Verantwoording literatuuronderzoek

Module Meermalig gebruik van parenterale medicatie

Inhoudsopgave

Uitgangsvraag
Wat is de plaats van het meermalig gebruik van medicatie in flacons bestemd voor eenmalig gebruik?

Methode
Onderzoeksvraag
A systematic review of the literature was performed to answer the following question:
What is the effect of using single-use parenteral medication as multiple-use medication on the prevalence of healthcare related infections and contamination of the product?

P	Single-dose vials
I	Multiple-use
C	Single-use
O	Healthcare related infections or contamination of the product

Relevant outcome measures
The guideline development group considered healthcare related infections and contamination of the product as critical outcome measures for decision making.

A priori, the working group did not define the health care related infection and contamination but used the definitions used in the studies.

The working group defined a 25% difference for dichotomous outcomes (RR < 0.8 or > 1.25), and 10% for continuous outcomes as a minimal clinically (patient) important difference.

Search and select (Methods)
The databases Medline (via OVID), Embase (via embase.com) and CINAHL were searched with relevant search terms until 1 December 2022. The detailed search strategy is available upon reasonable request via info@SRI-richtlijnen.nl. The systematic literature search resulted in 304 hits. Studies were selected based on the following criteria: systematic reviews, randomized controlled trials, or observational studies answering the research question. Forty-three studies were initially selected based on title and abstract screening. After reading the full text, 41 studies were excluded (see the table with reasons for exclusion), and 2 studies were included.Results
Three studies were included in the analysis of the literature, two for PICO-1 and one for PICO-2. Important study characteristics and results are summarised in the evidence tables. The assessment of the risk of bias is summarised in the Risk of bias tables.

Results
Two studies were included in the analysis of the literature (Das, 2015; Orneck, 2008). Important study characteristics and results are summarized in the evidence tables. The assessment of the risk of bias is summarized in the risk of bias tables.

Summary of literature

Description of studies

Das et al. (2015) conducted an observational study determining the stability, sterility, and safety of bevacizumab multiple dosing from a single vial without prior aliquoting (Das, Volety et al. 2015). Six vials of bevacizumab used on multiple patients on a single day and stored thereafter at 4°C in sterile condition for variable length of time were included as the test vials for all the laboratory studies. One new bevacizumab vial was used as a control. The six bevacizumab test vials were stored after a single day use for 1, 1.5, 3, 3.5, 5.5 and 6 months. Each vial was used on an average for 11 patients on a single day within 4 hours. All intravitreal bevacizumab were given in the operating room under strict aseptic conditions. At the end of all scheduled intravitreal procedures of the day, the vial was packed in a sterile pouch and left in the refrigerator at 4°C. Fifty microliter of bevacizumab from each bottle was withdrawn aseptically and inoculated in four media (5% sheep blood agar, brain heart infusion broth, thioglycolate broth and Sabouraud dextrose agar) and incubated for 7 days.

Following the in vitro results, the institute used single-dose bevacizumab vials for multiple injections for one week in 221 consecutive patients after obtaining written and informed consent. A new vial of bevacizumab was opened on every first working day of the week (Monday) and used till the last working day (Saturday) of the same week. All procedures were done in the operating room under sterile conditions.

Orneck and colleagues conducted a prospective observational study evaluating the sterility of bevacizumab when used as multiple doses from a single-use vial (Ornek, Karahan et al. 2008). Four groups of vials were used to simulate the storage and use conditions for bevacizumab. Each group contained 11 doses of 0.2 mL of bevacizumab. In group A, each syringe was packed in a sterile drape and stored in a sterile stainless-steel container. In group B, all syringes were kept in the same sterile stainless-steel container covered with a drape. In group C, all syringes were stored in one nonsterile stainless-steel container. In group D, the material was kept in the vial; each day, a single dose was drawn up with a sterile needle. All samples were initially drawn up from the same 16 mL vial, using an 18-gauge needle, in the operating room, under sterile conditions, by the principal investigator, and were transferred into 1 mL tuberculin syringes. Each vial was refrigerated at 4°C for 2 weeks until it was used again. Each group contained 11 doses of bevacizumab 0.2 mL. In total, 44 syringes were prepared for microbial examination. Each day for 10 days, one sample from each group was cultured once at 37°C; one sample from each group was left for 15 days. MacConkey agar, blood agar, thioglycollate broth, and Sabouraud medium were used to assess bacterial and fungal growth. Fifty microliters of material were inoculated directly into each plate. All media except Sabouraud agar plates were incubated at 37°C for 48 hours and checked for microbial growth after 24 and 48 hours. The Sabouraud agar plates were incubated at 30°C for up to 7 days and evaluated for growth each day. Significant growth was considered to be a growth on the main inoculation site. All of the culturing events were done by the same microbiologist.

