheters included S-L PICCs, nontunneled S-L and D-L SC CVCs) (n=182 catheters)	No impregnation, otherwise catheters as in Arm 1 (n=174 catheters)	D	Y	Y	N	CRBSI	Until catheter removal or 100 days (whichever came first)	CRBSI: 14 in control group, 3 in M-R group (8.0% v 1.6%; RR=1.8; 95% CI, 1.4 - 2.3; P=.003). Rate of CRI: 1.28/1,000 catheter-days in control group v 0.25/1,000 catheter-days in M-R group (P=.003). M-R catheters associated with lower risk of CRI over time (P=.003; Kaplan-Meier analysis, log-rank test). M-R catheters independently protective against CRBSI (OR, 0.1; 95% CI, 0.01 to 0.44; P<.001; mult log reg. analysis). [Asepatientic thrombophlebitis: all associated with use of PICC. 7 in M-R arm (P=.001); 8 in control arm (P<.001); no cases in SC CVCs].

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Harter Cancer 2002	Polyurethane catheters coated with a silver alloy may be associated with a higher rate of catheter-related thrombosis; U/S used for placement Study power not given	Hematologic-oncologic (n=233), undergoing chemotherapy	Silver impreg.nation of external surface (polyurethane, S-L) catheter (n=120)	Uncoated standard (polyurethane, S-L) catheter (n=113)	N	N	Y	N	Thrombosis-Patency of internal/external jugular veins (assessed by U/S just before or after catheter removal)	Until catheter removal (median, 10.25 days)	CRI: 21.2% in control group, 10.2% in silver-coated group (p=0.011) IJ vein thrombosis: 3 in control group, 1 in silver-coated group (p=NS)
Heaton Int Med J 2002	Determine if a daily minidose of warfarin reduces the incidence of thrombosis in, or asssociated with, CVCs in patients with heme malignancies; whether minidose warfarin causes prolong of patient or bleeding complications; study had 80% power (significance level 0.05) to detect 37.5% vs. 9.5% rate of thrombosis.	Adult patients with heme malignancies requiring insertion of double-lumen, subclavian CVCs (n=88; 102 catheters)	Warfarin 1mg by mouth every day (n=51)	No warfarin (n=51) Both arms started on day of catheter insertion	N	N	N	N	X-ray confirmed catheter thrombosis. X-ray confirmed venous thrombosis related to the catheter. Removal of the catheter for any reason before day 90.	Until study endpoint(s) or day 90 (warfarin d/c'd if INR >1.5) Mean time on warfarin was 41 days	11 patients had 2 or more catheters. There was a high incidence of thrombosis in these patients (5 thrombi in 14 of the 2nd or 3rd catheters, but only 1 patient had a thrombus in the first catheter). Results were re-analyzed using only first catheters (88 catheters in 88 patients).] Thrombosis (catheter or vein): 8 on warfarin, 5 in control (p=NS); Onset of thrombosis: NS; Clot-free catheter survival no difference across groups. For first 65 patients, warfarin discontinued during severe thrombocytopenia requiring platelet transfusion; for remainder of patients, warfarin was continued despite severe thrombocytopenia
Heden, PediatrBlood Cancer, 2009	Determine if use of midazolam during needle procedures reduces fear and distress.	Pediatric patients with cancer	With Midazolam	Without Midazolam	N	N	N	N	Fear and distress according to parents, nurses and children		Fear and distress was lower in the group that received midazolam during needle procedures with a port, according to parents (P=0.001), nurses (P=0.001) and children (P=0.015).
Henneberg Paed Anaesth 1996	To compare the durability of traditional percutaneous CVCs and tunneled catheters with a subcutaneous cuff.	Children (median age, 7 yrs) with known/strongly suspected cancer, requiring long lasting IV access (n=20; 16 evaluable)	Tunneled cuffed catheter (n=8)	"Conventional" CVC (n=8)	N	N	Y	N	Duration of catheters (catheter life) Infection, emboli, thrombosis, displacement	Not stated	Median duration of catheters: 224d (range, 25-846) for tunneled, 39.5d (range, 9-228) for conventional (p=0.014) 6/8 conventional catheters removed accidentally, none in tunneled group. Catheter-related sepsis: 2 in tunneled group, 1 in conventional group. Tunneled CVCs are less prone to displacement than traditional percutaneous CVCs when used in children with malignant diseases
Henrickson JCO 2000	Determine whether antibiotic flush solution with vancomycin/Heparin/cipro can prevent line infections; study power not given	Pediatric oncology (n=126; 153 evaluable lines)	1)vancomycin+heparin flush (n=28; 35 lines) 2)vancomycin+heparin+cipro flush (n=34; 38 lines) All arms used tunneled CVCs	Heparin flush (n=64; 80 lines)	D	Y	Y	Y	CVC line infections (further subdivided into Gram+ and Gram-)	Median number of line days per patient was 200 to 247 (36,944 line days total)	Time to definite catheter infection: increased using either antibiotic flush (Vanco+heparin, p=0.063; vancomycin+heparin+cipro, p=0.036). Both antibiotic flushes dramatically decreased the amount of catheter infections (both G+ and G-) and the time to first infection Time to possible/probable/definite catheter infection: increased using either antibiotic flush (Vanco+heparin, p=0.011;vancomycin+heparin+cipro, p=0.036) Occlusive episodes significantly t reduced in the vancomycin+heparin+cipro group (p=0.0005) compared to heparin group (but episodes not reduced in vancomycin+Heparin group)

RefID	Study Purpose/Hypothesis	Patient Population	Intervention/Arm 1	Control/Arm 2	B	AC	W/	ITT	Outcomes Assessed	Followup	Results
Hinds J Ped Onc Nurs 1991	To determine if the usual clean nursing procedure used with the blood reinfusion step, compared with an exaggerated unclean alternate procedure, could contribute to new microbial pathogens being acquired during the interval between removal and reinfusion of the blood sample	Pediatric oncology outpatients (majority leukemia) with S-L Hickmans, >2 y/o, non-neutropenic, clinically well (n=42)	Syringe left uncapped and placed on a table ("unclean" procedure) (n=21)	Syringe containing blood sample that represented the reinfusion step was capped and placed on a sterile 4x4 gauze for remainder of procedure (usual nursing procedure) (n=21)	N	N	N/A	N/A	Microbial organisms isolated in the residual blood in the Hickman. Microbial organisms isolated in the systemic blood collected immediately after the residual blood. Microbial organisms in the reinfusion blood sample that remained in the syringe during the entire collection procedure. Microbial organisms among the 3 samples collected from each patient.	All patients followed for 2 wks after samples drawn; each child participated in the study only one time	No microbial organisms were detected in any of the samples from either group. Study provides evidence that a carefully executed blood reinfusion step used in patients with Hickman catheters does not increase the risk of infection for nonneutropenic pediatric oncology patients.
Horne JCO 1997	To determine the role of low-dose urokinase infusions in treating fibrinous occlusions of CVCs in cancer patients	Cancer patients >18 y/o with radiographically-proven CVC occlusions (fibrin sleeves at catheter tips) refractory to routine urokinase instillations (n=42)	Urokinase + Heparin (320 U/h) (n=21) Both arms: drugs infused through occluded lumen and checked at 1, 3, 6, and 12 hours of infusion	Urokinase (40,000 U/h) (n=21) Both arms: When function restored, infusion stopped and radiographic study done; if sleeve still visible, infusion continued until next scheduled eval; if obstruction not relieved after 12h infusion, treatment d/c'd and scored as failure	D	N	N/A	N/A	Radiographically-proven resolution of thrombus	CVCs reopened by infusions were evaluated at least once/mo by PCP; if catheter needed >2 urokinase instillations/wk to maintain function, success considered ended When functional CVC removed, period of observation concluded and time since the previous urokinase infusion was recorded as the censored duration of success	Each arm: 16 "successes" and 5 "failures" Proportion of successes after 1h treatment: NS difference (p=0.47) Probability 0.28 that a reopened CVC would reocclude within 6 months, 0.79 that it would be removed for some other reason Llow-dose urokinase infusions is the preferred treatment for catheter occlusions that are refractory to urokinase instillations and that are shown radiographically to be related to fibrin sleeves.
Horne, Pharmacotherapy. 2006	To determine whether lepirudin flushes are more effective than Heparinized saline in preventing withdrawal occlusion of central venous access devices. 95% CI P=0.05	49 adults undergoing bone marrow transplantation for hematologic malignancies or metastatic solid tumors.	25/49 lepirudin dose was 3 ml of lepirudin 100 ug/ml (300 ug) per catheter at least once a day; Lepirudin was given for a mean of 19 ± 7.5days (range 2–34 days	24/49 Heparin dose was 3 ml of porcine Heparin 100 U/ml (300 U) per catheter lumen at least once a day	Y	Y	Y	Y	Efficacy was assessed by the frequency with which the patients were treated with alteplase instillations for withdrawal occlusion of their central venous access devices during the first 4 months of catheterization.	After 3-4 weeks all patients received Heparin flushes	Three (12.5%) patients treated with Heparin alone and five (20%) treated initially with lepirudin required alteplase instillations for an estimated relative risk with lepirudin versus Heparin of 1.6 (95% confidence interval [CI] 0.40–13.86, p=0.70). The drug lepirudin was discontinued prematurely (i.e., before 21 days) in nine patients for a variety of reasons. Lepirudin was not more effective than Heparin, which may have been related to the conservative dose of lepirudin administered.

