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Health Policy Review

Assessment of Infection Control Practices for Interventional Techniques: A Best Evidence Synthesis of Safe Injection Practices and Use of Single-Dose Medication Vials

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Background: It is universally accepted that transmission of bloodborne pathogens during health care procedures continues to occur because of the use of unsafe and improper injection, infusion, and medication administration practices by health care professionals in various clinical settings. This resulted in development of multiple guidelines based on case reports; however, these case reports are confounded by multiple factors without causal relationship to a single factor. Even then, single-dose vials used for multiple patients have been singled out and became the focus of infection control policies resulting in inordinate expenses for practices without improving patient safety. The cost of implementation of single dose vial policy in Interventional Pain Management for drugs alone may cost $750 million, whereas with single use radional gloves may exceed $1 billion per year.

Study Design: Best evidence synthesis.

Objective: To critically appraise and synthesize the literature on infection control practices for interventional techniques, including safe injection and medication vial utilization.

Methods: The available literature on infection control practices was reviewed. Due to the nature of the studies involved, with the majority being case reports, and a few prospective evaluations, quality assessment and clinical relevance criteria were not applied.

Data sources included relevant literature identified through searches of PubMed and EMBASE from 1966 through June 2012, literature from the Centers for Disease Control and Prevention (CDC), the U.S. Food and Drug Administration (FDA), and manual searches of the bibliographies of known primary and review articles.

Outcome Measures: The primary outcome measure was correlating infection to a breach of standards in infection control practices. The secondary objective was to assess the contribution of single-dose vials independently for infection.

Results: A total of 60 reports met inclusion criteria, with 16 reports related to pain management and other procedures, of which 9 reports were attributed to issues related to interventional techniques.

Based on an estimated 37 infections occurring during 200 million interventional techniques from 1997 through 2011, the rate of infection is speculated to be one infection for every 5 million interventional pain management procedures. However, if 10 times more infections are estimated, the infection rate appears to be one infection for every 500,000 interventional pain management procedures.

The evidence is good for infection related to a breach of infection control practices. There is good evidence that contamination of multi-dose or single-dose vials can contribute to infection.

There was poor evidence that the use of single-dose vials on multiple patients with appropriate infection control practices cause infection in interventional pain management.

Limitations: The limitations of this comprehensive best evidence synthesis include the paucity of literature and dependence of governmental agencies on their literature without applying Institute of Medicine (IOM) criteria for guideline synthesis.

Conclusion: There is good evidence that any breach of sterile practice may result in serious and life threatening infections. There is poor evidence for single-dose vials as a sole factor causing infections when used in multiple patients in interventional pain management settings.

Key words: Infection, safe injection practices, single-dose vials, multi-dose vials, surgical face masks, relative risk, interventional pain management, interventional techniques, sterile precautions

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Of the numerous regulations in the health care arena, infection control practices, including safe injection and medication vial utilization, has become a burdensome and expensive regulations for interventional practices and facilities in 2012. The regulation is hampered by a lack of evidence, lack of evidence-based guidelines, and the inability of the Centers for Disease Control and Prevention (CDC) to consider cost-effective safety measures (1-46). It is universally accepted that the transmission of bloodborne pathogens during health care procedures continues to occur in various clinical settings due to the use of unsafe and improper injection, infusion, and medication administration by health care professionals (28,29,32,42,47-58). Consequently, multiple guidelines and regulations have been developed and imposed (14-33,42,45,46). Unfortunately, these guidelines are not based on high quality evidence or relative risk reduction. These issues once again confirm that the most entrenched conflict of interest in medicine is a disinclination to reverse a previous opinion (59).

In a review of unsafe injections in the developing world and transmission of bloodborne pathogens (58), it was illustrated that unsafe injections accounted for a significant proportion of all new Hepatitis B and C infections. This review showed that each person in the developing world received 1.5 injections per year on average by 1999. However, institutionalized children and adults who are ill or hospitalized, including those infected with human immunodeficiency virus (HIV), were often exposed to 10 to 100 times as many injections. On average, 95% of all injections were therapeutic, the majority of which were judged to be unnecessary, with at least 50% of the injections being unsafe in 14 of 19 countries for which data were available, excluding the United States. In this review, it was also shown that 5 studies attributed 20% to 80% of all new Hepatitis B infections to unsafe injections, while 3 implicated unsafe injections as a major mode of transmission of Hepatitis C. This review did not consider the use of single-dose vials for multiple patients. An unsafe injection is defined as one in which the syringe, needle, or both, have been reused without sterilization. They also considered an unnecessary injection as one where oral alternatives were available, where the injected substance was inappropriate or harmful, or where the symptoms or diagnosis did not warrant treatment by injection. Overall, multiple studies were shown linking unsafe injections to the transmission of bloodborne pathogens in developing countries (60-95). The CDC has published multiple reviews; however, they were all based on case reports (31).

Recently, the Government Accountability Office (GAO) has undertaken an evaluation of unsafe injection practices (32). The GAO examined available information on the extent and cost of bloodborne pathogen outbreaks in ambulatory care settings related to unsafe injection practices, changes since 2009 in federal oversight to prevent unsafe injection practices that may lead to bloodborne pathogen outbreaks in selected types of ambulatory case settings, and other federal efforts or plans to improve current injection safety practices in order to prevent bloodborne pathogen outbreaks. They examined the changes in federal oversight designed to prevent unsafe injection practices in selected types of ambulatory case settings since 2009, the year of the last report on health care acquired infections emerged.

The GAO also reviewed the Centers for Medicare and Medicaid Services' (CMS) policies and procedures, as well as documentation from accrediting organizations that survey facilities, to ensure that they meet CMS health and safety standards. They also examined federal oversight of injection safety in terms of the scope and content of CMS health and safety standards, and the processes that CMS used to ensure compliance among the facilities to which those standards apply. The GAO included those types of ambulatory care settings in which the CDC has identified one or more bloodborne pathogen outbreaks from 2001 through 2011, specifically ambulatory surgery centers (ASCs) and physician

offices. The GAO study results showed that data on the extent of bloodborne pathogen outbreaks related to unsafe injection practices in ambulatory care settings were limited and that the full extent of such outbreaks would most likely be underestimated. Additionally, while comprehensive data on the cost of bloodborne pathogen outbreaks to the health care system do not exist, the CDC and other officials believe these costs may be substantial for those affected by such outbreaks, including individuals, state and local health departments, and clinicians and health care facilities (42).

According to CDC records, as shown in the GAO report (32), from 2001 through 2011, there were 18 known outbreaks – episodes of infection transmission where 2 or more patients became infected – of viral hepatitis associated with unsafe injection practices at ASCs and other ambulatory care settings in the United States. In these known ambulatory care setting outbreaks, nearly 100,000 individuals were notified to seek testing for possible exposure to viral hepatitis and HIV, and of these, 358 were infected with viral hepatitis (23,31,32). Furthermore, over 17,000 other patients were also notified of possible exposure to bloodborne pathogens because of the unsafe injection practices in ambulatory care settings outside of these 18 recognized outbreaks. However, these notification events were not identified as outbreaks because they did not meet the CDC's definition of bloodborne pathogen outbreak, which is an episode of transmission where 2 or more patients become infected and where these infections could be epidemiologically linked to a specific health care facility or clinician (32).

The GAO recommended that the Department of Health and Human Services (HHS) resume collecting data on unsafe injection practices that will permit continued monitoring of such practices, that HHS use those data for continued monitoring of ASCs, and that they strengthen the targeting efforts of the sole campaign for health care settings not overseen by CMS. HHS agreed with the GAO's recommendations (32).

In a review published in 2009, Thompson et al (22) found 33 outbreaks in non-hospital health care settings in the past decade with 12 in outpatient clinics, 6 in hemodialysis centers, and 15 in long-term care facilities, resulting in 448 persons acquiring a HBV or HCV infection. In each setting, the putative mechanism of infection was patient-to-patient transmission through the failure of health care personnel to adhere to fundamental principles of infection control and aseptic techniques, including the reuse of syringes or lancing devices. They recommended a comprehensive approach involving better viral hepatitis surveillance and case investigation, health care provider education and training, professional oversight, licensing, and public awareness. These were considered essential to ensure that patients were always afforded basic levels of protection against viral hepatitis transmission.

Guh et al (48) examined records of events that involved communications to groups of patients, conducted from 2001 through 2011, resulting in bloodborne pathogen testing stemming from potential exposures to unsafe injection practices. The authors identified 35 patient notification events related to unsafe injection practices in at least 17 states resulting in an estimated total of 130,198 patients notified. Among the identified notification events, 83% involved outpatient settings and 74% occurred since 2007, including the 4 largest events (greater than 5,000 patients per event). The primary breach identified in 44%, or more than 16 events, was syringe reuse to access shared medications either from a single-dose or multidose vials. Twenty-two, or 63% of notifications stemmed from the identification of viral hepatitis transmission. Thirteen, or 37% of notifications were prompted by the discovery of unsafe injection practices, absent evidence of bloodborne pathogen transmission. The authors concluded that unsafe injection practices represent a form of medical error that have manifested as large-scale adverse events, affecting thousands of patients in a wide variety of health care settings. The authors also suggested that increased oversight and attention to basic infection control are needed to maintain patient safety, along with research to identify best practices for figuring and managing patient notifications.

In a randomized trial, Anthony et al (35) evaluated an evidence-based bundle for preventing surgical site infection. In this evaluation, patients received either a combination of 5 evidence-based practices (extended arm) or were treated according to their current practice (standard arm). The interventions in the extended arm included 1) omission of mechanical bowel preparation; 2) preoperative and intraoperative warming; 3) supplemental oxygen during and immediately after surgery; 4) intraoperative intravenous fluid restriction; and 5) use of a surgical wound protector. The overall rate of surgical site infection was 45% in the extended arm of the study and 24% in the standard arm ($P = .003$). A multivariate analysis of this suggested that allocation to the extended arm of the trial conferred a

2.49-fold risk independent of other factors traditionally associated with surgical site infections. The authors concluded that an evidence-based intervention bundle did not reduce surgical site infections. The bundling of interventions, even when the constituent interventions have been individually tested, does not have a predictable effect on outcome.