Results

Healthcare related infections

Das et al. gave a total of 973 injections in 221 consecutive patients (average 4.4 injections per patient). There was no infection or inflammation noted in any of these eyes at day 1 and on subsequent visits when bevacizumab was stored at 4°C and used for one week (Das, Volety et al. 2015).

Contamination of the product

Das et al. found that all samples (6 samples stored for 1, 1.5, 3, 3.5, 5.5 and 6 months and 1 control) were negative for bacteria and fungi in culture after 7 days of incubation (Das, Volety et al. 2015).

Orneck and colleagues found that all samples were negative for bacterial growth at 24 and 48 hours. The Sabouraud agar analysis indicated no growth of any fungal organism from the contents of the 44 tested syringes for a period of 7 days. There were no differences between groups A, B, C and D (Ornek, Karahan et al. 2008).

Level of evidence of the literature

The level of evidence of the included studies was not assessed using GRADE(Grading Recommendations Assessment, Development and Evaluation) methodology, because of the absence of comparative data on contamination between single use and multiple use of single-dose parenteral medication.

Conclusies

Healthcare related infections

No GRADE	Because of the absence of comparative data, no conclusions could be drawn about the effect of using single-dose vials as multi-dose vials on the prevalence of healthcare related infections. *Source:* Das et al. (Das, Volety et al. 2015).

Contamination of the product

No GRADE	Because of the absence of comparative data, no conclusions could be drawn about the effect of using single-dose vials as multi-dose vials with regard to the contamination of medication.

Referenties

Bennet SN, McNeil MM, Bland LA, Arduino MJ, Villarino ME, Perrotta DM, Burwen DR, Welbel SF, Pegues DA, Stroud L, Zeitz PS, Jarvis WR. Postoperative infections traced to contamination of an intravenous anesthetic propofol. N Engl J Med 1995 July;333:147-154.

Cohen AL, Ridpath A, Noble-Wang J, Jensen B, Peterson AM, Arduino M, Jernigan D, Srinivasan A. Outbreak of Serratia marcescens Bloodstream and Central Nervous System Infections after interventional pain management procedures. Clin J Pain 2008 June;24(5):374-380.

Das T, Volety S, Ahsan SM, Thakur AK, Sharma S, Padhi TR, Basu S, Rao ChM. Safety, sterility and stability of direct-from-vial multiple dosing intravitreal injection of bevacizumab. Clin Exp Ophthalmol. 2015 Jul;43(5):466-73. doi: 10.1111/ceo.12489. Epub 2015 Apr 14. PMID: 25545882.

De Smet B, Veng C, Kruy L, Kham C, van Griensven J, Peeters C, Ieng S, Phe T, Vlieghe E, Vandamme P, Jacobs J. Outbreak of Burkholderia cepacia bloodstream infections traced to the use of Ringer lactate solution as multiple-dose vial for catheter flushing, Phnom Penh, Cambodia. Clin Microbiol Infect. 2013 Sep;19(9):832-7. doi: 10.1111/1469-0691.12047. Epub 2012 Nov 23. PMID: 23173820.