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Jaeg.er Ann Hem 2005	To investigate the efficacy of CH-SS-impregnated CVCs in preventing catheter-related colonization and CVC-related BSI in immunocompromised leukemic patients following intensive antineoplastic chemotherapy; a sample size of 50 catheters in each group was needed to detect with 80% power (beta error=0.20) a significantdifference in rates of catheter-related colonization (significantlevel p=0.05)	Leukemia patients requiring CVCs for chemotherapy (n=106)	CH-SS-impregnated catheter (n=51)	Standard T-L polyurethane CVC (n=55)	N	N	N/A	N/A	Catheter-related colonization CRBSI	Until catheter removal (because no longer needed or adverse event) BCxs obtained from catheter and peripheral vein at catheter removal and when suspected catheter-related colonization or bacteremia	Catheter colonization on catheter removal: 9 (16.4%) of controls, 5 (9.8%) of CH-SS group (p=0.035) Catheters removed due to clinical evidence of CRBSI: 1 in CH-SS group, 8 in control group (p=0.02) Meticulous attention to sterile technique during catheter insertion and routine maintenance still remain essential factors in the prevention of catheter-associated infection.
Jaeg.er chemotherapy 2001	To determine the efficacy of a benzalkonium chloride-impregnated CVC in preventing catheter-related infection in patients suffering from cancer and undergoing chemotherapy; precise estimate of CVC-related infectious complications not possible, study planned as pilot aimed to detect reduction in CRBSI of 25% between groups (significantlevel p=0.05)	Cancer patients requiring CVCs for chemotherapy (n=50)	Benz-chlor-impreg. CVC (n=25)	Standard T-L CVC (n=25)	N	N	N/A	N/A	Catheter-related colonization catheter-related bacteremia	CVCs removed when no longer necessary or upon suspicion of infection	catheter colonization: 4 in benz-alk group, 4 in control group (p=NS). Unable to prove any benefit with the use of CVCs bonded with benzalk chloride. Catheter-related bacteremia: once in each group (p=NS)
Johansson Supp Care Can 2004	To evaluate the use of a D-L port in patients with acute leukemia undergoing induction chemotherapy; study had 80% power (one-sided, p<0.05) with 29 patients in each group to detect a difference in CVC survival time from a mean of 100d in standard CVC to a mean of 200d in port group	Patients with acute leukemia, with planned induction chemotherapy (n=43; 37 evaluable). Due to lower than planned recruitment of patients, results have to be interpreted with caution	D-L port (n=17) All patients received prophylactic single dose of dicloxacillin IV prior to procedure Antifungal and antiviral prophylaxis given to all patients during neutropenia, but not antibiotic. Platelet transfusions given prior to placement if count <50x10-9 (no significant difference between groups)	Tunneled D-L CVC (n=20) All patients received prophylactic single dose of dicloxacillin IV prior to procedure Antifungal and antiviral prophylaxis given to all patients during neutropenia, but not antibiotic. Platelet transfusions given prior to placement if count <50x10-9 (no significant difference between groups)	N	N	Y	Y	CVC survival time Complication rate and function	Until CVC removal	Study closed early due to high rate of extensive local bleeding after port placement. ITT analysis did not show significantdifference between the 2 groups in CVC survival time. Per protocol analysis CVC survival time: 113 d in port group, 55 d in CVC group (p=0.15). Extensive SQ hematoma: 5 in port group, 0 in CVC group (p=0.01.) Exit site infection: 8 in port group for median of 19 d, 9 in CVC group for median of 15 days (p=NS). positive BCx findings per CVC days: 3.6/100 d in CVC group, 0.9/100 d in port group (p=0.02). Time to first coag-neg.ative staph positive BCx: 14 d in CVC group, 52 d in port group (p=0.02). Number of positive coag-neg.ative staph cultures per CVC day: 0.6/100 d in CVC group, 0/100 d in port group (p=0.02).
Kappers-Klunne Cancer 1989	To compare the D-L Hickman with the smaller S-L catheter connected to a port-a-catheter to evaluate the superiority of either system with special emphasis on infectious complications	Patients with acute leukemia (n=44) or NHL (n=3) in whom adequate venous access had become impossible due to prior treatment (n=47; 43 evaluable)	D-L Hickman (n=23)	S-L portacatheter (n=20)	N	N	N	N	Infectious complications	Until catheter removal	Mean days of catheter use: 59 d in Hickman, 57 d in portacatheter (p=1.00). Catheter removal due to infection: 7 documented in Hickmans, 2 documented in portacatheters, 2 clinically suspected in portacatheters (p=0.66). D-L catheters are comparable with those of S-L Hickman catheter in heme patients. Totally implantable portacatheter systems appeared to be at least as safe as D-L Hickmans in our patients. Results should be confirmed in larger study.

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Karthaus, Annal Oncol, 2006	To evaluate whether prophylactic treatment with a low molecular weight Heparin could prevent clinically relevant catheter-related thrombosis.	Patients with cancer undergoing chemotherapy for at least 12 weeks (n = 439) were randomly asSignificantned, in a 2:1 ratio, t or placebo, by subcutaneous injection, once daily for 16 weeks	Received either dalteparin (5000 IU) by subcutaneous injection, once daily for 16 weeks	Placebo (0.2 ml saline), by subcutaneous injection, once daily for 16 weeks	Y	Y	Y	Y	Primary end point was the occurrence of a catheter related complication (CRC), defined as the first occurrence of any one of the following: clinically relevant catheter-related thrombosis that was symptomaticor that required anticoagulant or fibrinolytic therapy; catheter-related clinically relevant pulmonary embolism; or catheter obstruction requiring catheter removal.	Assessed at 1, 2, 4, 8, 12, 16 weeks	There was no significant difference in the frequency of CRCs between the dalteparin arm (3.7%) and the placebo arm (3.4%; P = 0.88), corresponding to a relative risk of 1.0883 (95% confidence interval 0.37–3.19). No difference in the time to CRC was observed between the two arms (P = 0.83). There was no significantdifference between the dalteparin and placebo groups in terms of major bleeding (1 versus 0) or overall safety. Dalteparin prophylaxis did not reduce the frequency of thromboembolic complications after CVC implantation in cancer patients. Dalteparin was demonstrated to be safe over 16 weeks of treatment in these patients.
Kovacs, J Throm Haem, 2007 not rct, pilot study only	To assess the safety and effectiveness of a management strateg.y for central venous catheter-related DVT in cancer patients consisting of dalteparin and warfarin without the need for line removal.	74 patients with active malignancy (,2 years) and PICC line (77%) or portcatheters (19%) who had sympatientomatic, acute, or objectively documented UE DVT	Adults patients were treated with dalteparin 200 IU kg)1 per day for 5–7 days and warfarin with a target International Normalized Ratio of 2.0–3.0.	none	N	N	Y	Y	Rate of CVC failure, infusion failure that did not resopnd to 2 mg of tPA (which could be administered twice) or removal of line because of progressive or recurrent VTE within the 3 mo followup period. Secondary endpoints recurrent VTE major bleeding, death	3 months	Forty-two (57%) patients still had the central venous catheter in place and functional at 3 months. Thirty-two (43%) patients had the line removed prior to the 3-month endpoint but none were removed because of recurrent DVT or line blockage that was resistant to tPA infusion as per the efficacy criteria. The majority (21, 28%) were removed because of the end of therapeutic need; two were removed because of infection; nine were removed for other reasons that were not study endpoints (line fell out, patient request, skin irritation, etc.). Hence, overall, the efficacy of our management strateg.y as per our predetermined criteria was 100% (42/42; 95% CI = 91.6–100%); There were no episodes of recurrent venous thromboembolism and three (4%) (4.7%; 95% CI = 0.8–11.4%) major bleeds. No lines were removed because of infusion failure or recurrence/extension of DVT.

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La Quaglia J Ped Surg 1994	To evaluate the efficacy of 12-hour-interval slow-push UK infusion in addition to standard antibiotic treatment in the treatment of catheter sepsis in a pediatric oncology population; if 92 patients, study had 80% power (0.05 2-sided test) if catheter losses 50% for placebo group and 25% for UK group	Pediatric patients with Hickman catheters, undergoing chemotherapy with culture-confirmed catheter sepsis (n=41)	UK q 12h x 4 doses (n=23) Study drugs administered by slow IV push, given at 12-h intervals for 4 doses; catheters aspirated after 1 h	Placebo q 12h x 4 doses (n=18)	D	Y	N/A	N/A	Catheter salvage rate Number of catheters removed because of sepsis; rate of bacterial clearance from transcatheter cultures		Placebo arm (3.4%; P = 0.88), corresponding to a relative risk of 1.0883 (95% confidence interval 0.37–3.19). We conclude that bolus infusions (via slow IV push) are associated with adverse events such as fever, shaking chills, and hemodynamic instability. Urokinase infusion did not improve catheter salvage or the bacterial clearance rate.
Laura Haematol 2000	To compare 2 difference time interval protocols for CVC dressing in order to assess the effects on local infections and toxicity. Multicenter study.	Patients undergoing BMT; Group A had tunneled CVCs (n=230), Group B had non-tunneled (n=169), both groups randomly allocated (total n=399; 259 evaluable)	Dressing change at 5 days (Group A) (n=79) Dressing change at 2 days (Group B) (n=49) Transparent impermeable polyurethane dressings used for all arms.	Dressing change at 10 days (Group A) (n=81) Dressing change at 5 days (Group B) (n=50) Transparent impermeable polyurethane dressings used for all arms	N	N	Y	N	Rate of local infections at insertion site (microbiological assay) every 10 days Severity of skin toxicity (ECOG scale)	patient hospital stay	Difference in the time to CRC was observed between the two arms (P = 0.83). There was no significant difference. The increase in time interval between CVC dressing changes in BMT patients did not raise the risk of local infections, while significantly reducing patient discomfort and costs.
Lazarus JPEN 1984	To determine the appropriate criteria for catheter removal and to determine the usefulness of empirically administered amphotericin B in patients underoing intensive chemotherapyradiotherapy	42 14/42 randomized. Adult cancer patients (solid tumors and heme malignancies) undergoing intensive chemotherapyradiation treatment; patients with neutropenia and unexplained fever for 5 days despite broad-spectrum antibiotic or those who became afebrile initially after empiric antibiotic but later devleoped unexplained fever for 5 days comprised the actual study group (n=14)	catheter removal (n=6)	catheter stayed in place and patient received amphotericin B (n=8)	N	N	Y	N	Fever	catheters remained in place for a median of 27 days (12 - 56 days)	Between the dalteparin and placebo groups in terms of major bleeding (1 versus 0) or overall safety. Persistent unexplained fever in neutropenic patients in this study was not due to the presence of the catheter, since none of the patients became afebrile after its removal. The present study suggests that the catheter should not be removed but should be left inplace for administration of empiric ampho B treatment.

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Lim J Antimic Chem 1991	To determine if prophylactic teicoplanin given immediately before insertion of Hickman catheters reduced the early incidence of catheter-related soft tissue infections and G+ sepatienticemia in patients with heme malignancies needing intensive chemotherapy	Patients with heme malignancies, some undergoing BMT, requiring insertion of a Hickman catheter for chemotherapy radiotherapy (n=88)	Prophylactic teicoplanin, 1 single IV bolus within 2 h before catheter insertion (n=43)	No teicoplanin (n=45)	N	N	N/A	N/A	catheter-related soft tissue infection catheter-related sepatienticemia catheter tunnel infection	Until episode of fever or catheter-relatd soft tissue infection	catheter-related soft tissue infections: 14 (32.6%) in teicoplanin group, 20 (44.4%) in control group (p=NS) catheter tunnel infections: 3 (7%) in teicoplanin group, 6 (13%) in control group (p=NS). catheter-related G+ sepatienticemia: 7 (17.5%) in teicoplanin group, 16 (40%) in control group (p<0.05).
Ljungman Supp Care Can 1997	To investigate whether 2 doses of teicoplanin administered at the time of insertion of CVCs could reduce the frequency of G+ infections in patients with an expected episode of neutropenia; study deSignificantned as a group sequential study, max number of patients to be inlcuded with p=0.05 and 90% power if hazard rate of teicoplanin was 0.3 compared with no treatment was 220.	Adult patients scheduled for placement of CVC for treatment of acute leukemia or aplastic anemia or before allogeneic or autologous stem cell transplant; patients were expected to develop neutropenia with duration of at least 7 d (n=66; 65 evaluable)	Two doses of teicoplanin at time of catheter insertion (n=33; 32 evaluable)	No antibiotic therapy (n=32; 30 evaluable) All patients received tunneled catheters	N	N	Y	Y	Days to treatment failure	Study duration 21 d from time of inclusion in study	Study stopped early after interim analysis because the preset efficacy estimation could not be met with max estimated inclusion of 220 patients. Failures: 15/32 (47%) in teicoplanin arm, 11/30 (37%) in control arm. No statistical differences between 2 groups in any of the defined subgroups of infection episodes
Logghe J Hosp Infec 1997	To evaluate the effectiveness of CH-SS catheter impreg.nation in patients suffering from heme malignancy treatment'd by chemotherapy through a CVC. A reduction in the risk of BSI and/or delay in occurrence was hypothesized; study had power of 80% (significantlevel 0.05) with 332 catheters in each group to detect a change from 4.7% to 1%.	Patients with heme malignancy with treatment via CVC (n=538; 680 catheters)	M-L CH-SS-impreg. catheter (n=338 catheters)	M-L non-impreg. catheter (n=342)	D	N	N	N	CRBSI catheter-related infection Time to infection	Until catheter removal	Mean duration of catheter insertion: 20 d in each group Rate of BSI: 16.3% non-impreg. group, 14.5% CH-SS group (RR 1.13; 95% CI 0.79 - 1.61). Risk of catheter-related infection: 4.4% in non-impreg. group, 5.0% in CH-SS group (RR 0.87; 95% CI 0.44 - 1.72). Cumulative risk of all BSIs did not differenceer between types of catheters (p=0.53).