In a study of interventions aimed at reducing the transmission of resistant bacteria in intensive care (76), expanded barrier precautions or interventions, when compared to the existing practice (control), showed the interventions to be ineffective in reducing the transmission of methicillin-resistant staphylococcus aureus (MRSA) and vancomycin-resistant enterococci (VRE).

In a major study performed by Schaefer et al (43) on infection control assessment at ASCs, 68 centers were evaluated; lapses were found in 68% of them. Major issues were related to blood glucose monitoring equipment (46%), followed by reprocessing of equipment (28%), and single-dose medication vials for more than one patient (28%); however, none of these resulted in any infections.

The Association for Professionals in Infection Control and Epidemiology (APIC) position paper, which is not based on evidence, also mistakenly follows CDC guidance on safe injection practices (42). Furthermore, in an online survey of injection practices among clinicians in US health care conducted in May and June of 2010, the majority of the 5,446 eligible respondents who administer parenteral medications reported injection practices consistent with current recommendations. However, some unsafe practices were identified, with 6% sometimes or always using single-dose/single-use vials for more than one patient with 51.1% reusing a syringe to enter a multidose vial and then 6.5% saving that vial for use on another patient. In contrast, it was admitted that only 6% used single-dose/single-use vials for more than one patient. This is most likely an underestimation.

Manchikanti et al (33) assessed the rates of infection in patients undergoing interventional techniques. In approximately 3,200 patients and over 18,000 procedures performed during a 20-month period in an ASC. Simple precautions were utilized for clean procedures with the use of single-dose vials for multiple patients, while using safe injection practices, showing no evidence of infection.

Recently, the CDC proposed that single-dose vials may be divided into multi-dose vials by a compounding pharmacy (96). However, previous reports illustrate some issues related to compounding pharmacies (56,97). Given that there was not even a single report of infections with single-dose vials when appropriate precautions were taken, it may be that the CMS and CDC are suggesting that practitioners use practices which have been illustrated to cause infections replace practices which have not been shown to cause any infections.

The CDC issues recommendations for clinicians to follow in order to prevent and control health care-associated infections (HAIs). The GAO stated that the CDC issues these recommendations in the form of evidence-based guidelines and other informal communications, such as clinical reminders, which are generally recognized as authoritative interpretations of the current scientific knowledge base regarding the prevention of HAIs (31,32). Based on the GAO report, it is understood that the CDC develops these guidelines in collaboration with the Healthcare Infection Control Practices Advisory Committee (HICPAC) - a federal advisory committee that provides recommendations to the secretary of HHS and to the CDC and includes members from outside the federal government selected for their expertise on infection control (32). Representatives from CMS, the Agency for Healthcare Research and Quality (AHRQ), the Food and Drug Administration (FDA), the National Institute of Health (NIH), the Health Resources and Services Administration (HRSA), and the Department of Veterans Affairs are included.

In 2007, the CDC issued its most recent infection control guidelines outlining standard precautions, which serves as the foundation for preventing transmission of infections during patient care in all health care settings, and includes recommendations for safe injection practices (46). In May 2002, the CDC released a paper restating its position on the appropriate use of single-dose and single-use vials (31). The CDC recommends that clinicians limit the sharing of medications whenever possible. Furthermore, the CDC also recommended that in times of critical need, qualified health care personnel may repackage unopened single-dose or single-use vials for multiple patients when performed in accordance with standards in the United States pharmacopeia on sterile preparations for pharmaceutical compounding, as well as the manufacturer's recommendations for safe storage. In addition, the CDC also helps to provide assistance to state and local health departments in their investigations of pos-

sible bloodborne pathogen outbreaks resulting from unsafe injection practices, and maintains information on bloodborne pathogen outbreaks. In addition, CMS, consistent with statute, has established and overseen compliance with health and safety standards for ASCs as a condition of their participation in Medicare (45). However, not all ambulatory care settings are subject to CMS's health and safety standards. Patients may receive a wide array of services similar to those provided at ASCs, such as endoscopy and pain management services, in facilities designed as physician offices, ranging in scale from a small office facility with a single physician to a large clinic with multiple physicians and extensive medical or surgical capabilities (32).

A systematic analysis of the literature was not performed in the development of these guidelines. In contrast to the methodology standards for clinical guidelines, the guidelines were based entirely on case reports (31,32). When followed, the standards based on the Institute of Medicine (IOM) methodology result in reliable guidelines (34). Furthermore, among the studies quoted by multiple publications, all associated with the CDC (20-31,48) and the GAO (32), there were no studies causally relating infections to single-dose vials used for multiple patients with appropriate precautions. In the preparation of guidelines, statistics should not be derived from only limited and selected examples.

Thompson et al (22) published 33 outbreaks from 1998 to 2008 (24,29,48,50,51,87,89,92,93,98-114), the CDC published that 16 outbreaks occurred in patient notification events (57,77-91), and the GAO study presented results from 2001 through 2011 that presented 18 infection case reports (28,50,51,79,83,86,87,89,92,93,95,96,98-101,115-117). In contrast, Guh et al (48) reported 35 infection outbreaks occurred (28,50-52,83,84,86-89,91-93,98-100,106,115-132).

As indicated, there have been multiple variations in presenting results. For example, the GAO study did not include 11 cases included in the CDC report (57,77,78,80-82,84,85,88,90,91), Guh et al's (48) report, and Thompson et al's report (22). However, single-dose vials as a causal and sole reason for infection has not been illustrated in any of the reports. All the studies included a breach of infection practices; thus, the description of the inappropriate use of single-dose vials is appropriate for these cases. It is also possible from some of the articles that the CDC experts may be misunderstanding exactly what is involved in these issues as they note that the procedure tray did not include masks and the radiation protection gowns were not washed between cases.

The CMS and CDC issued a memorandum in June of 2012 (133,134) in reference to repackaging regulations. These regulations permit compounders to divide multidose vials into multiple single-dose vials under sterile conditions. It is interesting to note , however, that multiple infections have been reported from compounding pharmacies caused by contaminations occurring in those compounding facilities. Thus, repackaging and compounding facilities may exacerbate this issue further and increase the expense and the risk of infection, rather than decreasing it (135-147).

Thus, the recommendations for infection control which have been universally applied since January 2010 are based on weak evidence from case reports involving inaccurate and incomplete information and pure conjuncture. Multiple issues related to a sanitary environment, traffic flow, environmental conditions related to the monitoring of the airflow exchanges or infiltration systems for hospitals and ASCs, regular facility cleaning and disinfection, and routine hand washing are essential and common sense approaches. However, the regulations about safe injection practices with single-dose and multi-dose vials with one vial per patient and utilization of expensive radiation gloves for each and every procedure may be overreaching, expensive, and burdensome to the practice of medicine, specifically for closed procedures, including interventional techniques, and may ultimately result in reduced access. The cost of implementation of single dose vial policy in Interventional Pain Management for drugs alone may cost $750 million, whereas with single use radiation gloves may exceed $1 billion per year.

Consequently, we have taken this best evidence synthesis comprehensive review to evaluate the risk of infection in patients undergoing interventional techniques, utilizing single-dose vials for multiple patients.

1.0 Methods

The methodology utilized in this systematic review followed the review process derived from evidence-based systematic reviews and a meta-analysis of randomized trials and observational studies (148-157), Standards for Reporting Observational Studies (STROBE) (158), Cochrane guidelines (153,154), and quality of reporting of analysis (150,151).

1.1 Criteria for Considering Studies for This Review

1.1.1 Types of Studies

Randomized controlled trials
Non-randomized observational studies
Case reports and reviews

1.1.2 Types of Facilities

Hospital outpatient facilities, ASCs, and office practices performing interventional techniques were included.

1.1.3 Types of Interventions

All types of interventions, from simple injections to major procedures such as disc decompression and implantables, were included.

1.1.4 Types of Outcome Measures

- The primary outcome measure was correlation of infection to breach of standards of infection control practices.
- The secondary objective was to assess the contribution of single-dose vials independently for infection.

1.2 Literature Search

Searches were performed from the following sources without language restrictions:

1. PubMed from 1966
   www.ncbi.nlm.nih.gov/sites/entrez?db=pubmed
2. EMBASE from 1980
   www.embase.com
3. Cochrane Library
   www.thecochranelibrary.com/view/0/index.html
4. U.S. National Guideline Clearinghouse (NGC)
   www.guideline.gov
5. Previous systematic reviews and cross references
6. Clinical Trials
   www.clinicaltrials.gov
7. CDC
   www.cdc.gov
8. FDA
   www.fda.gov

The search period was from 1966 through June 2012.

1.3 Search Strategy

The search strategy emphasized safe injection practices, single-dose vials, multi-dose vials, spinal infection, and infections related to injections.

At least 2 of the review authors independently, in an unblinded standardized manner, performed each search. Accuracy was confirmed by a statistician. All searches were combined to obtain a unified search strategy. Any disagreements between reviewers were resolved by a third author and consensus.

1.4 Data Collection and Analysis

The review focused on all types of reports including case reports and reviews. We reviewed all records and reports available from the CDC of outbreaks of infections in ASCs, outpatient pain management clinics, offices, and other settings when applicable. Apart from published articles, unpublished reports of outbreak investigations and communications with state and local health officials were also assessed. We also have considered other complications including meningitis, epidural abscess, and other infections related to interventional techniques.

For the purpose of this review, while we referenced multiple manuscripts related to the hospital setting, outpatient setting, and all infections and outbreaks, we only counted outbreaks of infections that involved 2 or more infected persons that could be epidemiologically linked to a specific health care facility. Patients were categorized as having a health care-associated infection on the basis of evidence that included epidemiologic findings, temporal associations between patients and procedures, signs and symptoms of infection, and absence of traditional risk factors for infection (22). Similar to Thompson et al (22), persons were considered potentially at risk for infection if they had received health care at the implicated facility when transmission was known to have occurred or when the infection control lapse considered responsible for transmission was present. Typically in the outbreak investigations, these persons were notified of their risk and recommended to undergo screening. The persons screened included those potentially at risk for whom the investigating health department was aware of the screening test results.