Dolan SA, Arias KM, Felizardo G, Barnes S, Kraska S, Patrick M, Bumsted A. APIC position paper: Safe injection, infusion, and medication vial practices in health care. Am J Infect Control. 2016 Jul 1;44(7):750-7. doi: 10.1016/j.ajic.2016.02.033. Epub 2016 May 13. PMID: 27184207.

Fischer GE, Schaefer MK, Labus BJ, Sands L, Rowley P, Azzam IA, Armour P, Khudyakov YE, Lin Y, Xia G, Patel PR, Perz JF, Homberg SD. Hepatitis C Virus Infections from Unsafe Injection Practices at an Endoscopy Clinic in Las Vegas, Nevada, 2007–2008. CID. 2010 Aug;51: 267-273.

Groshskopf LA, Roth VR, Feikin DR, Arduino MJ, Carson LA, Tokars JI, Holt SC, Jensen BJ, Hoffman RE, Jarvis WJ. Serratia liquefaciens Bloodstream Infections from contamination of epoietin alfa at a hemodialysis center. N Engl J Med 2001 May(20);344:1491-97. 147-154.

Gutelius B, Perz JF, Parker MM, Hallack R, Stricof R, Clement EJ, lin Y, Xia G, Punsalang A, Eramo A, Layton M, Balter S. Multiple Clusters of Hepatitis Virus Infections Associated With Anesthesia for Outpatient Endoscopy Procedures. Gastroenterology 2010;139:163–170.

Khan P, Khan L, Mondal P. Cluster endophthalmitis following multiple intravitreal bevacizumab injections from a single use vial. Indian J Ophthalmol. 2016 Sep;64(9):694-696. doi: 10.4103/0301-4738.99855. PMID: 27853027; PMCID: PMC5151169.

Manchikanti L, Malla Y, Wargo BW, Fellows B. Infection control practices (safe injection and medication vial utilization) for interventional techniques: are they based on relative risk management or evidence? Pain Physician. 2011 Sep-Oct;14(5):425-34. PMID: 21927046.

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Muller AE, Huisman I, Roos PJ, Rietveld AP, Klein J, harbers JBM, Dorresteijn JJ, van Steenbergen JE, Vos MC. Outbreak of severe sepsis due to contaminated propofol: lessons to learn. Journal of Hospital infection 2010;76:225-230.

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Ornek K, Karahan ZC, Ergin A, Tekeli A, Tekeli O. Bevacizumab sterility in multiple doses from a single-use vial. Ann Pharmacother. 2008 Oct;42(10):1425-8. doi: 10.1345/aph.1L270. Epub 2008 Sep 2. PMID: 18765834.

Ripoll Gallardo A, Meneghetti G, Ragazzoni L, Kroumova V, Ferrante D, Ingrassia PL, Ruzza P, Dell'Era A, Boniolo E, Koraqe G, Faggiano F, Della Corte F. Multiple withdrawals from single-use vials: a study on sterility. Int J Pharm. 2015 May 15;485(1-2):160-3. doi: 10.1016/j.ijpharm.2015.03.010. Epub 2015 Mar 9. PMID: 25769293.

Siegel JD, Rhinehart E, Jackson M, Chiarello L; Health Care Infection Control Practices Advisory Committee. 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Health Care Settings. Am J Infect Control. 2007 Dec;35(10 Suppl 2):S65-164. doi: 10.1016/j.ajic.2007.10.007. PMID: 18068815; PMCID: PMC7119119.

Zorrilla-Vaca A, Arevalo JJ, Escandón-Vargas KE, Soltanifar D, Mirski MA. Infectious disease risk associated with contaminated propofol anesthesia, 1989-2014. Emerging Infectious Diseases 2016 June;22(6):981-992.