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Long Cancer Nurs 1992	To compare the incidence of infection in patients having venous access ports accessed using the commercially prepared access kits with patients having venous access ports accessed using a nursing protocol developed by RNs in the chemotherapy unit. The hypothesis was that there would be no significantdifference in the occurrence of infection between groups of patients	Adult cancer patients (majority solid tumors) receiving outpatient chemotherapy and had a surgically implanted venous access port inserted for >1 mo (n=26; ports accessed 171 times)	Nurse-developed access protocol (n=14; 102 accesses)	Commercially prepared access kit protocol (n=12; 69 accesses) Only difference between groups was the use of sterile gloves (commercial kit) or "clean" gloves (RN-developed protocol)	N	N	N/A	N/A	Incidence of infection Febrile episodes, drainage, pain, redness, swelling or warmth at port site	Data collected over a period of 6 mos	No instances of documented infection in either group over 6-mos study period. No evidence of any febrile episodes, drainage, pain, redness, swelling, or warmth at any port site.
Mansfield NEJM 1994	To evaluate the factors associated with complications and failures of SC vein catheterization and determine whether U/S guidance in locating the SC vein could minimize complications and failures	Adult cancer patients requiring catheterization (n=824; 821 evaluable)	U/S (not real-time) guidance to locate SC vein (n=411) If first physician failed to insert catheter, defined as failure; 2nd physician tried in most patients, and outcomes recorded	Standard insertion procedure (n=410)	N	N	Y	N	Complications and failures	Not stated	Goal was to enroll 1,100 patients, but study closed after 824 patients because interim analysis showed that U/S guidance had no effect on success of catheterization. Complications: risk ratio, 1.00; 95% CI 0.66 to 1.52 Failures: risk ratio, 1.04; 95% CI 0.72 to 1.50 Factors associated with failed attempatients (by multivariate analyses): prior major surgery in the reg.ion (p=0.002); BMI >30 or <20 (p=0.009); previous catheterization (p=0.043) Complication rate rose from 4.3% with 1 needle pass to 24.0% with >2 needle passes
	To compare technical feasibility and complications of radiologically arm port device implantation using arm venography exclusively (API Group B) with chest port placement using cephalic vein cutdown (CVC-Group A)	225 patients	Chest port placement using cephalic vein cutdown (CVC-Group A),	Radiologically arm port device implantation using armvenography exclusively (APIGroup	N	N	N	N	Technical feasibility and success rate	Median follow-up was 5.55 months (range: 0.032-9.6] in Group A versus 5.90 months [range: 0.06-27.6] (p = ns) in Group B.	Technical success was statistically higher in Arm Port Group (99.1%) compared to Chest Port Group (75.2%). Device specific duration rate of the whole population was 53% (95%CI) [0.47-0.60] at 6 months, 44.1% (95%CI) [24.4-37.8] at 12 months and 8% (95%CI) [4.4-14.5] at 24 months. Complication rate was 15.9% in Group A versus 8.9% in Group B corresponding to a complication rate per patient-implantation-days of 0.66/1000 patient-days (A) versus 0.42/1000 patient-days (B). Premature port device explantationrate was 4.4% (A) versus 5.4% (B). Premature port device explantation rate was 4.4% (A) versus 5.4% (B). Axillary and subclavian venous thrombosis was the main complication and occurred in 12 Group A patients and three Group B patients. Venous thrombosis rate was 0.37/1000 patient-days (A) and 0.13/1000 patient-days (B) (p ¼ 0.03).

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Mimoz, Arch Intern Med, 2007	To compare the effectiveness of chlorhexidine-based antiseptic solution vs alcohol -based povidone-iodine for CVC care; jugular or subclavian placement; jugular	195 patients (242 catheters) chlorhexidine group, and 204 patients (239 catheters) povidine group 538 catheters were randomized and 481/538 (89%) evaluable	Combination of 0.25% chlorhexidine gluconate, 0.025% benzalkonium chloride, and 4% benzylic alcohol	B)	N/ Y	N	Y	Y	Rates of catheter colonization; CRBSI		Of 538 catheters randomized, 481 (89.4%) produced evaluable culture results. Compared with povidone iodine, the chlorhexidine-based solution was associated with a 50% decrease in the incidence of catheter colonization (11.6% vs 22.2% [P=.002]; incidence density, 9.7 vs 18.3 per 1000 catheter-days) and with a trend toward lower rates of catheter-related bloodstream infection (1.7% vs 4.2% [P=.09]; incidence density, 1.4 vs 3.4 per 1000 catheter-days). Independent risk factors for catheter colonization were catheter insertion into the jugular vein (adjusted relative risk, 2.01; 95% confidence interval, 1.24- 3.24) and use of povidone-iodine (adjusted relative risk,1.87; 95% confidence interval, 1.18-2.96). It was estimated that for every 1000 catheter-days when sites are disinfected with a chlorhexidine-based solution rather than povidone-iodine, 9 episodes of catheter colonization and 2 episodes of catheter-related bloodstream infection would be prevented,
Miser J Pain Symp Man 1994	To study the safety and efficacy of administering topical local anesthesia using EMLA cream in pediatric cancer patients; based on preliminary info from pilot studies, sample size of 30 patients completing both study procedures with a 1-month period would provide 90% power for detecting a 30% reduction in the patients' VAS scores using a one-sided 0.025-level t test	Pediatric cancer patients undergoing implanted central venous port injections (scheduled to undergo 2 CV port injections within a 1-month period) (n=52; 47 evaluable	Crossover study; one group rec'd EMLA then placebo, other group placebo then EMLA EMLA cream (n=47)	Placebo cream (n=47)	D	N	Y	N	4 sets of pain scores; 5 - 15 mins following each procedure patient completed a cartoon face scale (CFS) and visual analogue scale (VAS) Independent health care observer completed same scales	Patients rec'd both treatments within 1 month period; children who chose EMLA after data collection from 2 randomization arms were followed for toxicity due to repeated doses	Crossover analysis performed for each of the 4 types of pain score (VAS and CFS for patients and health professionals) All 4 t-tests had p values <0.002 (Significant less pain after EMLA compared to placebo). Two-sample Wilcoxon test done to compare sum of the scores recorded for the two procedures between the 2 treatment-sequence groups; all 4 of these tests had p values of >0.3, so concluded no evidence of differenceerential carryover effects between the 2 study creams. In longer-term toxicity followup, 2 reports of "beet redness" and "blistering" at EMLA application site; both patients had used EMLA 10 to 12 times previously without incident, and receiving EMLA at approx. 3-day intervals when the toxicity occurred. The topical application of EMLA cream 5% provides highly effective superficial anesthesia, and promises to be extremely useful for pain relief during percutaneous access procedures in cancer patients

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Mismetti Haematologica 2003	Compare antithrombotic efficacy and safety of warfarin with LMWH (nadroparin); because study was a pilot, patient number empirically set at 30 patients/arm	Adult patients with non-heme cancers undergoing placement of a long-term implantable subclavian CVC (n=60; 45 evaluable)	Nadroparin SQ qd (n=21)	Warfaring 1mg po qd (n=24)	N	Y	Y	Y	Upper extremity thrombosis by day 90, confirmed by bilateral venography performed routinely 90 +/- 5 days after catheter insertion, or earlier if sxs of thrombosis appeared Any thromboembolic events catheter complications (infection, removal, obstructions) Safety endpoints: death, major bleeding, lab-confirmed HIT	Patients treatment'd for 90 +/- 5 days or until venographically confirmed thrombosis, then followed up at 6 months	[More lymphatic malignancies in warfarin group, p=0.027] Day 90 Results: Thrombosis (sympatiento, asympatiento, and catheter): 6 in nadroparin group, 4 in warfarin group (p=0.48) Overall total thromboembolic events: 31.8% nadroparin, 16.7% warfarin (p=0.23). One catheter removal in each group for CRI 6-month Followup Results: Events reported, but no statistical analysis provided Study did not demonstrate that a fixed, low dose of warfarin and a fixed, prophylactic dose of nadroparin has statistically differenceerent efficacies in preventing upper extremity thrombosis in cancer patients with indwelling long-term CVCs; safety satisfactory with both treatments
Mitchell, Cancer, 2003	To determine the prevalence of TEs. The secondary objective was to detect any association of TEs with the presence of congenital or acquired prothrombotic disorders. Not powered for third outcome.	60 children with Acute Lymphoblastic Leukemia treated with Asparaginase (ASP) (PARKAA) study	The dose of ASP for the POG protocol was 6000 units/m2 on Days 2, 5, 8, 12, 15, and 19 of induction therapy; for the CCG protocol, the ASP dose was 6000 units/m2 on Mondays, Wednesdays, and Fridays for 3 weeks during induction therapy.	No antithrombin	N	Y	Y	Y	Primary - Prevalence of thrombosis (fibrin sheath or loss of CVC patency) in the patients that received no antithrombin supplementation; Secondary assess the relation of TE to presence of prothombotic disorders; Third prelim data on efficacy and safety of prophylaxis with antithromin	not stated	22/60 children had TEs, a prevalence of 36.7% (95% confidence interval, 24.4–48.8%). TEs were located in the sinovenous system of the brain in 1 patient, the right atrium in 3 patients, and the upper central venous system in 19 patients. TEs detected by venography resulted in 1) 25–100% occlusion, with 1 in 3 patients showing occlusion of 75% of the greatest vessel dimension, and 2) the presence of collaterals in 60% of patients, with 40% categorized as major. No children with TEs were positive for factor V Leiden or prothrombin gene 20201A, and four of eight children with antiphospholipid antibodies had a TE.
Moller, J Hosp Infect, 2005	To investigate the impact of patient education reg.arding provision of their own catheter care on the frequency of CVC-related infections (CRIs). Slightly underpowered 80% -	82 patients with hematological cancers were fitted with tunnelled double-lumen Hickmans	42/82 received individualized training and supervision by a clinical nurse specialist, with the aim of becoming independently responsible for their own catheter care.	40/82 followed the standard CVC procedures carried out by nurses inside and outside the central hospital.	Y	Y	Y	Y	Primary CRI and CRBSI; Secondary BSI	At least 2 months	A significantreduction in CRIs was found in the intervention group, with a 50% reduction in the incidence rate of CRIs. 61 local exit site cultures, comprising 9 positive and 530 blood cultures that included 52 positive cultures with corresponding sepatienticaemia, were found in the control group.42 infections (12 local and 30 systemic) were determined as CRIs. CRBSIs represented 58% (30/52) of all cases of sepatienticaemia and were detected in 52.5% (21/40) of the control group patients. 50 local exit site cultures, comprising 4 positive and 406 blood cultures that included 36 positive cultures with corresponding sepatienticaemia,were found in the intervention group.16 infections (four local and 12 systemic) were determined as CRIs. CRBSIs represented 33% (12/36) of all cases of sepatienticaemia and were detected in 26% (11/42) of the intervention group patients. Systematic individualized, supervised patient education is able to reduce catheter-related infections.