1.4.1 Selection of Studies

- In an unblinded standardized manner, 2 review authors screened the abstracts of all identified studies.
- All articles with possible relevance were then retrieved in full text for comprehensive assessment.

1.4.2 Methodological Quality or Validity Assessment

Due to the inherent difficulty with the literature describing adverse effects such as a rare occurrence of infection, all available literature was included without methodologic quality or validity assessment; however, critical assessment of the literature was performed.

Each study was evaluated by at least 2 authors and any disagreements about conclusions were discussed with a third reviewer. Authors with a perceived conflict of interest for any manuscript were recused from reviewing the manuscript.

1.4.3 Data Extraction and Management

Two review authors independently, in an unblinded standardized manner, extracted the data from the included studies. Disagreements were resolved by discussion between the 2 reviewers; if no consensus could be reached, a third author was called in to break the impasse.

1.5 Summary Measures

Summary measures included probable evidence in favor of occurrence with a causal relationship to lack of infection control practices or independently of single-dose vials utilized for multiple patients.

1.6 Analysis of Evidence

Due to the nature of the issue and available literature, criteria developed by the United States Preventive Services Task Force (USPSTF) (159) or other criteria could not be utilized, thus, the evidence was analyzed based on a preponderance indicating causal relationship.

2.0 Results

An extensive search of the literature yielded multiple manuscripts (22,28,29,32,33,35,42,43,48,50,51,53-57,75-132,160-372).

Of all the reports of outbreaks available, there were 60 related to outpatient settings and of these, 15 reports directly related to spinal and non-spinal interventions. Numerous other reports failed to meet inclusion criteria of outbreaks in outpatient settings.

2.1 U.S. Infection Control Practices

Table 1 shows the results of studies of infection control practices in the United States (23,33,43). Of these 3 studies, Pugliese et al (23) assessed infection practices among clinicians in United States health care settings by an online survey in May and June 2010. Manchikanti et al (33), in a prospective evaluation, assessed infection control practices for interventional techniques over a period of 18 months. This evaluation included 12,000 patient encounters with approximately 18,500 procedures. The third study was performed by Schaefer et al (43). They evaluated infection control practices in ambulatory surgical centers.

2.2 Injection Related Infections

There have been numerous reports of injection-related infections in all types of outpatient and inpatient settings.

Thompson et al (22), in a review of non-hospital health care-associated hepatitis B and C virus transmission in the United States from 1998 through 2008, described 33 outbreaks, with 12 in outpatient clinics, 6 in hemodialysis centers, and 15 in long-term care facilities, resulting in 448 persons acquiring HBV or HCV infection.

Guh et al (48) assessed patient notifications for bloodborne pathogen testing due to unsafe injection practices in US health care settings from 2001 through 2011. The authors examined records of events that involved communications to groups of patients, conducted from 2001 through 2011, advising bloodborne pathogen testings stemming from potential exposure to unsafe injection practices. They identified 35 patient notification events related to unsafe injection practices in at least 17 states resulting in an estimated total of 130,198 patients notified. In this report, they also included multiple hospital-related infections, along with hospital-related outpatient clinics.

The GAO study (32) described 18 case reports involving infections. They described that these incidents were associated with one or more types of unsafe injection practices and most were related to improper use of syringes that led to contaminated medication vials or saline bags that were then reused for multiple patients. Table 2, adapted from the GAO report, shows unsafe injection practices that led to known bloodborne pathogen outbreaks in ambulatory care settings from 2001 through 2011 based on infection control lapses. In this description, they show that there were 12 instances of medication reuse, such as the use of saline bags or single-dose vials for more than one patient, or multiple dose vials used for multiple patients without appropriate infection control practices. They also stated that according to CDC officials, there had been no known HIV infections linked to unsafe injection practices from 2001 through 2011.

Table 3 shows bloodborne pathogen outbreaks re-

Table 1. *U.S. studies of infection control practices.*

Study/Year	Methods	Results	Conclusions by the Study Authors	Author Conclusions of the Review
Pugliese et al (23) 2010 Injection practices among clinicians in United States health care settings. Online survey.	An online survey in May and June of 2010 of clinicians in U.S. health care settings that prepare injections and are administered parenteral medications. The majority of the 5,446 eligible respondents reported injection practices consistent with current recommendations.	Unsafe practices: • 15.1% reuse a syringe to enter a multidose vial • 6.5% save that vial for use on another patient (1.1% overall) • 6% use single-dose/single-use vials for more than one patient, sometimes or always • 0.9% reuse a syringe but change the needle for use on a second patient, sometimes or always.	Unsafe injection practices present an ongoing threat to patient safety. Ensuring safe injection practices in all health care settings will require a multifaceted approach that focuses on surveillance, oversight, enforcement, and continuing education.	The study shows that the majority of problems are related to reusing a syringe to enter a multidose vial and then saving that vial for use on another patient. However, as in all self-reporting studies, the value of the study results are questionable. due to underreporting of practices
Manchikanti et al (33) 2011 Infection control practices (safe injection and medication vial utilization) for interventional techniques: Are they based on relative risk management or evidence?	3,179 patients undergoing interventional techniques from May 2008 to December 2009, were assessed for the rates of infections. A total of 12,000 encounters with 18,472 procedures were assessed. Prospective evaluation. During this period, single dose and multidose vials were utilized on multiple patients with appropriate precautions.	From a total of 3,179 patients undergoing 12,000 encounters with 18,472 procedures, 12 patients reported suspicion of infection. All of them were evaluated and found to have only superficial infections due to the patients' poor hygienic practice and requiring no antibiotic therapy.	There were no infections of any significance noted in approximately 18,000 procedures performed during a 20 month period in an ambulatory surgery center utilizing simple precautions for clean procedures with the use of single dose vials for multiple patients and using safe injection practices.	This is the first study conducted evaluating interventional techniques with simple sterile precautions performed in an ambulatory surgery center over a prolonged period of time in a large population involving >18,000 procedures illustrating no evidence of infections.
Schaefer et al (43) 2010 Infection control assessment of ambulatory surgical centers	68 ASCs were assessed between June and October 2008. Prospective evaluation. Assessment focused on 5 areas of infection control: • hand hygiene • injection safety and medication handling • equipment reprocessing •environmental cleaning • handling of blood glucose monitoring equipment Among the centers evaluated, interventional pain procedures were performed at 26% of centers with a 95% CI of 27.7%-50.8%.	Overall, 46 of 68 ASCs (67.6%; 95% CI, 55.9%-77.9%) had at least one lapse in infection control. • 25 of 54 ASCs (46.3%; 95% CI 33.4%-59.6% mishandled blood glucose monitoring equipment. • 19 of 67 ASCS (28.4%; 95% CI, 18.6%-40.0%) failed to adhere to recommended practices regarding reprocessing of equipment. • 18 of 64 ASCs (28.1%; 95% CI, 18.2%-40.0%) used single-dose medication vials for more than one patient. • 12 of the 68 ASCs (17.6%; 95% CI, 9.0%-28.1%) had lapses identified in 3 or more of the 5 infection control categories.	Infection control practices might be lacking and were not specific to a given state. Two-thirds of the pilot ASCs had lapses in infection control identified during the inspection. The study authors have not cultured the injection samples.	This study included interventional procedures performed at approximately 40% of centers.

ASCs = ambulatory surgery centers; CMS = Centers for Medicare and Medicaid Services; CI = confidence interval

Table 2. *Unsafe injection practices that led to the known blood-borne pathogen outbreaks in ambulatory care settings, 2001 through 2011.*

Infection control lapse that led to outbreak	Number of outbreaks	Settings	States	Years of outbreaks	Type of infection
Syringe reuse or suspected reuse that contaminated medication vials or saline bags, and syringe reuse from one patient to another or from clinician to patient	16	Alternative medicine clinic, cardiology clinic, endoscopy clinic, hematology-oncology clinic, hospital-based outpatient radiology clinic, hospital-outpatient pain management clinic, outpatient surgery clinic, pain management clinic, physician office	CA, FL, NE, NV, NY, NC, OK	2001, 2002, 2003, 2005, 2006, 2007, 2008, 2009, 2010, 2011	Hepatitis C, hepatitis B, or both
Medication reuse, such as the use of saline bags or single-dose vials for more than one patient, or multi-dose vials used for multiple patients without appropriate infection control practices	12	Alternative medicine clinic, cardiology clinic, endoscopy clinic, hematology-oncology clinic, outpatient surgery clinic, pain management clinic, physician office	CA, FL, NE, NV, NJ, NY, NC	2002, 2005, 2006, 2007, 2008, 2009, 2010, 2011	Hepatitis C, hepatitis B, or both
Other infection control lapses, such as mishandling of medication vials or medication preparation, such as preparing medication in contaminated environment or failure to store or prepare medication in aseptic conditions	9	Alternative medicine clinic, hematology-oncology clinic, pain management clinic, physician office	CA, FL, NJ, NY	2001, 2005, 2009, 2010	Hepatitis C, hepatitis B, or both

Source: GAO analysis of CDC data (32).

Notes: The total number of outbreaks does not add up to 18 because for some outbreaks there was more than one infection control lapse that contributed to the outbreak. Moreover, because of variation in the way the investigations are conducted by health departments that typically lead outbreak investigations, additional lapses may have occurred that were not observed or recorded.

According to CDC officials, there were no known HIV infections linked to unsafe injection practices from 2001 through 2011.

lated to unsafe injection practices in ambulatory care settings. The table was adapted from Appendix 1 of the GAO study (32) with the addition of studies not included in the GAO report.

A total of 60 reports were identified from multiple sources (28,29,50-52,54,56,57,77-133). These have been divided into pain management and related facilities, endoscopy facilities, hospital outpatient facilities, other outpatient settings, dialysis centers, and long-term care facilities.