Evidence table

Study reference	Study characteristics	Patient characteristics	Intervention	Control	Follow-up	Outcome measures and effect size	Comments
Das, 2015	Type of study: observational study Setting and country: laboratory, USA Funding and conflicts of interest: no conflicts of interest.	Not applicable	Six vials of bevacizumab used on multiple patients on a single day and stored thereafter at 4°C in sterile condition for variable length of time were included as the test vials for all the laboratory studies. The six bevacizumab test vials were stored after a single day use. Each vial was used on an average for 11 patients on a single day within 4 hours.	One new bevacizumab vial was used as a control.	1, 1.5, 3, 3.5, 5.5 and 6 months	Healthcare related infections a total of 973 injections in 221 consecutive patients (average 4.4 injections per patient). There was no infection or inflammation noted in any of these eyes at day 1 and on subsequent visits when bevacizumab was stored at 4°C and used for one week. Contamination of the product	

			At the end of all scheduled intravitreal procedures of the day, the vial was packed in a sterile pouch and left in the refrigerator at 4°C. Fifty microliter of bevacizumab from each bottle was withdrawn aseptically and inoculated in four media (5% sheep blood agar, brain heart infusion broth, thioglycolate broth and Sabouraud dextrose agar) and incubated for 7 days. Following the in vitro results, the institute used single-dose bevacizumab vials for multiple injections for one week in 221 consecutive patients after obtaining written and informed consent. A new vial of bevacizumab was opened on every first working day of the week (Monday) and used till the last working day (Saturday) of the same week.			All samples (6 samples stored for 1, 1.5, 3, 3.5, 5.5 and 6 months and 1 control) were negative for bacteria and fungi in culture after 7 days of incubation.	
Ornec k, 2008	Type of study: observ	Not applicable	Four groups of vials were used to simulate the storage and use	Not applicable	7 days	Contamination of the product	

	ational study Setting and country: laboratory, USA Funding and conflicts of interest: no conflicts of interest.		conditions for bevacizumab. Each group contained 11 doses of 0.2 mL of bevacizumab. In group A, each syringe was packed in a sterile drape and stored in a sterile stainless-steel container. In group B, all syringes were kept in the same sterile stainless-steel container covered with a drape. In group C, all syringes were stored in one nonsterile stainless-steel container. In group D, the material was kept in the vial; each day, a single dose was drawn up with a sterile needle. All samples were initially drawn up from the same 16 mL vial, using an 18-gauge needle, in the operating room, under sterile conditions, by the principal investigator, and were transferred into 1 mL tuberculin syringes. Each vial was refrigerated at 4°C for 2 weeks until it was used again. Each group contained 11 doses of			all samples were negative for bacterial growth at 24 and 48 hours. The Sabouraud agar analysis indicated no growth of any fungal organism from the contents of the 44 tested syringes for a period of 7 days. There were no differences between groups A, B, C and D (Ornek, 2008).	

			bevacizumab 0.2 mL. In total, 44 syringes were prepared for microbial examination. Each day for 10 days, one sample from each group was cultured once at 37°C; one sample from each group was left for 15 days. MacConkey agar, blood agar, thioglycollate broth, and Sabouraud medium were used to assess bacterial and fungal growth. Fifty microliters of material were inoculated directly into each plate. All media except Sabouraud agar plates were incubated at 37°C for 48 hours and checked for microbial growth after 24 and 48 hours. The Sabouraud agar plates were incubated at 30°C for up to 7 days and evaluated for growth each day				

Exclusietabel

Reference	Reason for exclusion
CDC (Centers for Disease Control and Prevention) grand rounds: preventing unsafe injection practices in the U.S. health-care system. MMWR: Morbidity & Mortality Weekly Report. 2013; 62 (21) :423-425	Not a comparative study