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Monreal Throm and Hemo 1996	Whether long-term dalteparin reduces incidence of upper extremity DVT, and try to confirm if patients with high platelet counts at higher risk of developing UE DVT; originally planned sample size of 100 was calculated assuming a probability of a control group event of 0.40 and intervention 0.20	Cancer patients undergoing placement of long-term Port-a-catheter (n=32; 29 evaluable)	Dalteparin SQ qd x 90d (n=16)	No dalteparin (n=13)	N	N	Y	N	Upper extremity DVT (demonstrated by routinely performed venography 90d after catheter insertion or at sympatientom appearance) Infection, major bleeding	90 days (study period)	Study closed early due to an excess of thrombotic events in control arm Subclavian DVT: 6% of dalteparin group, 62% control group (RR: 6.75; 95% CI: 1.05-43.58; p=0.002) Tendency toward higher platelet count at moment of catheter insertion in patients who developed DVT, but difference not Significant No serious bleeding, no PE
Mueller JCO 1992	Compare frequency of infection, mechanical or thrombotic complications between 2 arms. Whether complications could be managed without catheter removal. Whether one type of catheter was preferable to other in certain patient populations; study power not given	Adult and pediatric cancer patients requiring prolonged access (n=100; 92 evaluable)	External catheter (Hickman) (n=48; 46 evaluable)	Subcutaneous (Port-a-catheter) (n=52; 46 evaluable)	N	N	Y	N	Catheter-related infections Mechanical problems Thrombosis	Minimum of 180 days following catheter insertion All patients monitored until device removal, death, or protocol termination	After first 6 months, no difference between groups for all complications [excepatiention: episodes of unexplained fever more frequent in Port-a-catheter patients, p=0.0072]. At device removal/death/study termination, no difference in number of catheters removed due to complications, mean device life was comparable, rate of complications similar. No difference between groups in incidence of documented infections or mechanical or thrombotic complications.
Niers, J Thromb Haemost, 2007	To determine the efficacy and safety of thromboprophylaxis with s.c.low-molecular-weight Heparin (nadroparin) administered once daily in a randomized placebo-controlled, double-blind trial in patients with hematologic malignancies	113 patients randomized to nadroparin but 87/113 (77%) underwent venography	Nadroparin LMWH 2850 antifactor Xa units once daily for 3 wks sc	Placebo sc	Y	Y	Y	Y	Thrombosis; Secondary outcomes were bleeding and CRI	day of CVC removal or 3 weeks	11 venographically Venography was performed on day 21 after CVC insertion) proven catheter-related CVTs were diagnosed. The frequency of catheter-related CVT was not significantly differenceerent between study groups, namely four catheter-related CVTs in the placebo group [9%; 95% CI: 0.002–0.16] vs. seven catheter-related CVTs in the nadroparin group (17%; 95% CI: 0.06–0.28). In addition, no difference in the incidence of catheter related infection or bleeding was observed between the groups.
Olson J Infus Nurs 2004	Whether CVC-related sepsis could be reduced by removing a hypothesized reservoir for pathogens, the CVC exist site dressing; 116 cases required to detect a 12.5% difference between groups (power of 80%, p=0.05)	Cancer patients with newly inserted CVCs upon site healing (3 wks) (n=78)	No dressing, exit site left uncovered (n=43)	Dressing provided (gauze); changed daily if neutropenic or qod if not (n=35)	N	N	N/A	N/A	Rate of catheter-related sepsis	catheter removal or patient death	Study closed early - patients with sepsis: 10 in no dressing group, 12 in dressing group (p=0.28)

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Ostendorf Supp Care Can 2005	To determine the efficacy of antisepatientic coating (CH-SS coated catheters) in preventing catheter-related infections among heme patients undergoing chemotherapy	Patients with heme malignancy needing a CVC for at least 7 days (n=245; 184 evaluable)	D-L CH-SS coated catheter (n=90)	D-L non-coated catheter (n=94)	D	N	Y	N	catheter colonization catheter-related bacteremia catheter-related sepatienticemia Local infection	Until catheter removal; BCxs obtained from catheters and peripheral vein at time of catheter removal	Mean length of catheter placement: 11 days Local infection: 35 in CH-SS group, 39 in control group. Overall BSI rate 10/184 (5.43%) and 4.7/1,000 catheter days Significant bacterial growth on tip or SQ seg.ment: 26% in CH-SS group, 49% in control group (tip: 8.8% vs 24.4%, p=0.0028; SQ seg.ment: 6.6% vs 28.7%, p=0.00004) catheter colonization: 33% in controls, 12% in CH-SS group (p=0.01). CRBSI: 3 in CH-SS group, 7 in controls (p=0.21). The use of CH-SS catheters is an effective tool in patients with heme malignancy.
Raad Cancer 1998	To test the efficacy of a prophylactic oral antibiotic combining novobiocin and rifampin to prevent staph infections in patients with metastatic melanoma treatment'd with biochemotherapy; assuming incidence of infection of 55% in untreatment'd patients, study needed 28 patients in each group for 80% power (one-tailed, significantlevel 0.05) to detect decrease in incidence to 20%	Crossover study patients with metastatic melanoma treatment'd with IL-2 and IFN-a plus chemotherapy (biochemotherapy) (n=26; 17 evaluable)	Novobiocin 500mg + rifampin 300mg po q12 h x 35 d (n=12 originally randomized, 17 total evaluable, crossover study)	Observation (n=14 originally randomized, 17 total evaluable, crossover study) All patients received D-L nontunneled silicone catheter	N	N	Y	N*	Incidences of infection Number of episodes of infection per patient course Adverse events	70 day study duration; catheter remained in place until no longer needed or specific reason for removal	Study stopped early because interim analysis after 26 patients showed significantresults Infectious complications: 71% during control course, 12% during antibiotic prophylaxis (p=0.001) catheter-associated bacteremia: 41% during control course, 6% during antibiotic prophylaxis (p=0.04) Local catheter infection: 53% during control course, 12% during antibiotic prophylaxis (p=0.008) 36 episodes of catheter infections during 17 control courses, 3 episodes during antibiotic prophylaxis courses (p<0.001).
Raad Inf Cont Hosp Epi 2001	To determine the safety and cost-effectiveness of replacing the IV tubing sets in hospitalized patients at 4- to 7-day intervals instead of q 72 h; rate of tubing set contamination at 72 h estimated to be 2%; equivalence deSignificantn yielded sample size of 340 patients/arm, assuming contamination incidence of 3% at 7 d, with a limit of 4% within which the two rates were considered to be equivalent (alpha error of 0.05, beta error of 0.2). Criteria for high- and low-risk patients were defined post-hoc, not a preplanned analysis	Adult cancer patients (most solid tumor) requiring infusion treatment via IV administration sets for >2 d (n=512)	IV tubing sets changed between 4 and 7 days (n=232)	IV tubing sets changed q 3 d (n=280)	N	N	N/A	Y	Infusion- or catheter-related contamination or colonization of IV tubing (determined by quantitative cxs of infusate) Infusion- or catheter-related BSI (determined by quantitative cx of the infusate in association with BCxs in febrile patients)	All patients followed prospectively for 1 wk after the IV tubing was removed to monitor for development of BSI	Study protocol required interim analysis after accrual of >50% of patients, and study was to be stopped if there was a trend toward a higher rate of infusion- or catheter-related BSI in the 4- to 7-days arm. Preplanned interim analysis performed after 75% of patients entered (512 patients) showed that all 3 episodes of infusion-related BSI occurred in patients whose IV administration set was changed 4 to 7 days after insertion (p=0.09); this led to early study termination, as specified in study protocol ITT analysis demonstrated no significantdifference in frequency of infusate contamination between the 2 groups (5 (2%) in 3-d group, 8 (3%) in 4-7 d group, p=0.2). Number of colonies from infusate: 50 in 3-d group, 145 in 4-7 d group (p=0.02). Number with infusion- or catheter-related infection: 0 in 3-d group, 3 (1%) in 4-7 d group (p=0.09, all 3 patients received IL-2). Subset analysis on patients at low risk for infection who did not receive IL-2, TPN, or blood transfusions; no significant difference in frequency of infusate contamination (2% in each arm, p=0.6); also no infusion- or catheter-related BSIs. Subset analysis on patients at high risk (rec'd IL-2, TPN, or blood transfusions) had a trend toward higher frequency of contamination of infusate in 4-7 d group (0% vs. 9%, p=0.07)