2.3 Evaluation of Infections with Spinal and Non-Spinal Interventions

Table 4 shows the reports evaluating interventional techniques (28,54,56,57,79,81,84,85,92-97,99,109,115,117,125). A total of 16 reports were identified involving all types of interventional techniques. Of these, 2 reports (96,115) were related to procedures performed in a hospital outpatient setting related to intravenous sedation rather than infection control practices related to interventional techniques, with 107 infected individuals. Two reports (56,97) were related to inappropriate preparation of compounded betamethasone and methylprednisolone with 16 individuals being infected. There were a total of 3 ambulatory surgery centers involved (56,79,99). Of these, one report was related to issues of a compounding pharmacy with betamethasone (56). In the other 2 surgery centers, a total of 6 individuals were infected (79,99). In addition, 2 reports were related to orthopedic clinics (85,94), and a third one was related to an outpatient radiology clinic (81) with 12 individuals being infected. Consequently, 9 reports were related to interventional techniques. In one report (93), investigators showed that there were no infections reported and there was no breach of infection control practices.

Thus, among the 9 reports (54,57,79,84,92-95,99) constituting interventional techniques, there was a total of 37 individuals infected. In contrast, 117 individuals were infected with intravenous sedation, whereas 16 individuals were infected with compounding related issues. Seven individuals were infected in an orthopedic clinic and 8 individuals were infected in radiology clinics. In reference to hospital outpatient centers, a total of 114 of 148 infections were involved. However, a

Table 3. *Bloodborne pathogen outbreaks related to unsafe injections practices in ambulatory care settings.*

Health Care Setting (State)	Year	Number of Individuals Notified	Number of Individuals Screened	Number of Individuals Infected	Infection Control Lapses	Medication(S) Involved	Comments Causal Relationship to Single-Dose Vials with Proper Sterile Precautions
Pain Centers And Other Spinal And Non-Spinal Injections							
Pain Management Clinic (AZ) (94)	2012	NA	NA	4	Use of diluted contrast divided into 2 separate bottles in the morning and afternoon mixed with 10 treatment of single-dose vial of saline solution	Contrast mixed w/ sodium chloride solution diluted and separated to 2 different vials.	No
Ambulatory Surgery Center (Pain Management Clinic) (CA) (79,109)	2010	2,293	NA	2	Syringe reuse contaminating medication vials; use of single-dose vials of contrast, lidocaine, and sodium bicarbonate for more than one patient; failure to use aseptic technique when accessing medication vials	Lidocaine, sodium bicarbonate contrast	No
Pain Management Clinic (NY) (57)	2008/2010	NA	54	4 confirmed 5 suspected	Lack of hand hygiene, lack of masks, improper cleaning of injection sites, single-dose vials for multiple patients with contaminated needles	Contrast, local anesthetic, steroid, saline bags	No
Pain Management Clinic (WV) (84)	2009/2012	110	NA	6	Syringe reuse contaminating medication vials	Triamcinolone, lidocaine, iopamidol (contrast)	No
Primary Care Clinic (GA) (85)	2009	NA	NA	5	Mishandling of multi-dose vials used for >1 patient (e.g., handling in the immediate patient treatment area and failure to store according to manufacturer instructions) Inadequate hand hygiene Incorrect cleaning and disinfection of medical equipment	Steroid	No
Pain Management Clinic, Physician Office (NY) (92)	2005/2007	98	84	3	Syringe reuse contaminating medication vials; use of single-dose vials of contrast (and possible Ketorolac) for more than one patient	Bupivacaine, ketorolac, triamcinolone, iohexol (contrast)	No
Pain Management Clinic, Physician Office (NY) (93)	2005/2007	8,500	NA	0	None	None	No
Pain Management Clinic, University Hospital (MA) (54)	2005/2008	NA	35	7	Multiple medications accessed with a common needle and syringe; single-dose vials of medication, including contrast solution; used for multiple procedures with technique involving contamination	Contrast, local anesthetic, steroid	No
Ambulatory Surgical Center (Pain Management Clinic) (CA) (99)	2003	52	35	4	Suspected syringe reuse contaminating medication vials	NA	No
Pain Management Clinic Affiliated With A Hospital (OK) (28,115)	2002/2004	908	795	31 and 71	Reuse of syringes on multiple patients to deliver midazolam, fentanyl, and propofol through a heparin lock	Midazolam, fentanyl, propofol	No

Table 3 (cont.). *Bloodborne pathogen outbreaks related to unsafe injections practices in ambulatory care settings.*

Health Care Setting (State)	Year	Number of Individuals Notified	Number of Individuals Screened	Number of Individuals Infected	Infection Control Lapses	Medication(S) Involved	Comments Causal Relationship to Single-Dose Vials with Proper Sterile Precautions
Ambulatory Surgery Center (CA) (56)	2001/2006	NA	78	11	Compounding pharmacy	Betamethasone	No
Pain Management Clinic (NC) (97)	2002	NA	NA	5	Inappropriate preparation of compounded methylprednisolone	Depo-Medrol	No
Pain Management Clinic (NY) (95,117)	2011	466	NA	2	Suspected syringe reuse contaminating medication vials; single-dose vials of propofol used for more than one patient	Propofol, midazolam, lidocaine	No
Orthopedic Clinic (DE) (94)	2012	NA	NA	7	Patients received single-dose vial bupivacaine provided to multiple patients from a single-dose vial with breach of safe practice identified without sterile technique. There was also storage of the solution overnight.	Bupivacaine	No
Outpatient Radiology Clinic (MO) (81)	2010/2012	NA	35	3	Lack of sterile technique without a face mask, reuse of single-dose vials for multiple patients.	Contrast	No
Acute Care Hospital And Affiliated Multispecialty Clinic – Interventional Radiology (FL) (96,125)	2010/2012	3,929	3,444	5	Syringe reuse; narcotics diversion by clinician	Narcotics	No
ENDOSCOPY CLINICS							
Endoscopy Clinic (NY) (95,120)	2009	3,287	NA	2	Suspected syringe reuse contaminating medication vials; use of single-dose vials of propofol for more than one patient	Propofol	No
Endoscopy Clinic (NY) (117)	2008	259	NA	NA	Suspected mishandling of single-dose vials for multiple patients	Propofol	No
Ambulatory Surgical Centers (Single Purpose and Endoscopy Clinics) (NV) (52,87,133)	2008	63,000	712,000	9	Syringe reuse contaminating medication vials; use of single-dose vials of propofol for more than one patient	Propofol	No
Multiple Endoscopy and Ambulatory Surgical Centers (NY) (89)	2006/2007	4,490	841	6	Suspected syringe reuse contaminating medication vials; use of single-dose vials of propofol for more than one patient	Propofol	No
Endoscopy Clinic (NY) (98,117)	2002/2003	1,199 At risk=84	78	4	Suspected needle or syringe reuse contaminating medication vials	Unspecified anesthesia medications	No
Endoscopy Clinic (NY) (28,117)	2001	2,009	1,315	19	Suspected syringe reuse contaminating medication vials	Unspecified anesthesia medications	No

Table 3 (cont.). *Bloodborne pathogen outbreaks related to unsafe injections practices in ambulatory care settings.*

Health Care Setting (State)	Year	Number of Individuals Notified	Number of Individuals Screened	Number of Individuals Infected	Infection Control Lapses	Medication(S) Involved	Comments Causal Relationship to Single-Dose Vials with Proper Sterile Precautions
HOSPITAL-AFFILIATED CENTERS							
Orthopedic Clinic (DE) (94)	2012	NA	NA	7	Patients received single-dose vial bupivacaine provided to multiple patients from a single-dose vial with breach of safe practice identified without sterile technique. There was also storage of the solution overnight.	Bupivacaine	No
Hospital (WI) (132)	2011	56	NA	NA	Overt reuse of insulin demonstration pen from one patient to another	Saline or possibly non-sterile water	No
Hospital (NJ) (121)	2010	80	NA	NA	Suspected mishandling of single-dose vials for multiple patients	Propofol	No
Multispecialty Clinic Affiliated with a Hospital (FL) (125)	2010	3,929	NA	5	Syringe reuse, narcotics diversion by provider	Fentanyl	No
Hospital-Based Outpatient Radiology Clinic (FL) (96)	2010	3,929	3,444	5	Syringe reuse; narcotics diversion by clinician	Narcotics	No
Outpatient Clinic Affiliated with a Hospital (PA) (130)	2010	250	NA	NA	Overt syringe reuse from one patient to another	Botulinum toxin	No
Primary Care Clinic (GA) (85)	2009	NA	NA	5	Mishandling of multi-dose vials used for >1 patient (e.g., handling in the immediate patient treatment area and failure to store according to manufacturer instructions) Inadequate hand hygiene Incorrect cleaning and disinfection of medical equipment	Steroid	No
Hospitals, Ambulatory Surgical Centers (CO, NY) (123,124)	2007/2009	8,690	NA	NA	Syringe reuse, narcotics diversion by provider	Fentanyl	No
Hospital (TX) (128)	2007/2009	2,114	NA	NA	Overt reuse of insulin pen from one patient to another	Insulin	No
Hospital (FL) (129)	2009	1,851	NA	NA	Overt reuse of saline bag and intravenous tubing from one patient to another	Saline	No
Hospital (NY) (127)	2008	185	NA	NA	Suspected overt reuse of insulin pen from one patient to another	Insulin	No
Hospitals (TX, VA, District of Columbia) (122)	2004	543	NA	NA	Contamination of vials/syringes, narcotics diversion by provider	Fentanyl	No
Pain Management Clinic Affiliated with a Hospital (OK) (28,115)	2002	908	795	31 and 71	Reuse of syringes on multiple patients to deliver midazolam, fentanyl, and propofol through a heparin lock	Midazolam, fentanyl, propofol	No

Table 3 (cont.). *Bloodborne pathogen outbreaks related to unsafe injections practices in ambulatory care settings.*