Focus on five. Switching to single-dose containers: moving away from multiple-dose vials. Joint Commission Perspectives on Patient Safety. 2006; 6 (1) :10-10	Not available
TJC raises an alarm about misuse of vials. Nursing. 2014; 44 (9) :27-27	Not available
Alam, Murad and Yoo, Simon S. and Wrone, David A. and White, Lucile E. and Kim, John Y. S. Sterility assessment of multiple use botulinum A exotoxin vials: a prospective simulation. Journal of the American Academy of Dermatology. 2006; 55 (2) :272-5	Not a comparative study
Angrup, A. and Krishnamoorthi, S. and Biswal, M. and Gautam, V. and Ray, P. and Agarwal, A. and Dogra, M. R. and Singh, R. and Katoch, D. and Gupta, V. and Angrup, Archana and Krishnamoorthi, Sivanantham and Biswal, Manisha and Gautam, Vikas and Ray, Pallab and Agarwal, Aniruddha and Singh, Ramandeep and Katoch, Deeksha and Gupta, Vishali Utility of MALDI-TOF mass spectrometry in an outbreak investigation of acute endophthalmitis following intravitreal injection. Journal of Hospital Infection. 2018; 100 (4) :e253-e256	Wrong I/C (does not compare multiple use of SUV vs single use)
Baniasadi, Shadi and Dorudinia, Atosa and Mobarhan, Mandana and Karimi Gamishan, Masoumeh and Fahimi, Fanak Microbial contamination of single- and multiple-dose vials after opening in a pulmonary teaching hospital. The Brazilian journal of infectious diseases : an official publication of the Brazilian Society of Infectious Diseases. 2013; 17 (1) :69-73	Wrong I/C (does not compare multiple use of SUV vs single use)
Barrow, Emily M. and Rosen, Clark A. and Hapner, Edie R. and Smith, Sarah and Hatcher, Jeanne L. and Simpson, Blake and Johns, Michael M., 3rd Safety and efficacy of multiuse botulinum toxin vials for intralaryngeal injection. The Laryngoscope. 2015; 125 (5) :1149-54	Not a comparative study on single/multi use
Bjornson, Lindsay and Bucevska, Marija and Tilley, Peter and Verchere, Cynthia Is it safe to re-access sodium bicarbonate bottles for use in minor surgery?. Journal of pediatric surgery. 2018; 53 (11) :2290-2293	Wrong I/C (does not compare multiple use of SUV vs single use)
Buck, D. and Subramanyam, R. and Varughese, A. A quality improvement project to reduce the intraoperative use of single-dose fentanyl vials across multiple patients in a pediatric institution. Paediatric Anaesthesia. 2016; 26 (1) :92-101	Study on implementation of measures
Carlson, Alexandra R. and Nixon, Emma and Jacob, Megan E. and Messenger, Kristen M. Sterility and	Veterinary study

concentration of liposomal bupivacaine single-use vial when used in a multiple-dose manner. Veterinary surgery: VS. 2020; 49 (4) :772-777	
De Giorgi, I. and Sadeghipour, F. and Favet, J. and Bonnabry, P. Sterility validity period of vials after multiple sampling under vertical laminar airflow hood. Journal of oncology pharmacy practice: official publication of the International Society of Oncology Pharmacy Practitioners. 2005; 11 (2) :57-62	Wrong I/C (does not compare multiple use of SUV vs single use)
De Smet, B. and Veng, C. and Kruy, L. and Kham, C. and van Griensven, J. and Peeters, C. and Ieng, S. and Phe, T. and Vlieghe, E. and Vandamme, P. and Jacobs, J. Outbreak of Burkholderia cepacia bloodstream infections traced to the use of Ringer lactate solution as multiple-dose vial for catheter flushing, Phnom Penh, Cambodia. Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases. 2013; 19 (9) :832-7	Not a comparative study on single/multi use
Eaton, Tim, et al. "Investigation of the transfer of septum microbial contamination by hypodermic needles." European Journal of Parenteral and Pharmaceutical Sciences 25.1 (2020).	Wrong I/C (does not compare multiple use of SUV vs single use)
Falavarjani, Khalil Ghasemi and Modarres, Mehdi and Hashemi, Masih and Parvaresh, Mohammad M. and Naseripour, Masood and Zare-Moghaddam, Abbas and Nekoozadeh, Shahbaz Incidence of acute endophthalmitis after intravitreal bevacizumab injection in a single clinical center. Retina (Philadelphia, Pa.). 2013; 33 (5) :971-4	Wrong I/C (does not compare multiple use of SUV vs single use)
Gerrard, C. and Moore, S. and Ryan, B. Biological tissue adhesive for multiple use in the accident and emergency department. Journal of accident & emergency medicine. 2000; 17 (5) :341-3	Wrong P
Khalili, Hossein and Sheikhbabayi, Mehdi and Samadi, Nasser and Jamalifar, Hossein and Dalili, Dina and Samadi, Nasrin Bacterial contamination of single- and multiple-dose vials after multiple use and intravenous admixtures in three different hospitals in iran. Iranian journal of pharmaceutical research: IJPR. 2013; 12 (1) :205-9	Wrong I/C (does not compare multiple use of SUV vs single use)
Khan, Perwez and Khan, Lubna and Mondal, Prosenjit Cluster endophthalmitis following multiple intravitreal bevacizumab injections from a single use vial. Indian Journal of Ophthalmology. 2016; 64 (9) :694-696	Not a comparative study on single/multi use