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Raad Infec Con Hosp Epi 1994	To determine whether the use of MSB precautions, consisting of sterile gloves, gowns, and a large drape as well as nonsterile masks and caps, would result in a lower rate of catheter colonization and infection than using only sterile gloves and a small drape during insertion	Adult cancer patients with a nontunneled non-cuffed silicone CVC (n=402; 343 evaluable)	MSB at time of catheter insertion (n=176)	"Standard" practice: sterile gloves and small drape (n=167)	N	N	Y	N	catheter infections Time to infection	3 mos post-insertion or until catheter removal, whichever came first	MSB group: 106 patients kepatient CVC during f/u, 70 patients had CVC removed during f/u period Control group: 95 patients kepatient their CVC during f/u, 72 patients had CVC removed during f/u period (p=0.53) Significant colonization of catheters: 12 (7.2%) of controls, 4 (2.3%) of MSB patients (p=0.04) Catheter infections: 4 in MSB group, 12 in control group (p=0.03). Time to infection: 67% of control group occurred in first 2 mos, 25% of MSB group occurred in first 2 mos (p<0.01)
Rackoff J Pediatr 1995	To determine whether adding vaco my CVC flush sol'n would Significant reduce the incidence of bacteremia attributable to luminal colonization with VSO; study had 80% power (significantlevel 0.05) with 36 patients per arm if assume 30% infection in heparin group [paper cut off, couldn't see percentage invancomycin group]	Pediatric patients (most with cancer) with indwelling cuffed CVCs (n=63)	heparin +vancomycin flush (n=32)	heparin flush (n=31)	N	N	N/A	N/A	Fever positive BCxs Bacteremia Bacteremia with VSO Bacteremia attributable to luminal colonization with VSO	Median time on study 136 d	Study stopped early (after 63 patients) because after >9,000 catheter days interim analysis showed 2 groups not significantdifference, and given the results study would have needed approx. 200 patients/arm to show a difference positive BCx: 35% in heparin, 37.5% in heparin-vanco (p=0.87) Bacteremia: 32.3% in heparin, 31.3% in heparin-vanco (p=0.93) Bacteremia with VSO: 19.4% in heparin, 21.9% in heparin-vanco (p=0.81) Bacteremia attributable to luminal colonization with VSO: 6.5% in heparin, 15.6% in heparin-vanco (p=0.43)
Ranson J Hosp Infec 1990	To investigate whether prophylactic IV vacomycin was effective in reducing the subsequent incidence of catheter-related sepsis in patients undergoing chemotherapy for malignant disease	Cancer patients requiring CVCs for chemotherapy, some undergoing leukemia treatment or BMT (n=98; 72 evaluable)	Vancomycin IV x 2 at time of catheter placement (n=36)	Saline infusions (n=36)	D	Y	Y	N	Coag-neg.ative staph bacteremia Tunnel sepsis catheter-related sepsis	catheters were in place across groups for 80 - 126 days (4 means fall within this range across 4 groups)	Coag-negative staph bacteremia episodes total: 10 in vancomycin group, 11 in control group Episodes in first 30 days: 3 in each group Tunnel sepsis episodes total: 3 invancomycin, 1 in control Episodes in first 30 days: 1 in vancomycin, 1 in control catheter-related sepsis total episodes: 18 in vancomycin, 20 in control catheter-related sepsis first 30 days: 9 in each group. This trial confirms that the incidence of catheter-related sepsis is higher in patients who have more severe and prolonged immunosuppression.
Ray JVIR 1999	Determine efficacy and safety of prophylactic urokinase in the prevention of delayed tunneled CVC-related complications; study power not given. Most patients received Hickman with silver-impregnated cuffs, but some received Pheres-flow catheters specifically for plasma pheresis.	Adult cancer patients undergoing radiologic placement of a tunneled CVC, expected to require catheter for >6 mos (n=105)	Twice-daily Heparin flushes + once-weekly urokinase flushes, dwell time 12h (n=53) [note that the urokinase replaced the Heparin flush on the days urokinase was given]	Twice-daily Heparin flushes (n=52)	N	N	Y	N/A	Complications: local and systemic infections, clinically evident venous thrombosis, catheter occlusions, bleeding complications	Up to 6 mos after CVC implantation	Occlusion: 16% of Heparin group, 4% of urokinase group (p<0.05). "Infectious complications": 6% of Heparin group, 2% of urokinase group (p not given but assume NS). Infectious and occlusive complications combined: 21% of Heparin group, 6% of urokinase group (p=0.02). Catheter-related venous thrombosis: 10% in Heparin group, 11% in urokinase group (p>0.05). Bleeding complications: 2% Heparin group, 0% urokinase group

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Ruschulte, Annals of Hematology, 2008	To evaluate the effectiveness of chlorhexidine-impregnated sponges (Biopatch, Ethicon, Germany) for reducing catheter-related infections of central venous catheters inserted for cancer chemotherapy. (three step group sequential analysis protocol); IJ or SC; underpowered.	601 adult patients with hematological or oncological malignancies with 9731 catheter days all had CHSS impreg.. CVC (Arrogard blu, Arrow, Germany)	301/601 patients - Chlorhexidine gluconate-impreg.nanted wound dressing	300/601 patients - Standard sterile wound dressing	Y	Y	Y	Y	Rate of CVC-related infection; Insertion site sympatientoms (swelling, pain, redness) temperature' WBC and C-reactive protein count; infection diagnosis requires removal of CVC	Until CVC no longer needed or a CVC related infection was suspected	Overall, the rate of CVC-related infections was 46% less in the study group than in the control group (RR of 0.54; confidence interval [CI] 0.31–0.94); The incidence of CVC-related infections were 11.3% (34 of 301) and 6.3% (19 of 300) in the control and chlorhexidine-impregnated wound dressing groups, respectively (p=0.016, relative risk 0.54; confidence interval 0.31–0.94). Especially, catheter-related infections at internal jugular vein insertions could be reduced (p=0.018). No adverse effects related to the intervention were observed.
Ruud, Acta Paediatr, 2006	To perform a study of adjusted low-dose warfarin for the prevention of CVC-related VTE in children with malignancies. IJ; 90% power p=0.05	73 children enrolled, 62 completed	31/73 (29 treated) warfarin (Marevan†, Nycomed Pharma, Norway) for 6 mo with an intended INR between 1.3 and 1.9.	40/73 (33 treated) no prophylaxis	Y	Y	Y		VTE in a jugular vein diagnosed with ultraonography; CVC related infections measured as days on antibiotics or positive blood culture	6 months	Asymptomatic CVC-related VTE was frequent (42%), but often transient. Regardless of severity, timing and duration, CVC-related VTE was equally frequent among children on warfarin as compared to controls (p =0.44). Low-dose warfarin (p =0.59) or jugular CVL-related VTE (p =0.91) did not have any impact on days on antibiotics, but we observed a tendency towards an association between CVL-related VTE and positive blood cultures (p =0.15). Study did not show any benefit of warfarin adjusted to maintain INR between 1.3 and 1.9.
Ruud, Pediatr Blood Cancer, 2008	Evaluated the interaction of warfarin and CYP2C9 polymorphisms and concomitant corticosteroids in 29 children with cancer. Children with heterozygous polymorphisms of CYP2C9 achieved target INR sooner and more frequently had INR above the target level, compared to children without mutations. Children on concomitant steroids had Significantnifi cantly lower warfarin requirements. Thus, awareness of CYP2C9 genotype and steroid-induced responsiveness to warfarin may be important when administrating oral anticoagulation in children.	Children (median age, 7 yrs) with known/strongly suspected cancer, requiring long lasting IV access (n=20; 16 evaluable)	29/62 children (mean age 7.3 years) received low dose warfarin with a target INR 1.3-1.9; 15 had concomitant high dose steroids (ALL)	no thromboprophylaxis	U	U	U	U	Warfarin requirements(1.3-1.9) for children with CYP2C9 genotype	not stated	The required warfarin dose to achieve the target INR (1.3–1.9) ¼0.89). Children receiving intermittent steroid treatment (n=15) had significantly lower warfarin requirements while on steroids as compared to periods without steroids (P<0.001). Mean warfarin dose was 0.057 mg/kg/d (SD=0.03) in periods on high-dose steroids, while the mean dose increased to 0.12 mg/kg/d (SD=0.04). in periods without steroids. This was observed both during first and second induction phase in children with ALL, as well as in the child with sarcoma. There was no significantdifference in dose requirements between heterozygous children as compared to those without mutations (0.09 mg/kg/d vs. 0.11 mg/kg/d) (P=0.57). Children with CYP2C9 polymorphisms achieved the target INR more rapidly and more frequently had an INR above the target level than children with normal CYP2C9 genotype.
Sanders, J Antimicro chemotherapy, 2008	Prospectively evaluate the use of intraluminal ethanol for the prevention of CRBSI in immunosuppressed haematology patients. Powered , two tailed p=0.05	64 patients with tunnelled cuffed CVC inserted in subclavian haematological malignancy	n=34 Prophylactic treatment using 70% ethanol	n=30 Heparinized saline flushes	Y	N/Y	Y	U	Primary endpoint was episode of CRBSI (bacteraemia in febrile patient with CVC within 48 hours and no identified focus of infection. Secondary endpoint was febrile episodes	not stated; until the end of treatment	Varied substantially during the treatment period of 6 months. Patients had identical dual lumen Hickman CVC: Patients receiving prophylactic antibiotics, as occurred routinely inthe early part of the study were not excluded.

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Schwartz JCO 1990	Determine whether addition ofvancomycin to Heparin flush sol'n would alter incidence of symptomaticbacteremia (suscepatientible tovancomycin) secondary to colonization of catheter lumen; study power 80% (5% significantlevel) to detect bacteremia reduction from 50% to 5%	Pediatric; neutropenic or to receive chemotherapy (n=45)	Heparin +vancomycin flush (n=21)	Heparin flush (n=24) Tunneled catheters in both arms, flushed daily	D	N	N/A	N/A	symptomaticbacteremia secondary to colonization of catheter lumen withvancomycin-suscepatientible bacteria	Average of 247 catheter days/patient patients followed until catheter was removed, patient died, or patient was transferred to an institution where study sol'ns could not be given	Data analyzed 2 mos after 44th patient enrolled (pre-planned analysis of data after every five episodes of bacteremia after 44 patients enrolled); study stopped because no episodes ofvancomycin-sensitive bacteremia associated with heparin+vanco flush [note: one episode ofvancomycin-resistant infection in heparin+vanco flush group reported] Bacteremia withvancomycin-sensitive organisms, attributed to luminal colonization: 5 in Heparin flush group, 0 in heparin+vanco group (p=0.035; does not account for the number of catheter days/patient.
Shivnan Onco Nurs For 1991	To compare transparent adherent dressings and dry sterile gauze dressings in patients undergoing BMT; study allowed a detectable difference of 35% or more in complication rates between the 2 groups, power of 80% (p<0.05, one-sided)	patients undergoing BMT (adult & pediatric) (n=103; 98 evaluable)	Teg.aderm changed q 4d (n=51)	Gauze changed daily (n=47)	N	N	Y	Y	Incidence/severity of local and systemic complications Patient assessment of comfort Nursing time	30-day study period	Skin irritation: 2.7 days (mean) in Teg.aderm group, 7.4 days (mean) in gauze group (p=0.0005). Frequency of positive skin cxs between arms: p=NS. Nursing time to change dressings over 30 days: $46.86 for Teg.aderm, $125.07 for gauze. Teg.aderm patients reported Significantly higher levels of satisfaction on all days (p<0.008)
Smith Am J Ped Hem Onc 1991	Compare standard approach (Heparin BID) to weekly saline flush. Randomized crossover study.	Pediatric cancer patients with Broviacs (n=14)	Isotonic saline flush q week (all patients, crossover study) patients crossed over after 3 1/2 mos for another 3 1/2 mos	Heparinized saline flushes BID (all patients, crossover study)	N	N	N	N	Catheter thrombus formation (presence of clot on echo or a blocked catheter)	7 mos	No stat significantdifference between groups (no statistical analysis provided). Heparin is not necessary in the maintenance of the patency of indwelling CVCs.
Smith Antimic Agents and chemotherapy 1989	To comparevancomycin and teicoplanin in the treatment of S-L Hickman-associated infections in patients with heme malignancies. Single center study.	Patients with heme disorders with fever >38 C on 2 consecutive occasions 2 hours apart OR fever spike of >38.5 C (n=59; 72 febrile episodes, 60 evaluable)	Teicoplanin IV (n=32 episodes)	Vanco IV (n=28 episodes)	N	N	Y	N	Infection (microbiologically documented, clinically documented, possible)	Until infection resolution or removal of catheter for infection	Median treatment time: 7 days for vancomycin, 8 days for teicoplanin. Response rates for micro and clinically documented infections: 80% forvancomycin, 69% for teicoplanin (p=0.316). Number of responders for micro/clinically documented infections: 16 invancomycin group, 18 in teicoplanin group (p=0.52). Exit site infections, micro/clinically documented: 10 invancomycin group, 11 in teicoplanin group (p=0.055) Tunnel infections: 4 invancomycin group, 7 in teicoplanin group (p=0.21). Toxicity: adverse events in 9vancomycin patients and 3 teicoplanin