Health Care Setting (State)	Year	Number of Individuals Notified	Number of Individuals Screened	Number of Individuals Infected	Infection Control Lapses	Medication(S) Involved	Comments Causal Relationship to Single-Dose Vials with Proper Sterile Precautions
OTHER OUTPATIENT CLINIC(S)							
Outpatient Clinic (CO) (131)	2011	171	NA	NA	Overt syringe reuse from one patient to another	Influenza vaccine	No
Oncology Clinic (MS) (119)	2011	623	NA	NA	Overt syringe reuse from one patient to another, and syringe reuse over multiple days contaminating saline bags and heparin bags	Heparin and saline flushes	No
Primary Care Clinic (WI) (120,132)	2011	2,345	NA	NA	Overt reuse of insulin demonstration pen from one patient to another	Saline or possibly non-sterile water	No
Urology Clinic (NV) (77)	2011	101	NA	NA	Single-use needle guides (for prostate biopsy) used for >1 patient	NA	No
Pediatric Clinic (CO) (78)	2011	NA	NA	NA	Syringe reuse (i.e., using the same syringe to administer influenza vaccine to >1 patient)	Influenza vaccine	No
Physician Office (NY) (118)	2010	25	NA	NA	Suspected overt syringe reuse from one patient to another	Influenza vaccine	No
Health Fair (NM) (80)	2010	50	NA	NA	Same fingerstick device used on >1 patient to obtain blood samples for blood glucose monitoring	NA	No
Outpatient Radiology Clinic (MO) (81)	2010/2012	NA	35	3	Lack of sterile technique without a face mask, reuse of single-dose vials for multiple patients	Contrast	No
Alternative Medicine Clinic (FL) (116)	2009	163	NA	9	Syringe reuse contaminating medication vials; mishandling of medication preparation; use of single-dose vials of magnesium sulfate for more than one patient	Various infusion therapies, including EDTA and vitamin C	No
Allergy Clinic (TX) (82)	2009	NA	NA	25	Inappropriate selection and dilution of skin disinfectant	NA	No
Hematology-Oncology Clinic (NJ) (83)	2009	4,600	NA	29	Mishandling of medication vials; medication preparation in contaminated environment; common-use of saline bag for multiple patients; use of single-dose vials for more than one patient	Saline flush, possible unspecified chemotherapy agents	No
Physician Office (Ob/Gyn) (NY) (88)	2008	36	NA	NA	Overt syringe reuse from one patient to another	Influenza vaccine	No
Cardiology Clinic (NC) (86)	2008	1,205	NA	5	Suspected syringe reuse contaminating multi-dose vials of saline used for more than one patient	Saline flush	No
Physician Office (Dermatology) (MI) (91)	2007	13,500	NA	NA	Suspected overt syringe reuse and reuse of surgical instruments from one patient to another	Unspecified	No
Pediatric Oncology Clinic (GA) (90)	2007	None	NA	13	Contents from single-dose vials used for >1 patient Predrawing saline flush solutions	Saline	No

Table 3 (cont.). *Bloodborne pathogen outbreaks related to unsafe injections practices in ambulatory care settings.*

Health Care Setting (State)	Year	Number of Individuals Notified	Number of Individuals Screened	Number of Individuals Infected	Infection Control Lapses	Medication(S) Involved	Comments Causal Relationship to Single-Dose Vials with Proper Sterile Precautions
Alternative Medicine Clinic (FL) (100)	2005	253	106	7	Mishandling of medication vials; failure to prepare and store intravenous infusions under aseptic conditions	Intravenous fluids	No
Alternative Medicine Clinic (CA) (101)	2005	15	15	7	Reuse of syringes, resulting in contamination of a saline bag used for more than one patient	Saline solution	No
Physician Office (RI) (126)	2005	669	NA	NA	Overt syringe reuse from one patient to another	Vitamin B12	No
Nuclear Imaging (3 facilities (MD) (102)	2004	88	75	16	Reuse of syringes used to dilute radiopharmaceuticals, resulting in contamination of technetium-99m sestamibi vial used for multiple patients	Radio-pharmaceuticals	No
Hematology-Oncology Clinic (NE) (28,50)	2002	613	494	99	Syringe reuse contaminating saline bags used as a source of flush for more than one patient	Saline flush	No
Physician Office (NY) (28,51)	2001/2002	1,042	222	38	Mishandling of medication vials and injection equipment; medication preparation in contaminated environment	Atropine, dexamethasone, and vitamin B12	No
HEMODIALYSIS							
Hemodialysis Center (NY) (105)	2006	183	183	7	Use of mobile cart to deliver injectable medications to multiple patients; reuse of single-dose epoetin alfa vials on multiple patients; failure to clean dialysis equipment between patients	Epoetin-alpha vials	No
Hemodialysis Center (VA) (103)	2006	64	64	7	Use of mobile cart to deliver injectable medications to multiple patients; reuse of single-dose epoetin alfa vials on multiple patients; failure to clean environmental surfaces between patients	Epoetin-alpha vials	No
Hemodialysis Center (IL) (104)	2001	75	73	11	Preparation of injections in contaminated environment; failure to separate clean and contaminated areas; failure to change gloves and perform hand hygiene after handling contaminated dialysis equipment	Equipment contamination	No
Hemodialysis Center (OH) (103)	2000	95	95	5	Preparation of injections in a contaminated environment; failure to clean environmental surfaces between patients; use of mobile cart to transport clean and used supplies among multiple patients	Equipment contamination	No
Hemodialysis Center (WI) (103)	2000	24	24	3	Use of mobile cart to transport clean and used supplies among multiple patients	Equipment contamination	No
Hemodialysis Center (MD) (103)	1998	51	51	7	Preparation of injections in a contaminated environment; failure to clean environmental surfaces between patients	Equipment contamination	No

Table 3 (cont.). *Bloodborne pathogen outbreaks related to unsafe injections practices in ambulatory care settings.*

Health Care Setting (State)	Year	Number of Individuals Notified	Number of Individuals Screened	Number of Individuals Infected	Infection Control Lapses	Medication(S) Involved	Comments Causal Relationship to Single-Dose Vials with Proper Sterile Precautions
LONG-TERM CARE							
Long-Term Care Facility (NJ) (121)	2010	182	NA	NA	Suspected mishandling of insulin pens for multiple patients, mishandling of medication preparation	Insulin, other unspecified medications	No
Assisted-Living Facility (IL) (104)	2008	105	21‡	7	Failure to use gloves and perform hand hygiene between fingerstick procedures on diabetic residents	Equipment contamination	No
Assisted-Living Facility (PA) (114)	2008	151	25‡	9	Shared use of fingerstick devices, and shared use of glucometers without cleaning among diabetic residents	Equipment contamination	No
Assisted-Living Facility (NY) (112)	2007	120	44‡	7	Shared use of fingerstick device among diabetic residents	Equipment contamination	No
Assisted-Living Facility (IL) (104)	2007	120	108	7	Shared use of glucometers without cleaning among diabetic residents	Equipment contamination	No
Assisted-Living Facility (FL) (113)	2007	6	6	2	Common storage of used and unused blood glucose monitoring equipment (fingerstick devices, glucometers)	Equipment contamination	No
Assisted-Living Facility (VA) (111)	2005	84	39‡	7	Shared use of fingerstick devices, and shared use of glucometers without cleaning among diabetic residents	Equipment contamination	No
Assisted-Living Facility (VA) (111)	2005	120	29‡	4§	Shared use of fingerstick devices, and shared use of glucometers without cleaning among diabetic residents	Equipment contamination	No
Assisted-Living Facility (CA) (29)	2004	22	22	8	Shared use of fingerstick devices, and shared use of glucometers among diabetic residents, failure to wear gloves or perform hand hygiene	Equipment contamination	No
Nursing Home (NC) (29)	2003	192	192	11	Shared use of glucometers without cleaning among multiple diabetic residents	Equipment contamination	No
Nursing Home (MS) (29)	2003	160	160	15†	Shared use of fingerstick devices, and shared use of glucometers without cleaning among diabetic residents; possible contamination of insulin vials	Insulin	No
Nursing Home (CA) (101)	2002	38	24‡	3§	Shared use of glucometers w/out cleaning among multiple diabetic residents	Equipment contamination	No
Nursing Home (CA) (110)	2002	145	46	3	Shared use of glucometers without cleaning among multiple diabetic residents	Equipment contamination	No
Nursing Home (TX) (108)	2001	110	110	5	Shared use of fingerstick device among diabetic residents	Equipment contamination	No
Nursing Home (CA) (106)	1999	59	38	4†	Reuse of disposable end-caps on fingerstick device shared by multiple diabetic patients	Equipment contamination	No
Nursing Home (CA) (107)	1999	269	55‡	5	Shared use of fingerstick devices, shared use of glucometers without cleaning among multiple diabetic residents	Equipment contamination	No

§ = Screening partially restricted to diabetic residents and persons undergoing blood glucose monitoring. † = Two deaths associated with acute hepatitis B infection. ‡ = One death associated with hepatitis B infection.

Table 4. *U.S. outbreaks associated with unsafe injection practices in outpatient setting of spinal and non-spinal injections.*