King, Cecil A. and Ogg, Mary Safe injection practices for administration of propofol. AORN journal. 2012; 95 (3) :365-72	Not a comparative study
Lin, Sandra Y. and Lay, P. Chase and Hughes, Larry F. and Bass, Richard The safety of multi-dose vials in allergy immunotherapy. Otolaryngology--head and neck surgery: official journal of American Academy of Otolaryngology-Head and Neck Surgery. 2008; 139 (2) :195-7	Focussess on multi-dose vials
Liu, D. and Zhang, L. P. and Huang, S. F. and Wang, Z. and Chen, P. and Wang, H. and Cheng, Y. Outbreak of Serratia marcescens infection due to contamination of multiple-dose vial of heparin-saline solution used to flush deep venous catheters or peripheral trocars. Journal of Hospital Infection. 2011; 77 (2) :175-176	Letter to the editor
Longfield, R. and Longfield, J. and Smith, L. P. and Hyams, K. C. and Strohmer, M. E. Multidose medication vial sterility: an in-use study and a review of the literature. Infection control : IC(Intensive care). 1984; 5 (4) :165-9	Wrong I/C (does not compare multiple use of SUV vs single use)
Manchikanti, L. and Malla, Y. and Wargo, B. W. and Fellows, B. Infection control practices (safe injection and medication vial utilization) for interventional techniques: Are they based on relative risk management or evidence?. Pain Physician. 2011; 14 (5) :425-434	Wrong I/C (does not compare multiple use of SUV vs single use)
Manchikanti, Laxmaiah and Falco, Frank J. E. and Benyamin, Ramsin M. and Caraway, David L. and Helm Ii, Standiford and Wargo, Bradley W. and Hansen, Hans and Parr, Allan T. and Singh, Vijay and Hirsch, Joshua A. Assessment of infection control practices for interventional techniques: a best evidence synthesis of safe injection practices and use of single-dose medication vials. Pain physician. 2012; 15 (5) :E573-614	Systematic review without meta-analysis
Marshall, K. A. and Brooks, A. C. and Hammac, G. K. and Thomovsky, E. J. and Johnson, P. A. Prevalence of bacterial contamination in 50% dextrose vials in varying storage conditions after multiple punctures. Journal of Small Animal Practice. 2018; 59 (12) :758-762	Veterinary study
Miller, David C. and Smith, Clark The Safe Use of Multidose and Single-Dose Vials. Pain Medicine. 2019; 20 (5) :1047-1048	Only recommendations, not a comparative study
Mishra, Chitaranjan and Lalitha, Prajna and Rameshkumar, Gunasekaran and Agrawal, Rupesh and	Not a comparative study on single/multi use