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Solomon Eur J Cancer 2001	Reg.ular instillation of urokinase into double-lumen Hickman catheters would be superior to Heparinized saline in reducing catheter-related complications; study power not given. Multicenter study.	Patients with heme malignancies requiring catheter for transplant or chemotherapy, >16 y/o; catheter life expected to be >6 wks (transplants) or >13 wks (chemotherapy) (n=100)	Urokinase lock, twice weekly (n=52)	Heparin lock, twice weekly (n=48)	N	Y	Y	Y	Incidence of microbiologically confirmed catheter-related sepatienticemic infections Other infections, catheter occlusions, catheter-related venous thrombosis, all combined catheter-related complications Separate analysis planned prospectively to compare endpoints by treatment group (chemotherapy vs. transplant)	Mean duration of treatment 8.5 wks for Heparin group, 8.8 wks for urokinase group (removal of catheter led to withdrawal from study) Adverse events recorded up to 30d after removal of catheter	Heparin is not necessary in the maintenance of the patency of indwelling CVCs. Of 1,700 treatments, incorrect drug given on 32 occasions Low rate of removal of catheters, but high rate of complications; within 2 wks of catheter insertion, approx. 50% of patients in both groups developed >1 catheter-related complications patients with solid tumors had more catheter-related venous thrombosis compared to patients with heme malignancies (p=0.027) patients with heme malignancies more likely to have infectious complications (p=0.006) Although 98% of all patients had adverse events, none could be attributed to study drugs
Starling, JCO, 2010	Data concerning the prevalence of and outcomes related to thromboembolic events (TEs) in patients with advanced gastroesophageal cancer and CVC who are undergoing chemotherapy are limited. prospective, exploratory analysis of TEs in a randomized, controlled trial	n=964 patients treated with epirubicin/platinum/ fluoropyrimidine combination chemotherapy for advanced/locally advanced gastroesophageal cancer. Reg.imens were epirubicin (E), cisplatin (C), fluorouracil (F; ECF); E, C, capecitabine (X; ECX); E, F, oxaliplatin (O; EOF); and EOX.	Continuously infused F was administered via a central venous access device (CVAD) with 1 mg of warfarin for thromboprophylaxis	none	N	N	N	N	Incidence of TEs (venous and arterial) in the whole treated patient cohort, according to chemotherapy, associated with CVADs and TE-related prognoses; OS		The incidences of any, of venous, and of arterial TEs among 964 treated patients were 12.1% (95% CI, 10.7 to 14.3), 10.1% (95% CI, 8.3 to 12.3), and 2.2% (95% CI, 1.4 to 3.4) respectively. There were fewer TEs in the O compared with the cisplatin groups (EOF/EOX v ECF/ECX: 7.6% v 15.1%; P = .0003). Cisplatin was identified as a risk factor for TE in multivariate analysis (hazard ratio [HR], 0.51; 95% CI, 0.34 to 0.76; P = .001). There was no difference in the incidence of TEs for the F group compared with the capecitabine groups. The incidence of CVAD-related thrombosis was 7.0% (ECF/EOF arms). Overall survival was worse for patients who experienced TEs versus no TEs (median survival, 7.4 v 10.5 months; HR, 0.8; 95% CI, 0.64 to 0.99; P = .043).
	To assess the possible benefits of a new polyurethane catheter impregnated with dispersed silver ions inimmunocompromised patients	Patients with cancer, heme malignancies, bone marrow or organ transplant, or immunosuppressed, requiring CVC (n=154; 97 evaluable)	T-L silver-impregnated catheter (n=50)	T-L conventional polyurethane catheter (n=47)	N	N	Y	N	"Contamination" (growth of more than 15 cfu on the blood agar plate) catheter-related infections	Until catheter removal; only data of catheters in place for at least 3 days were evaluated	Mean indwelling time of catheter: 10.5 d in silver group, 11.0 d in control group. Contaminated catheters: 10 in silver group, 14 in controls (p=NS). Contamination episodes per 1,000 catheter days: 15.6 in the silver group, 24.6 in controls (p=NS). Infections attributed to catheter according to paper's scoring system: 3 in silver group, 3 in control group (p=NS).

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Teichgraber, Cardio Intervent Radiol, 2009	The purpose of this study was to evaluate whether low-profile totally implanted central venous port systems can reduce the late complication of skin perforation.	Patients with cancer (N=80) Indications for port catheter implantation were malignant disease requiring chemotherapy.	40 patients (age, 57 +/- 13 years; 22 females, 18 males) were randomized for the implantation of a low-profile port system,	40 patients (age, 61 +/- 14 years; 24 females, 16 males) received a reg.ular port system as control group.					Procedure time, number of complications (procedure-related immediate, early, and late complications), and number of explantations were assessed.	Follow up at 6 months	All port implantations were successfully completed in both study groups. There were two incidents of skin perforation observed in the control group. One skin perforation occurred 13 weeks and the other 16 weeks after port implantation (incidence, 5%) in patients with reg.ular-profile port systems. Two infections were observed, one port infection in each study group. Both infections were characterized as catheter-related infections (infection rate: 0.15 catheter-related infections per 1000 catheter days).
Timsit JAMA 1996	To assess the efficacy of tunnelization of IJ catheters in decreasing catheter-related sepsis in ICU patients (hypothesis was that tunnelization decreases rate of sepsis to that of SC catheter sepsis); study had power of 80% (type I error 5%) with sample size of 208 to detect a decrease in rate of systemic catheter-related sepsis from 15% to 4% .	Critically ill patients (27 with cancer) >18 y/o admitted to ICU and expected to need catheterization for >48h (n=241; 231 evaluable)	Tunneled IJ catheters (n=117)	Non-tunneled IJ catheters (n=114)	N	Y	Y	Y	Time to occurrence of systemic catheter-related sepsis catheter-related sepatienticemia and Significant catheter colonization	Catheters removed and cultures obtained according to pre-established rules in the event of Significantns of catheter-related sepsis, uselessness, malfunction, discharge of the patient from ICU, or death	Systemic catheter-related sepsis: 18 events in non-tunneled (1.9/100 catheter-days), 7 events in tunneled (0.7/100 catheter-days) (p=0.02; RR=3). Time to bacteremic catheter-related sepsis: 13 events in non-tunneled group (1.3/100 catheter-days), 4 events in tunneled group (0.4/100 catheter-days) (p=0.02). Positive catheter colonizations: 29 in non-tunneled (3.1/100 catheter-days), 20 in tunneled (2/100 catheter-days) (p=0.10; RR of colonization estimated at 1.6 in non-tunneled vs tunneled group). Appears that MSB was used for both groups Median time to catheter placement Significant longer in the tunneled group (30 mins v 16.5 mins, p<0.001).
Unal Trans Aphere Sci 2003	To analyze the incidence of malpositioning for right and left side catheter insertion attempatients for Hickman catheters. Randomization inappropriate - used sequential (alternating) randomization.	patients who were candidates for stem cell collection and high dose chemotherapy, undergoing placement of long-term tunneled CVCs (n=82; 93 placement attempatients, 75 evaluable patients)	Hickmans inserted in left SC vein (n=36; 48 attempatients)	Hickmans inserted in right SC vein (n=39; 45 attempatients)	N	N	Y	N	Incidence of malpositioning (left vs right side)	Not stated	Malpositioning in attempatients: 2 in left side (5.55%), 8 in right side (20.51%) (p not given). No significant difference between right and left sided attempatients reg.arding mechanical complications excepatient malpositioning (p<0.05). Left sided attempatients had a lower incidence of malpositioning (p=0.032). Left SC Hickman cathetererization can be used as a safer method to avoid malpositioning to the IJ vein, and also is safer than a right SC approach reg.arding other mechanical complications. The left site approach may be preferred for long-term purposes, as it may be much more comfortable as the vast majority of patients are right handed.

RefID	Study Purpose/Hypothesis	Patient Population	Intervention/Arm 1	Control/Arm 2	B	AC	W/	ITT	Outcomes Assessed	Followup	Results
van Rooden, JCO, 2008	Investigate whether three times weekly urokinase rinsing of CVC reduces the incidence or severity of CVC-related infections by CoNS in patients undergoing intensive cytotoxic treatment for hematologic malignancies.	Of 181 consecutive patients , 20 excluded because they met exclusion criteria. 161 patients 18 yo or older (83 urokinase, 78 saline) with hematologic malignancies with CVC in subclavian or jugular, tunnelled, locked with Heparin	Urokinase rinses (5 mL of 5,000 U/mL n=83	Placebo saline rinses n= 78	D	Y	Y	Y	Primary- occurrence of any CVC related infection by CoNS (local or systemic); Secondary CVC infectinons caused by other microbial pathogens, premature CVC removal, secondary CVC related complications, major bleeding		% patients with 1 + culture with CoNS < in patients receiving urokinase compared with patients on placebo (26% v 42%, respectively; relative risk [RR] 0.61; 95% CI, 0.39 to 0.94). Major CVC-related CoNS infection occurred less frequently in patients receiving urokinase versus placebo (1.2% v 14.1%, respectively; RR 0.09; 95% CI, 0.01 to 0.50). Secondary complications, including CVC-related thrombosis, were observed less frequently in the urokinase group compared with the placebo group (1.3% v 9.0%, respectively; RR 0.14; 95% CI, 0.02 to 0.82). No severe bleeding complications attributable to urokinase were observed. Frequency of non CVC related sepsis was similar among patients with urokinase (8.5%) and saline (9%);
Vassilomanolakis BMT 1995	To investigate perioperative vancomycin prophlaxis for CVC-related infections in BMT. D-L Hickmans used.	Patients with solid tumors or leukemias undergoing BMT, requiring CVCs (n=40; 46 catheters)	Vancomycin IV x 3 at time of catheter placement (n=29; 35 catheters)	No vancomycin (n=11; 11 catheters)	N	N	Y	Y	CVC-related infections in post-transplant period	Up to 30 days after BMT	Infected CVCs: 4/35 catheters invancomycin group, 5/11 catheters in control group (p<0.05). Exit site infections: 2/35 invancomycin group, 3/11 in control group (p=NS). CVC-related bacteremia: 2/35 invancomycin group, 5/11 in control group (p<0.01) G+ infections: 4/35 in vancomycin group, 6/11 in control group (p<0.01).
Verso, JCO, 2005	To evaluate the efficacy and safety of the low molecular weight Heparin, enoxaparin, in the prevention of VTE. Second generation poly or silicone CVC including implantable were used.	385 randomized, 320/385 (83.4%) underwent venography. Adequate for 155 patients in each treatment group	n=155 patients Subcutaneous enoxaparin 40 mg once a day. Treatment was started 2 hours before CVC insertion and continued for 6 weeks.	n= 155 patients Placebo	Y	Y	Y	Y	DVT confirmed by venography of CVC limb performed 6 wks after randomization or clinically overt embolism, confirmed by objective testing during drug administration. Secondary - bleeding complications with decrease in hemoglobin at least 2g/dL or requiring a transfusion 2 or > units	3 months	A DVT was observed in 22 patients (14.1%) treated with enoxaparin and in 28 patients (18.0%) treated with placebo, corresponding to a relative risk of 0.78 (95% CI, 0.47 to 1.31). No major bleeding occurred. Five patients (2.6%) in the enoxaparin group and two patients (1.0%) in the placebo group died during the treatment period. No difference in the rate of CVC-related VTE was detected between patients receiving enoxaparin and patients receiving placebo.