Manuscript Author(s), Occurrence Year and/or Publication	Practice Type/Setting/Methods	Results	Infection Control Lapse(S)	Study Authors Conclusions	Author Review Conclusions
Centers for Disease Control and Prevention (94) Pain Management Clinic 2012	The CDC report presents invasive staphylococcus aureus infections associated with pain injections and reuse of single-dose vials in Arizona. Based on a report on April 8, 2012, to the Arizona Department of Health Services of a patient with acute mediastinitis with blood and pleural fluid culture positive for methicillin resistant staphylococcus aureus, the investigation was conducted. Clinic staff members typically prepared contrast medium each morning in the patient procedure room, before the arrival of patients. Two new syringes were used to withdraw 5 mL each from a 10 mL single dose vial of contrast medium (300 mg per liter/mL) and a 10 mL of single dose vial of saline solution. The contents from each syringe then were transferred to the alternative vial, resulting in two 10 mL vials of diluted contrast solution, one for use in the morning and one reserved for the afternoon.	All of the patients with MRSA infections received diluted contrast from the afternoon vial. Three patients with MRSA infections went to a local hospital 4 to 8 days after their outpatient pain procedures. They required inpatient care for severe infections, including acute mediastinitis, bacterial meningitis, epidural abscess, and sepsis. The 4th recipient of diluted contrast from the afternoon vial was found deceased at home, 6 days after treatment at the clinic. In addition to identifying improper reuse of single dose vials for more than one patient, county health officials also noted that health care personnel did not adhere to standard precautions because they failed to wear face masks when performing spinal injections.	Single-dose vials of contrast were diluted with saline and then used for >1 patient; masks not worn by staff performing spinal injections.	The CDC concluded that these invasive staphylococcus aureus infections were associated secondary to single dose vials.	Even though there appears to be a causal relationship to the procedure and MRSA, it is puzzling how the MRSA was introduced. The obvious reasons are that contamination and poor injection practices, rather than MRSA growing in the contrast vials after they were opened. It is also not certain if these 10 mL vials were compounded or not.
Centers for Disease Control and Prevention (94) Orthopedic Clinic 2012	The CDC reported invasive staphylococcus aureus infections associated with intraarticular injections (94) in an orthopedic practice in Delaware. The division of Public Health and Delaware of Health and Social Services was notified on March 19, 2012. All 7 patients required debridement of the infected sites and intravenous antimicrobial therapy with an average length of hospitalization of 6 days. Three additional patients who received injections during March 6-8 developed symptoms that suggested an infection but did not have cultures taken and were treated with oral antibiotics on an outpatient basis.	The reuse of single dose vials of the anesthetic bupivacaine for multiple patients was claimed to be the breach of safe practice identified during the investigation and represented a recent change due to the national shortage of the drugs . Only one 30 mL vial of bupivacaine was opened at any given time; each vial was accessed over a course of several hours for multiple patients until all contents were withdrawn. Further, an opened 30 mL vial was also stored in a medical cabinet for use the next day sometimes. When nasal swabs were collected from the 3 clinic medical providers and 4 ancillary staff members who were involved with the preparation or administration of injections, 2 staff members whose responsibilities included preparing injections were colonized with staph aureus	Single-dose vial with breach of infection control practices to multiple patients. Overnight storage of single-dose opened vials.	Breach of infection control and single-dose vials resulted in infection.	Even though single-dose vials were involved, there were proven breach of infections.
New York City Department of Health and Mental Hygiene (95,117) Pain management clinic 2011	A pain management clinic in New York was the subject of investigation in 2011 based on the reports of individuals being infected. The authorities investigated and notified 466 patients.	The authorities notified 466 individuals; however, the information on the number of individuals screened is not available. Two individuals were infected.	Suspected syringe reuse contaminating medication vials; single-dose vials of propofol used for more than one patient.	Suspected syringe reuse, contaminated medication vials; single-dose vials of propofol used for more than one patient were responsible.	Intravenous sedation issue with suspected syringe reuse contaminating medication vials.

Table 4 (cont.). *U.S. outbreaks associated with unsafe injection practices in outpatient setting of spinal and non-spinal injections.*

Manuscript Author(s), Occurrence Year and/or Publication	Practice Type/Setting/Methods	Results	Infection Control Lapse(S)	Study Authors Conclusions	Author Review Conclusions
Bancroft et al (79) Ambulatory Surgery Center (Pain Management Clinic) 2010	The Los Angeles County Department of Public Health, the Acute Communicable Disease Control Program, undertook an investigation of the clinic to determine the source of hepatitis C infection, identify other cases, and control potential spread of disease. The investigators performed laboratory investigations for hepatitis. Investigators also observed infection control procedures in the office.	Investigators identified 2 cases of hepatitis with one case receiving a total of 4 procedures on 4 separate days during January to April 2010. No other cases were identified in the evaluation of 40 patients. The second case had a total of 8 procedures from July 2009 to January 2010 leading to investigation of 120 patients without identification of any additional cases. Investigators observed multiple breaches in infection control.	Syringe reuse contaminating medication vialsfor >1 patient; failure to use aseptic technique when accessing medication vials.	The investigators concluded that both cases acquired acute hepatitis C while being treated at the clinic. The investigators believe	There is a clear causal relationship to saline being injected which was contaminated from hepatitis C patient. In the second case, they were unable to do so. However, based on the history of the first case and their infection control breakdowns, it appears that there is a causal relationship with this. However, even though the physician has stopped using single dose contrast vials, there was no causal relationship identified to single dose vials.
Chitnis et al (81) Outpatient Radiology Clinic 2010/2012	An outbreak of bacterial meningitis at an outpatient radiology clinic was investigated to determine the source and implement measures to prevent additional infections. Patients who underwent myelography and other procedures at a clinic in Missouri performed by a radiology assistant from October 11 to 25, 2010, were investigated.	Three cases were identified among 35 patients from this particular clinic who underwent procedures. All case patients required hospitalization, 2 in an intensive care unit. Case-patients had myelography performed by the same radiology physician assistant and technician on October 25, 2010. All patients who underwent myelography on October 25, 2010 were affected. Health care personnel did not wear face masks and reused single-dose iohexol vials for multiple patients. Streptococcus salivarius (a bacteria commonly found in oral flora) was detected in the CSF of 2 case patients, and in health care professional oral specimens.	Lack of sterile technique without a face mask, reuse of single-dose vials for multiple patients.	Bacterial meningitis likely occurred because health care personnel performing myelography did not wear face masks along with lapses in injection practices may have contributed to transmission.	Even though single-dose vials were involved in this case report it is clearly due to lack of sterile precautions.
Hellinger et al (96) Acute Care Hospital and Affiliated Multispecialty Clinic – Interventional Radiology 2010/2012	The investigation was performed in an interventional radiology clinic affiliated with multispecialty clinic in an acute care hospital setting in Florida based on the reports of infections.	A total of 3,929 individuals were notified and 3,444 individuals were screened. There were 5 infected individuals.	Syringe reuse; narcotics diversion by clinician	The authors concluded that infections were secondary to diversion of narcotics by a clinician.	There is no causal relationship to single-dose vials, rather this is related to syringe reuse and narcotic diversion.
Radcliffe et al (84) Pain Management Clinic 2009/2012	The Centers for Disease Control and Prevention, conducted a retrospective cohort study evaluating clinic patients who received injections during a 3-week period. A case was defined as the laboratory confirmed infection or clinical evidence of infection less than 14 days after a patient received an injection. Infection control procedures were assessed. Methicillin-susceptible staphylococcus aureus (MSSA) isolates from patient infections and clinic staff nasal swabs were genotyped by using pulsed-field gel electrophoresis.	Eight (7%) of 110 cohort patients met the case definition. Six (75%) cases were laboratory confirmed. Eight (12%) of 69 patients who received epidural injections were case patients compared with none of the other 41 patients (P = 0.02). During procedures, staff use of face masks and preparation of patients skin was suboptimal, epidural injection syringes were reused to access shared medication vials, MSSA isolates from 2 patients and one staff member were indistinguishable by pulsed-field gel electrophoresis.	Reuse of syringe to access medication vials used for >1 patient; Use of single-dose vials of contrast for >1 patient; improper storage of medication vials; masks not worn by staff performing epidural injections; suboptimal skin preparation.	Infection control breeches likely facilitates MSSA transmission to patients receiving epidural injections. Adhering to correct infection control practices in ambulatory care settings is critical to prevent disease transmission.	This was a retrospective cohort study of only 110 patients. The study illustrated only laboratory indicated cases with no clinical symptomatology. Further, the study also showed isolates from patients and staff member were very similar in some cases. Overall this illustrates no evidence of single-dose vials being incriminated, but lapse of common sense and commonly practiced precautions.
Archer et al (85) Primary Care Clinic (GA) 2009	Georgia Division of Public Health was notified of 5 patients who experienced joint injections after intraarticular corticosteroid injections at clinic A during one week. Intraarticular corticosteroid injections These infections were investigated by investigating clinic activity, injection logs, and medical records for case finding and infection control practices were assessed.	During December 1, 2008, to February 12, 2009, multidose vials and prepared syringes were tested for pathogen contamination. Five consecutive cases occurred among 15 patients who had received injections. All patients required hospitalization and prolonged intravenous antibiotic treatment. Four had culture confirmed methicillin-susceptible Staphylococcus aureus (MSSA).	• Mishandling of multidose vials • Inadequate hand hygiene • Incorrect cleaning and disinfection of medical equipment	The authors concluded that clinical isolates were generally indistinguishable indicating a common source of joint infections. Infection control errors increased likelihood of extrinsic contamination of multidose vials.	This report involves multidose vials with multiple infection control breaches. There were no single-dose vials involved.

Table 4 (cont.). *U.S. outbreaks associated with unsafe injection practices in outpatient setting of spinal and non-spinal injections.*