Balne, Praveen Kumar and Iswarya, Mani and Kannan, Naresh Babu and Ramasamy, Kim Incidence of Endophthalmitis after Intravitreal Injections: Risk Factors, Microbiology Profile, and Clinical Outcomes. Ocular immunology and inflammation. 2018; 26 (4) :559-568	
Mora, J. S. and Cevallos, V. and Whitcher, J. P. Risk of microbial contamination with multiple use of 5-fluorouracil vials. Journal of glaucoma. 1996; 5 (6) :371-4	Wrong I/C (does not compare multiple use of SUV vs single use)
Motamedifar, Mohammad and Askarian, Mehrdad The prevalence of multidose vial contamination by aerobic bacteria in a major teaching hospital, Shiraz, Iran, 2006. American journal of infection control. 2009; 37 (9) :773-7	Focussess on multi-dose vials
Muller, A. E. and Huisman, I. and Roos, P. J. and Rietveld, A. P. and Klein, J. and Harbers, J. B. and Dorresteijn, J. J. and van Steenbergen, J. E. and Vos, M. C. Outbreak of severe sepsis due to contaminated propofol: lessons to learn. Journal of Hospital Infection. 2010; 76 (3) :225-230	Not a comparative study on single/multi use
Nath, P. and Freiler, J. and Gomez, R. A. Safety of multidose immunotherapy vials after routine use. Journal of Allergy and Clinical Immunology: In Practice. 2018; 6 (6) :2110-2111	Letter to the editor
Neumann, M. E. Multi-dose drawing from single vials is safe, saves Medicare money, NRAA says. Nephrology News & Issues. 2008; 22 (11) :8-8	Not available
Nogler-Semenitz, Elisabeth and Lass-Florl, Cornelia and Nogler, Michael and Speer, Gerhard and Dierich, Manfred P. Bacterial contamination of solutions for parenteral administration for single- and multiple-dose vials after multiple use in the hospital. Wiener medizinische Wochenschrift (1946). 2007; 157 (15) :398-401	Wrong I/C (does not compare multiple use of SUV vs single use)
Pegues, D. A. and Shireley, L. A. and Riddle, C. F. and Anderson, R. L. and Vess, R. W. and Hill, B. C. and Jarvis, W. R. Serratia marcescens surgical wound infection following breast reconstruction. The American journal of medicine. 1991; 91 (3) :173S-178S	Wrong I/C (does not compare multiple use of SUV vs single use), not a comparative study
Perez, F. and Deshpande, A. and Kundrapu, S. and Hujer, A. M. and Bonomo, R. A. and Donskey, C. J. Pseudo-outbreak of Klebsiella oxytoca spontaneous bacterial peritonitis attributed to contamination of multidose vials of culture medium	Wrong I/C (does not compare multiple use of SUV vs single use)

supplement. Infection Control and Hospital Epidemiology. 2014; 35 (2) :139-143	
Reiter, P. D. and Sims, C. and Harmes, L. and Paisley, J. and Rosenberg, A. A. and Valuck, R. J. Calfactant sterility in multiple doses from single-use vials. Annals of Pharmacotherapy. 2003; 37 (9) :1219-1223	Wrong I/C (does not compare multiple use of SUV vs single use)
Shortliffe, Edward H. and Lyman, Gary H. and Amankwah, Francis K. Medications in Single-Dose Vials and Implications of Discarded Injectable Drugs: A National Academies Report. JAMA: Journal of the American Medical Association. 2021; 325 (15) :1507-1508	Viewpoint, not a comparative study
Smith, Timothy C. and Lee, Lawrence R. Rate of microbiological contamination in vials of bevacizumab used for multiple intravitreal injections. Retinal cases & brief reports. 2008; 2 (2) :133-5	Not a comparative study
Whitehead, Michelle C. and Vanetten, Chelsey L. and Jacob, Megan E. and Harrison, Tara M. Microbial integrity of preservative-free alfaxalone in a multiple-use system for two storage conditions and three handling techniques. American journal of veterinary research. 2018; 79 (7) :704-710	Veterinary study
Wong, Melissa R. and Del Rosso, Paula and Heine, Lisa and Volpe, Veronica and Lee, Lillian and Kornblum, John and Lin, Ying and Layton, Marcelle and Weiss, Don An outbreak of Klebsiella pneumoniae and Enterobacter aerogenes bacteremia after interventional pain management procedures, New York City, 2008. Regional anesthesia and pain medicine. 2010; 35 (6) :496-9	Not a comparative study on single/multi use