RefID	Study Purpose/Hypothesis	Patient Population	Intervention/Arm 1	Control/Arm 2	B	AC	W/	ITT	Outcomes Assessed	Followup	Results
Verso, Intern Emerg Med, 2008	To identify the risk factors for CVC-related thrombosis in patients aimed at assessing the efficacy and safety of enoxaparin for prophylaxis of CVC-related thrombosis (ETHIC study) Same data, differenceerent analyses as Verso, JCO, 2005.	385 randomized, 310/385 (80.5%) underwent venography (Adequate for 155 patients in each treatment group)	n=155/310 patients received 40 mg once daily of enoxparin given 6 wks after insertion of CVC	n= 155/310 patients received placebo	Y	Y	Y	Y	DVT confirmed by venography of CVC limb performed 6 wks after randomization or clinically overt embolism, confirmed by objective testing during drug administration. Secondary - bleeding complications with decrease in hemoglobin at least 2g/dL or requiring a transfusion of 2 or > units; assessment of position of CVC tip	not stated (3 months?)	The incidence of CVC -related DVT was 16.1% (50/310); 14.1% in the enoxaparin group(22/155) compared to 18.0% in the placebo group (28/155) corresponding with a RR of 0.78 (95% CI, 0.470 1.31) . In the overall study population (univariate analysis), an adequate position of CVC tip (RR 0.26, 95% CI 0.17-0.43; P<0.0001) and right-sided CVC insertion (RR 0.39; 95% CI 0.25-0.65 P< 0.0001) were found to be 'protective" factors for CVC-related DVT. Also weekly CVC care with Heparin (in comparison with CVC care at interval longer tahn 1 wk or after each infusion of chemotherapy) was a "protective" factor for DVT (RR 0.45, 95% CI 0.23-0.83 P=0.010); In overall study population (multiple logistic reg.ession analysis) - CVC tip (OR 4.05, 95% CI 1.64-10.02 P=0.002; left isde insertion (OR 2.29, 95% CI 95% 1.01-5.51 P=0.05, chest radiotherapy (OR 7/01, 95% CI 1/42-34.55 P=0.017) and were independent risk factors for DVT. In patients with placebo - position of CVC tip)OR 5.67, 95% CI 1.43-22.40, P=0.01) and left sided insetion (OR 6.01, 95% CI 1.47-24.56 P=0.01) were confirmed to be independent risk factors. The presence of distant metastases (OR 9.36, 95% CI 1.53-57.05 P=0.01) increased the risk of CVC related thrombosis only in patients who received placebo. Enoxaparin reduced the incidence of thrombosis from 21%012% in patients with mets (OR 0.5, 95% CI 0.21-1.10 and from 24% to 13% in patients older than 60 (OR 0.5, 95% CI 0.21-1.10)
Vokurka, Med Sci Monitor, 2009	Determine opatientimal frequency interval for dressing CVC	n=81 patients with AML with non-tunneled polyurethane CVC subclavian insertion site covered with a polyurethane semi permeabel occlusive dressing	n=42 2x week dressing change group Note: 80% of the changes were performed according to the protocol interval and the real mean interval between dressing changes was 3.8 days. The main reason for the 20% of unplanned early dressing changes were local bleeding in 50% of the cases, unstitched or soiled dressings in 34%, insertion site infl ammation in 8%, and other reasons in 8% of the cases.	n=39 1 x week dressing change group Note: In the once-weekly group, only 58% of the dressing changes were performed according to the protocol interval. Because 42% of the changes were performed early, the real mean interval was reduced to 5.4 days in this group, instead of the 7 days originally planned. The main reason for these unplanned early dressing changes were an unstitched or soiled dressing in 52%, local bleeding in 28%, insertion site infl ammation in 10%, and other reasons in 10% of the cases.					Primary - Frequency of dressing change and skin damage, insertion site inflamation, fevers and CVC blood cultures and tolerance and pain		No differences were observed between the groups with respect to local cutaneous damage, fevers, or positive catheter blood cultures. There were more insertion-site inflammations in the twice-weekly group (55% vs. 25%, p=0.008). In the once-weekly group it was necessary to change the occlusive dressing sooner in 42% of the cases, mostly due to a soiled dressing and local bleeding, and the real mean interval of changes was 5.4 days. Significantly more incidences of infl ammation were observed in the twice-weekly group (55% vs. 25%, p=0.008), with a median diameter of the infl ammation of 5 mm (range: 3–30 mm). Only 13% out of 294 skin swabs performed on the occasion of occlusive dressing change were positive (coagulase-neg.ative staphylococci-positive in 76% of the cases) with no Significantnifi cant difference between the two groups. No correlation between insertion site inflammation and age, gender, number of CVC lumina, or dose of Ara-C was observedin univariate and multivariate analysis. The prolonged interval of dressing changes, with a real mean interval of 5.4 days, did not lead to an increased number of local cutaneous complicationsor CVC blood culture positivity and even contributed to reduced insertion-site inflammation occurrence.

RefID	Study Purpose/Hypothesis	Patient Population	Intervention/Arm 1	Control/Arm 2	B	AC	W/	ITT	Outcomes Assessed	Followup	Results
Warner J Am Coll Surg 1996	To compare Groshongs with Hickmans in a pediatric oncology patient population. No statistical analysis given for any results. Randomization inappropriate, based on MR number (even & odd last digits).	n=81 patients with AML	D-L Groshong (n=10)	D-L Hickman (n=10)	N	N	N/A	N/A	Mechanical and sepatientic complications	Until catheter removal	Study closed early due to Significant greater number of complications associated with Groshongs Average duration of catheter: 239 d for Groshong, 260 days for Hickmans. Five Groshongs removed prematurely due to catheter-related problems. Two Groshongs required conversion to daily flushes with Heparin to maintain patency.
Wiernikowski Am J Ped Heme/Onc 1991	To determine if the use of bacteriostatic saline (compared to sterile saline) would reduce the frequency of catheter colonization in pediatric oncology patients; study had 90% power (significantlevel 0.05) to show a 50% reduction in the incidence of colonized catheters with a sample size of 26 patients	n=81 patients with AML	Sterile saline + 1% benzyl alcohol (bacteriostatic solution) flush sol'n q 1 wk (n=13)	Sterile saline flush sol'n q 1 wk (n=17)	D	N	N	N	Catheter colonization (determined by weekly surveillance cxs) Attempatient to determine seasonal variation	6 months	Catheter colonization: 11/17 (65%) of sterile saline group, 6/13 (46%) in bacteriostatic group (p=NS). Average length of time to first positive event: 64 +/- 34 d for sterile saline group, 146 +/- 27 d for bacteriostatic group (p<0.001). Majority of infections in bacteriostatic group occurred during summer months.
Young, Lancet, 2009	Assessed whether warfarin reduces catheter-related thrombosis compared with no warfarin and whether the dose of warfarin determines the thromboprophylactic effect. Low event rate restricts the statistical power of all comparision.	n=81 patients with AML	84 [21%] on dose-adjusted) warfarin to maintain the international normalized ratio (INR) between 1.5 and 2.0.	Warfarin (n=408; 324 [79%] on fixed-dose of 1 mg/day (Compared with no warfarin (n=404),	Y		Y	Y	Primary - Rate of radiologically proven, symptomaticcatheter-related thrombosis; Secondary non catheter related trombotic events, catheter patency, bleeding, survival, infections, costs (not reported)		Compared with no warfarin (n=404), warfarin (n=408; 324 [79%] on fixed-dose and 84 [21%] on dose-adjusted) did not reduce the rate of catheter-related thromboses (24 [6%] vs 24 [6%]; relative risk 0·99, 95% CI 0·57–1·72, p=0·98). However, compared with fixed-dose warfarin (n=471), dose-adjusted warfarin (n=473) was superior in the prevention of catheter-related thromboses (13 [3%] vs 34 [7%]; 0·38, 0·20–0·71, p=0·002). Major bleeding events were rare; an excess was noted with warfarin compared with no warfarin (7 vs 1, p=0·07) and with dose-adjusted warfarin compared with fi xed-dose warfarin (16 vs 7, p=0·09). A combined endpoint of thromboses and major bleeding showed no difference between comparisons. We did not note a survival benefi t in either comparison.

Data Supplement #2: Evidence Table – List of Systematic Reviews or Meta-analyses

1. Akl EA, Kamath G, Yosuico V, et al: Thromboprophylaxis for patients with cancer and central venous catheters: a systematic review and a meta-analysis. Cancer 112:2483-92, 2008
2. Akl EA, Rohilla S, Barba M, et al: Anticoagulation for the initial treatment of venous thromboembolism in patients with cancer: a systematic review. Cancer 113:1685-94, 2008
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5. Chaukiyal P, Nautiyal A, Radhakrishnan S, et al: Thromboprophylaxis in cancer patients with central venous catheters. A systematic review and meta-analysis. Thromb Haemost 99:38-43, 2008
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18. Prandoni P, Falanga A, Piccioli A: Cancer and venous thromboembolism. Lancet Oncol 6:401-10, 2005

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American Society of Clinical Oncology Clinical Practice Guideline for Central Venous Catheter Care for the Oncology Patient

Data Supplement #3: Search terms

Catheter set

(("Catheterization, Central Venous"[MeSH] OR "Catheters, Indwelling"[MeSH] OR "Infusion Pumps, Implantable"[MeSH] OR "Venous Cutdown"[MeSH] OR "central venous catheter*"[tw] OR "femoral line"[tw] OR "CVAD"[tw] OR "central line"[tw] OR ("central venous"[tw] AND access[tw]) OR "PICC"[tw] OR (("peripherally inserted"[tw] OR "peripherally implanted"[tw]) AND "central catheter*"[tw]) OR Hickman[tw] OR Broviac[tw] OR Groshong[tw] OR Quinton[tw] OR Opti-flow[tw] OR Pheres-flow[tw] OR "Tesio Twin"[tw] OR "Ash Split"[tw] OR "Dacron cuff"[tw] OR "Vita cuff"[tw] OR "Hohn catheter"[tw] OR "subcutaneous port"[tw] OR "implantable port"[tw] OR "arm port"[tw] OR "chest port"[tw] OR (femoral[tw] AND "venous access"[tw]) OR (("single lumen"[tw] OR single-lumen[tw] OR "double lumen"[tw] OR "double-lumen"[tw] OR "triple lumen"[tw] OR triple-lumen[tw] OR "multi lumen"[tw] OR multi-lumen[tw]) AND catheter[tw])) NOT urinary catheterization[MeSH])