Manuscript Author(s), Occurrence Year and/or Publication	Practice Type/Setting/Methods	Results	Infection Control Lapse(S)	Study Authors Conclusions	Author Review Conclusions
Wong et al (57) Pain Management Clinic 2008/2010	The evaluation was performed in an interventional pain management office setting following the notification of New York City Department of Health and Mental Health in October 2008 of 2 cases of Klebsiella pneumoniae, blood stream infections in patients who had undergone invasive pain management treatments on the same day at the same outpatient pain management facility before their infections. Infection control assessment was conducted by an investigational team to assess infection control practices and identify potential modes of transmission. The inspections included observations of mock pain management to evaluate adherence to infection control practice.	Four confirmed and 5 suspected case patients were identified. Among the 4 confirmed case patients, 3 case patients had a positive blood culture for cultures for Klebsiella pneumoniae, and one case patient had a positive blood culture for Enterobacter aerogenes. All confirmed and suspected case patients had a sacroiliac joint steroid injection procedure and 3 case patients (2 suspected and 1 confirmed) also had a greater trochanter bursa steroid injection. The median number of days between the procedure and onset of the symptoms was one day, ranging from 0 to 2 days. Six case patients were hospitalized for their illness and all case patients recovered.	•. Hand hygiene before procedures. • Not wearing cap, gown, and mask • Injection site was not properly cleaned. • Single-dose medication vials were used for multiple patients.	Infection was associated with pain management procedures, specifically those involving infection to the sacroiliac joint. Authors correlated sacroiliac joint injections and dose of triamcinolone even though only E. aerogenes was grown from iodixanol.	Many of the described issues are irrelevant. Only growth observed was from an open 100 mL vial of iodixanol.
New York State Department of Health (92) Pain Management Clinic, Physician Office 2005/2007	The investigation identified 98 patients that were notified by letter of the need for testing due to possible risk of transmission, and 84 of them were tested. Laboratory evidence from December 2005 found 2 hepatitis C cases. This is a practice of an interventional pain physician, anesthesiologist, practicing at 2 practices when the New York State and Nassau County Health Departments first became aware of 2 cases of hepatitis C related to this physician.	Overall the patients identified in this physician's practice were about 1.5% which was in the range of what would normally be expected (1.6%). Authorities also stressed that there were no cases of acute or chronic hepatitis B or HIV transmission as a result of this physician's practice. There were also 4 cases of hepatitis C identified among those patients who were tested by their private physicians. None were causally related to this clinic.	Syringe reuse contaminating medication vials; use of single-dose vials of contrast (and possibly Ketorolac) for >1 patient.	While chance of transmission is low, it is important that every patient be made aware of facts that might affect their health so that they can act appropriately.	This report shows breach of infections resulting in either 2 or 4 hepatitis cases. However, there was no causal relationship to single-dose vials.
New York State Department of Health (93) Pain Management Clinic, Physician Office 2005/2007	This is a practice of an interventional pain physician, anesthesiologist, practicing at 2 practices when the New York State and Nassau County Health Departments first became aware of 2 cases of hepatitis C related to this physician.	Overall the patients identified in this physician's practice were about 1.5% which was in the range of what would normally be expected (1.6%). Authorities also stressed that there were no cases of acute or chronic hepatitis B or HIV transmission as a result of this physician's practice.	There were no reported infection control lapses	Investigators stressed that there were no cases of acute or chronic hepatitis B or HIV transmission as a result of this physician's practice or activities	This report shows breach of infections resulting in either 2 or 4 hepatitis cases. However, there was no causal relationship to single-dose vials.
Cohen et al (54) Pain Management Clinic, University Hospital 2005/2008	A case-control study was conducted at the pain clinic associated with the outbreak to identify risk factors for serratia marcescens infection. To identify potential sources of transmission, authors also observed use of equipment; evaluated the role of personnel, hand hygiene, and other infection control practices during a marked epidural injection; and collected environmental samples. They also assessed cleaning and disinfection practices performed between procedures. Microbiologic and environmental investigations were performed on various types of samples, including surfaces of the air vents in the 2 procedure rooms, samples of frequently touched surfaces, such as fluoroscopy machine, countertops, and patient tables.	The authors identified 5 culture-confirmed case patients and 2 presumptive case-patients who had no bacteria recovered from cultures. The 7 case-patients were compared with 28 controls who underwent procedures at the same clinic but did not develop symptoms of infection. All confirmed case patients had serratia marcescens bloodstream infections. Of these, 2 had concurrent serratia marcescens central nervous system infections. Case patients were more likely than controls to have procedures that used contrast solution or entered the epidural or intervertebral disc space. The authors also showed that serratia marcescens was shown to survive and grow in contrast solution that was experimentally contaminated for up to 30 days.	Multiple medications were accessed with a common needle and syringe. Single dose vials of medication, including contrast solution, were used for multiple procedures.	The authors concluded that the results of this investigation suggest contamination of a common medication, likely contrast solution, as the source of the outbreak.	The authors described their limitations. These are only propositions rather than confirmations. The strong causal relationship between contrast injection from single dose vials and development of serratia marcescens has not been established in this study.

Table 4 (cont.). *U.S. outbreaks associated with unsafe injection practices in outpatient setting of spinal and non-spinal injections.*

Manuscript Author(s), Occurrence Year and/or Publication	Practice Type/Setting/Methods	Results	Infection Control Lapse(S)	Study Authors Conclusions	Author Review Conclusions
Janowski et al (99) Ambulatory Surgical Center (Pain Management Clinic) 2003	In 2003, an ambulatory surgery center with pain management clinic was investigated by the CDC and the local authorities. In this investigation, 52 individuals were notified.	Based on the investigation, 52 individuals were notified and 35 individuals were screened. Total number of individuals infected were 4.	Suspected syringe reuse contaminating medication vials	The study authors concluded that suspected syringe reuse contaminating medication vials was responsible for the outbreak.	Since the report illustrates that suspected syringe reuse contaminating medication vials was the main factor, relationship to single-dose vials is not causally related.
Comstock et al (115) Pain Management Clinic Affiliated With A Hospital 2002/2004	Oklahoma State Department of Health and CDC conducted a retrospective cohort study of clinic patients, including a serologic survey, interviews of infected patients, and reviews of medical records and staff infection control practices, following a report of 6 patients with unexplained hepatitis C virus (HCV) infection treated in the same pain remediation clinic in August 2002.	Of the 908 patients, 795 (87.6%) were tested, and 71 HCV infected patients (8.9%) and 31 HBV infected (3.9%) met the case definition. Review of staff practices revealed the nurse anesthetist had been using the same syringe-needle to sequentially administer sedation medications to every treated patient each clinic day.	Reuse of needles and syringes throughout the clinic day to administer sedation medications.	Reuse of needles-syringes was the mechanism for patient-to-patient transmission of HCV and HBV in this large nosocomial outbreak.	The setting was a hospital outpatient clinic where sedation was administered by certified registered nurse anesthetist.
Centers for Disease Control and Prevention (97) Pain Management Clinic 2002	In September 2002, the North Carolina division of Public Health was notified of 2 cases of meningitis caused by a rare fungus in patients who had received epidural injections at outpatient pain management clinics. Consequently, this report described 5 cases of fungal infection associated with contaminated drugs prepared at a compounding pharmacy.	After epidural injections of contaminated steroids prepared in a compounding pharmacy, a woman aged 77 years developed meningitis with Exophiala dermatitidis infection and died 51 days after hospitalization. A second woman aged 61 years developed meningitis with Exophiala dermatitidis which was identified 27 days after the collection of the specimens.	Inappropriate preparation of compounded methylprednisolone	Investigation showed that compounding pharmacy was the source of infected methylprednisolone.	There was no relationship to single dose vials; however, it was related to breakdown in the compounding pharmacy procedures.
Civen et al (56) Ambulatory Surgery Center 2001/2006	Following the report of 4 patients with serratia marcescens meningitis who received epidural injection of betamethasone compounded at a community pharmacy, an outbreak investigation was initiated in June 2001. The California Board of Pharmacy reviewed the procedures used to prepare the betamethasone.	Eleven patients were identified with culture confirmed serratia marcescens (8 patients) or clinical infection (3 patients) following injection of compounded betamethasone from May 25 through May 31, 2001. Five patients had meningitis with 3 deaths, 5 patients had epidural abscesses, and one patient had infected hip. Serratia marcescens was isolated from 35 (69%) of 51 betamethasone vials recovered.	Compounded betamethasone	This outbreak of serratia marcescens infections followed improper compounding of betamethasone in a community pharmacy.	There was no relationship to single dose vials; however, it was related to breakdown in the compounding pharmacy procedures.

potential causal relationship was demonstrated in only one report, 4 cases from Arizona (94) concerning MRSA-infected patients due to multiple breakdowns in sterile technique. Further, it appears that infections at a pain management clinic in New York (95) were mainly related to narcotic medication and contamination of intravenous sedatives, possibly lidocaine. The remaining 7 reports (54,57,79,84,92,95,99) are only correlations and postulations without a definite causal relationship involving a total of 34 of 148 infections. However, this involvement may be even less if 2 cases (95) are excluded due to the main description involving intravenous sedation rather than single-dose vials, even though it was causally mentioned in reference to lidocaine.

2.4 Analysis of Evidence

Based on the available evidence and reports, there was only one report potentially establishing the relationship between a single-dose vial used on multiple patients (94). However, even in this case, questions still remain in reference to whether it was compounded and what issues were related to unsafe injection practices. The remaining 7 reports (54,57,79,84,92,95,99) do not show a definitive correlation between infections and single-dose vials used with appropriate precautions. Among the 7 reports, the evidence showed that in one report (93), 2 infections were related to compounding pharmacies (56,97). The physicians' infection control practices did not cause the infections. Two reports (96,115) and potentially a third report (95) were related to propofol and narcotics. There is good evidence that safe injection practices must be observed during interventional techniques. However, there is limited evidence to show that single-dose vials when utilized appropriately with sterile precautions are responsible for infections.

2.5 Summary of Evidence

In summary, there is fair evidence that injections from compounding pharmacies are not safe. There is good evidence for resultant outbreaks related to intravenous analgesia. A causal relationship between single-dose vials and infections has not been established due to poor evidence.

3.0 Discussion

For this comprehensive review, we evaluated 60 publications. This review of infection control practices for interventional techniques showed good evidence of unsafe injection practices resulting in multiple outbreaks. This comprehensive review also showed fair evidence for an increased risk for infection by compounded products used in clinical settings, specifically intrathecally or intravenously. There is also good evidence related to intravenous and general anesthetics being responsible for outbreaks of bloodstream infections. However, the relationship of single-dose vials to infection outbreaks is not established in interventional pain management settings. There is only limited evidence causally relating single-dose vials to infections when appropriate sterile precautions are observed.

The 60 reports were divided into pain management and related facilities, endoscopic facilities, hospital outpatient facilities, other outpatient settings, dialysis centers, and long-term care facilities. Of the 60 reports, there were 16 reports related to pain management facilities, whereas there were 6 reports describing endoscopy clinics, 13 reports in hospital-affiliated outpatient centers, 21 reports involving other outpatient clinics with oncology clinics, primary care clinics, radiology clinics, hematology clinics, etc., and the remaining were related to hemodialysis centers and long-term care facilities. Some reports were included in more than one category. The 16 reports originating from pain management related facilities including a total of 153 infections; however, of these, 37 were related to interventional techniques (in one report, it was predominantly contamination of intravenous sedatives), with 107 or 109 patient infections related to intravenous narcotics, 16 infections related to compounding pharmacies, and a total of 119 infections related to hospital outpatient settings. Of these, a total of 6 cases were related to ambulatory surgery centers after removing compounding pharmacy infections (which included 11 of them in an ambulatory surgery center), with endoscopy clinics contributing to 47 infections, hospital affiliated clinics contributing to 119 infections, and other clinics contributing to 213 infections. There was substantial data missing for hospital infections and other facilities. In addition, a single hematology and oncology clinic (50) reported 99 individuals infected, whereas another physician office reported 38 cases. However, missing information is of extreme importance. Thus, this report, while showing a large number of reports, 9 of 60 related to interventional techniques showed a maximum of 37 infections related to facilities performing interventional techniques. Only 4 cases may be directly related to single-dose vials; however, multiple questions remain on that issue (58,94). In addition to the outbreaks even in outpatient settings, there have

been multiple reports of infections which do not constitute outbreaks, including those in radiology suites, oncology clinics, interventional pain management clinics, and all other settings.