Cancer set

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RCT set

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Systematic review set

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OR metaanalysis [ti] OR meta-analyses [ti] OR evidence-based medicine OR (evidence-based AND (guideline [tw] OR guidelines [tw] OR recommendations)) OR ((evidenced-based OR evidence based) AND (guideline [tw] OR guidelines [tw] OR recommendation*)) OR consensus development conference [pt] OR health planning guidelines OR guideline[pt] OR practice guideline[pt] OR cochrane database syst rev OR acp journal club OR health technol assess OR evid rep technol assess summ OR evid based dent OR evid based nurs OR evid based ment health OR clin evid) OR ((systematic [tw] OR systematically OR critical [tw] OR (study [tiab] AND selection [tiab]) OR (predetermined OR inclusion AND criteri* [tw]) OR exclusion criteri* OR "main outcome measures" OR "standard of care") AND (survey [tw] OR surveys [tw] OR overview* OR review [tw] OR reviews [tw] OR search* OR (handsearch OR hand search) OR analysis[tw] OR critique [tw] OR appraisal OR (reduction AND risk AND (death OR recurrence))) AND (literature [tw] OR articles OR publications [tw] OR publication [tw] OR bibliography [tw] OR bibliographies OR published OR unpublished OR citation OR citations OR database OR internet [tw] OR textbooks [tw] OR references OR trials OR meta-analysis [mh] OR (clinical [tw] AND studies) OR treatment outcome)) NOT (case report [ti] OR editorial [ti] OR editorial [pt] OR letter [pt] OR newspaper article [pt]))

Venous Thrombosis

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"Heparin" set

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Dressing/Skin Cleansing/Sterile Precautions Set

(("infection"[MeSH Terms] OR infection[Text Word]) OR (chlorhexidine[mh] OR chlorhexidine gluconate[nm] OR chlorhexidine[tw] OR silver sulfadiazine[mh] OR silver sulfadiazine[nm] OR silver sulfadiazine[tw] OR silver[nm] OR silver[tw] OR povidone-iodine[mh] OR povidone-iodine[nm] OR “povidone-iodine”[tw] OR betadine[tw] OR hibiclens[tw] OR anti-infective agents, local[mh] OR anti-infective agents, local[nm] OR cross infection[mh] OR ((antisepsis[mh] OR antimicrobial[tw] OR anti-infective[tw] OR antiseptic[tw] OR aseptic[tw] OR antibiotic[tw]) AND (skin[tw] OR local[tw])) OR coated materials, biocompatible[mh] OR occlusive dressing[mh] OR dressing*[tw] OR bandages[mh] OR bandage*[tw] OR Opsite[tw] OR Tegaderm[tw] OR Biopatch[tw] OR Opsiture[nm] OR ((“transparent polyurethane”[tw] OR polyurethanes[nm] OR polyurethanes[mh]) AND (film[tw] OR dressing*[tw])) OR ((Maximum[tw] OR maximal[tw] OR full[tw] OR strict[tw]) AND sterile[tw] AND (precaution*[tw] OR technique*[tw] OR barrier[tw])) OR (skin[tw] AND (disinfection[mh] OR disinfect*[tw])) OR “site care”[tw] OR “skin care”[tw] OR “catheter care”[tw] OR “antibiotic lock”[tw] OR gauze[tw] OR tape[tw])

Impregnated Catheters Set

(chlorhexidine[mh] OR chlorhexidine[nm] OR chlorhexidine[tw] OR silver sulfadiazine[mh] OR silver sulfadiazine[nm] OR silver sulfadiazine[tw] OR silver[nm] OR silver[tw] OR anti-infective agents, local[mh] OR anti-infective agents, local[nm] OR antisepsis[mh] OR ((antimicrobial[tw] OR anti-infective[tw] OR antiseptic[tw] OR antibiotic[tw]) AND impregnate*[tw]) OR coated materials, biocompatible[mh] OR minocycline[mh] OR minocycline[nm] OR minocycline[tw] OR rifampin[mh] OR rifampin[nm] OR rifampin[tw])

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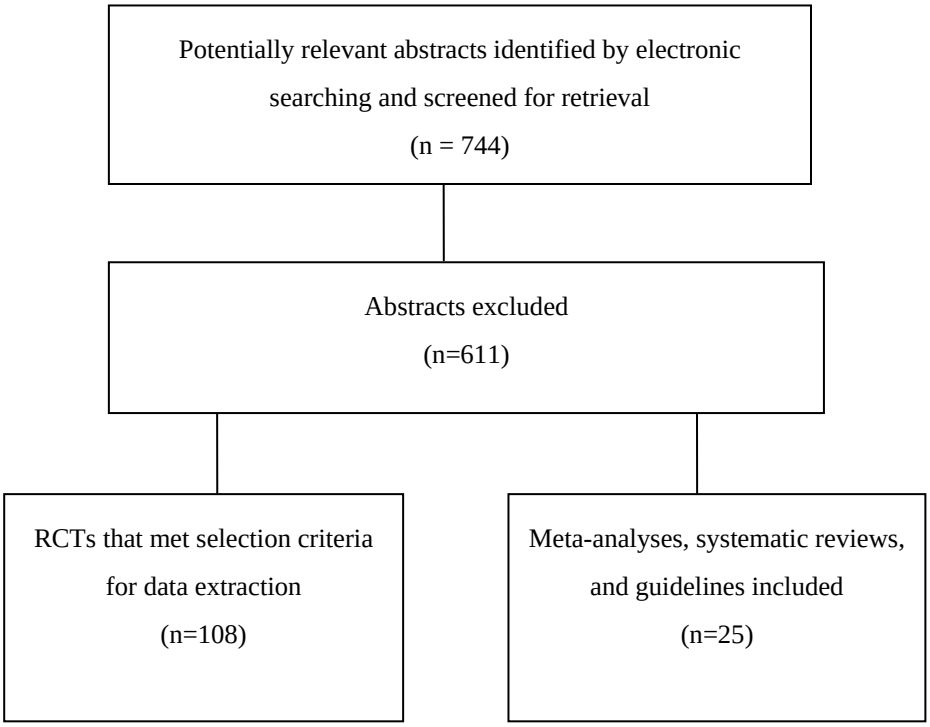
Data Supplement #4: Quorom Diagram: Publications Identified for Systematic Review



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Data Supplement #5: CVC Types and Risks of Infection

Catheter type	Entry site	Length	Advantages	Disadvantages	Comments
Nontunneled CVC	Percutaneously inserted into (subclavian, internal jugular, or femoral veins	>/= 8 cm depending on patient size	Choice of sites, easy to insert and remove, multiple lumen can be used	Short term use	Account for the majority of CRBSI
Tunneled CVC	Implanted into subclavian, internal jugular	>/=8 cm depending on patient size	Lower infection rates than nontunneled, good for long term use,	More complex insertion and removal	Cuff inhibits migration of organisms into catheter tract; lower rate of infection than nontunneled CVC
Peripherally inserted central venous catheters (PICC)	Inserted into basilic, cephalic, or brachial veins and enter the superior vena cava	>20 cm depending on patient size	Easy to insert and remove, Does not require platelet transfusion support or correction of clotting prior to insertion/removal	Higher thrombosis rate particularly with polyurethane variety, incidence of malposition greater than other types of CVC, longevity lower than tunneled devices	Lower rate of infection than nontunneled CVCs
Totally implantable	Tunneled beneath skin and have subcutaneous port accessed with a needle; implanted in subclavian or internal jugular veins	>/= 8 cm depending on patient size	No external catheter, cosmetically attractive, patient can bathe/swim as usual, lower maintenance, lower infection rates	Surgical insertion and removal, frequent repeated access may be more uncomfortable	Lowest risk for CRBSI; improved patient self-image; no need for local catheter-site care; surgery required for catheter removal

CVC – central venous catheter; CRBSI – catheter-related bloodstream infection
(Adapted from CDC Guidelines for the Prevention of Intravascular Catheter-Related Infections, 2011)[1]

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Data Supplement #6: Clinical Definitions of CVC-related Infections

Infections	Description
Catheter colonization	Growth of $\geq$ 15 cfu from a 5-cm segment of the catheter tip by semiquantitative (roll-plate) culture or growth of $>10^2$ cfu from a catheter by quantitative (sonication) broth culture reflects catheter colonization. Catheter tip should be cultured.
"Entrance or Exit-site" infection	Erythema, tenderness, induration within 2 -2.5 cm of the catheter entrance or exit site and distal to the catheter tunnel cuff, with or without purulence from the catheter entrance or exit site. Exudate at the catheter site that yields a microorganism, with or without a bloodstream infection.
Tunnel infection	Tenderness, erythema, and/or induration >2 -2.5 cm from the catheter entrance or exit site and above the catheter cuff extending along the subcutaneous tract of a tunneled catheter (e.g., Hickman or Broviac catheter), with or without concomitant entrance or exit site purulence or bloodstream infection.
Pocket infection in implanted catheter	Infected fluid in the subcutaneous pocket of a totally implanted intravascular device; may or may not be associated with tenderness, erythema, and/or induration over the pocket; spontaneous rupture and drainage, or necrosis of the overlying skin, with or without concomitant bloodstream infection.
Infusate-related bloodstream infection	Concordant growth of the same organism from the infusate and blood cultures with no other identifiable source of infection.
Catheter-related bloodstream infection	Isolation of fungi or bacteria from culture of a catheter segment and from the blood (preferably drawn from a peripheral vein) of a patient with accompanying clinical symptoms of bloodstream infection with no apparent source for bloodstream infection, with the exception of the CVC.

cfu , colony-forming units
(Adapted from IDSA Guidelines) [2] Refer to IDSA Guidelines Table 5 for "Intravenous antimicrobial treatment of catheter related bloodstream infection according to the specific pathogen related" (page 20-21)

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Data Supplement #7: Determining the Source of CVC-related Blood Stream Infection

Determining that the catheter is the source of blood stream infection is often difficult unless there is clinical evidence of local inflammation around the insertion site. Blood cultures must be done. Refer to the 2009 Update by the Infectious Diseases Society of America paper by Mermel et. al.[3] (the "Diagnosis" section and Table 5) for an extensive discussion about how to obtain an accurate blood culture.

Data Supplement #8: Suggested Future Research Directions

1. Conduct research on pharmaco-economic issues related to the use of antibiotic and anticoagulant impregnated CVCs.

2. Conduct trials to determine the incidence and management of asymptomatic CVC-related thrombosis and small peri-catheter clots detected by imaging studies in otherwise asymptomatic patients.

3. Research the importance of testing for thrombophlilia and inherited disorders such as Factor V Leiden in patients who experience thrombosis.

4. Conduct descriptive research on the use of different types of CVC in actual practice – Which cancers? Which treatment regimens?

5. Conduct research on the hematologic parameters (platelet count, coagulation assays) needed at the time of catheter insertion.

References

1. O'Grady NP, Alexander M, Burns LA, et al: Guidelines for the prevention of intravascular catheter-related infections. Clin Infect Dis 52:e162-93, 2011
2. Mermel LA, Allon M, Bouza E, et al: Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 Update by the Infectious Diseases Society of America. Clin Infect Dis 49:1-45, 2009
3. Mermel LA, Farr BM, Sherertz RJ, et al: Guidelines for the management of intravascular catheter-related infections. J Intraven Nurs 24:180-205, 2001