In a recent report, hospital infections have been linked to burned out nurses (269). In this survey, hospitals where higher numbers of nurses report burnout also had higher rates of surgical site and urinary tract infections than hospitals with fewer burned out nurses. This survey specifically showed that those nurses reporting 30% lower levels of burnout had patients with 6,329 fewer surgical site and catheter-associated urinary tract infections, which researchers estimated saved those hospitals $68 million a year. The report was drawn from a 2006 survey of 7,027 registered nurses working in 161 hospitals in Pennsylvania. In addition, an association between nurse staffing in intensive care unit with patient outcomes were demonstrated to be consistent with findings and studies of the general acute care population (368). Multiple other studies have shown nurse staffing ratios are associated with patient outcomes (373-387) such as mortality (373-375,378,379,381-383,387), adverse events, complications, failure to rescue (375,378,381-383), quality of care (377), costs (375,378,387), length of stay (375,378), as well as nurse burnout and job dissatisfaction (381). Most of these studies were performed in general acute care units or a conglomerate of hospital/unit types. Similarly, an infection control bundle of 5 evidence-based practices, as reported by Anthony et al (35) in a randomized trial, may also be related to nursing burnout and stress on professionals due to extensive protocol.

In reference to guideline preparation, the GAO report and the CDC have stated that these guidelines are considered as evidence-based guidelines. However, the IOM has released methodology standards for clinical guidelines, which when followed, result in guidelines that can be trusted (34). In this manuscript the IOM describes multiple challenges in developing guidelines. The IOM states that the literature assessing the best methods for guideline development have evolved dramatically in the 20 years since the IOM's first report on the subject. The new definition from IOM is as follows:

1. Be based on a systematic review of the existing evidence.
2. Be developed by a knowledgeable, multidisciplinary panel of experts and representatives from key affected groups.
3. Consider important patient subgroups and patient preferences, as appropriate.
4. Be based on an explicit and transparent process that minimizes distortions, biases, and conflicts of interest.
5. Provide a clear explanation of the logical relationships between alternative care options and health outcomes, and provide ratings of both the quality of evidence and the strength of recommendations.
6. Be reconsidered and revised as appropriate when important new evidence warrants modifications of recommendations.

The IOM also described standards for developing trustworthy clinical practice guidelines which include the following:

- Establishing transparency.
- Management of conflict of interest with appropriate disclosures reflecting all current and planned commercial, non-commercial, intellectual, institutional, and patient/public activities pertinent to the potential scope of the guidelines, with exclusion criteria to exclude members with conflicts of interest.
- Guideline development group composition.
- Clinical practice guideline – systematic review intersection.
- Establishing evidence foundations for and rating strength of recommendations.
- Articulation of recommendations.
- External review.
- Updating.

The committee derived several recommendations directly relevant to the ultimate effectiveness of 8 standards in increasing the quality and trustworthiness of clinical practice guidelines and enhancing health care quality and patient outcomes (34).

The issue of conflicting guidelines is a major issue in the era of comparative effectiveness research and evidence-based medicine (1,3,10,12,388-393). A publication, based on IOM standards, on adverse events in hospitals showed they were not accurately measured (394). In fact, they developed a new standard and illustrated that many years and much expense due to the extensive measures proposed by IOM standards have not improved care by reducing the number of adverse events in hospitals, but that adverse events in hospitals may be 10 times greater than previously measured (394). Multiple issues related to various regulations and

guidelines since the enactment of the American Recovery and Reinvestment Act (ARRA) (395) and the Patient Protection and Affordable Care Act (ACA) (396-398) along with various guidelines have been questioned. These guidelines are not only related to subjects such as infection control, but mammography, prostate cancer screening, fraud and abuse, and even the administering of sedation during procedures, just a few of the issues affecting medical practices in the modern era (399-416). At the same time, the present administration has attempted to liberalize regulations on how these procedures can be performed and by whom, issuing unneeded clarifications and expanding the role of certified registered nurse anesthetists (CRNAs) allowing them to perform interventional techniques (14,417,418).

Livingston and McNut have described the hazards of evidence-based medicine in assessing variations in care (419). They showed that, in their evaluation, multiple issues related to frequently used measures of processes of care by Medicare's 25 quality metrics (420) may have been causing harm rather than providing benefit. Traditionally it has been touted by authorities that adherence to these processes is thought to lead to improved outcomes.

One such program, the surgical care improvement project, was introduced in 2006 with a goal of reducing surgical complications by 25% by 2010 (421). This project was based on observational studies demonstrating associations between process and outcomes, leading the experts to conclude that adherence to the series of process measures would result in better care. In reality, for some process measures, studies have shown that adherence to these measures is not necessarily associated with improved outcomes, but may actually be harmful. This has been illustrated with perioperative antibiotic use and postoperative wound infection (422), and for acute myocardial infarction, heart failure, and pneumonia (423). Another measure which has been reported to be harmful was tight glucose control in critically ill patients (424).

It is often stated that most infection outbreaks are related to outpatient settings. However, among the many reports available, a significant proportion of them are related to hospital acquired infections (123,127-129,135,136,161,165,172,182-184,186,188-190,192-194,197,202,203,205-208,210,211,214,215,219-222,224,225,227,229-232,235-237,239,241-243,245-247,249,283,287,288,294,300,301,305,307,309,331-340). Apart from single-dose vials, multiple other techniques have been described to control infections. Surgical face masks have been shown to be effective in reducing bacterial contamination caused by dispersal from the upper airway (266). All reports of outbreaks failed to follow this simple infection control measure. Further, absolute sterile technique and storage in drawing these solutions is also of extreme importance (266-268).

A recent report from the CDC (94) showed MRSA infection occurred with a transfer of contrast medium into 2 separate bottles and using them later in the day. An additional factor was that they also mixed contrast with sodium chloride solution. They also were not wearing masks. The origin of these vials and infection control practices other than using them for more than one patient are not known. The issue relating to controlling MRSA infection is not limited to interventional settings, which involves only one case report (94). In fact, multiple policies have been developed to control MRSA in various hospital settings (273,274). Thus, the question of whether to screen patients for possible carriage of MRSA when they are admitted to hospitals has been one of the most controversial areas in infection control during the past decade and is not yet resolved (294). The conflicting evidence has led to diverse national policies and local strategies to identify those who should be screened and possibly undergo MRSA decolonization treatment (294). Even then, the prevalence of MRSA has now been reduced, even in high income countries that have not implemented universal MRSA screening and decolonization policies.

A study of universal screening for MRSA at hospital admission and nosocomial infection in surgical patients in the United States (273) concluded that a universal, rapid MRSA admission screening strategy did not reduce nosocomial MRSA infection in a surgical department with endemic MRSA prevalence but relatively low rates of MRSA infection. In contrast, another study in the United States (279) concluded that MRSA colonization of the nares, either present at admission to the hospital or acquired during hospitalization, increases the risk for MRSA infections. In addition, identifying MRSA colonization at admission could target a high-risk population that may benefit from intervention to decrease the risk for subsequent MRSA infection. Further, in a study of routine screening for MRSA, among patients newly admitted to an acute rehabilitation unit in the United States (275), published in 2002, based on an outbreak of MRSA in 1987, showed that the rate of MRSA isolation from one or more body sites increased significantly from 5% in 1987 to 12% in 2000 for new-

ly admitted patients and from 0% to 7% for in-house transfers. The results showed that a negative nasal culture was highly predictive (98% of a negative perianal culture). Prior history of MRSA infection or colonization and transfer from outside sources were independently associated with positive MRSA screening cultures. Thus, in the future, it may be essential to use appropriate measures of hand hygiene, sterile preparation, mask, and MRSA cultures. However, the role of MRSA infections when health care professionals use all the precautions is not known in acute care settings such as interventional pain management.

The majority of these infections are serious. Further, numerous factors are involved, including very ill patients and immunosuppressed individuals receiving catheterizations and infusions. None of these relate solely to single-dose vials, specifically the ones used in interventional pain management. The second major category is related to intravenous anesthetics and sedatives (55,87,89,140,225,240,241,246,248,256). The majority of them were related to propofol and fentanyl.

There were multiple reports of infections from reprocessing of equipment (43,299,306,310,320,341).

There was a report of catheter-related polymicrobial bloodstream infections among pediatric bone marrow transplant outpatients in Atlanta in 2007 (90). In this study, 30 outpatients treated at a new bone marrow transplant clinic September 10-21, 2007, were enrolled in a cohort study. Investigators speculated that infection prevention challenges in the new clinic, combined with successive needle punctures of vials, facilitated extrinsic contamination and transmission of health care-associated pathogens. Even though they recommended preservative-free single-use vials not be punctured more than once, there was no correlation for the infections. However, in this setting, with bone marrow pediatric transplant patients who were immunosuppressed, it was essential to take all precautions, including single-dose vials for one patient.

There was a case report of the transmission of the hepatitis C virus during myocardial profusion imaging in an outpatient clinic (86). The study was initiated following a report of HCV infection in a patient without identified risk factors who had undergone myocardial profusion imaging 6 weeks before diagnosis. Clinical and epidemiologic information was obtained for patients with HCV infection and molecular testing was performed to assess viral related evidence of HCV transmission among patients who had undergone myocardial profusion imaging at the cardiology clinic on 2 separate dates, involving 2 potential source patients and a total of 5 newly infected patients. Molecular testing also identified a high degree of genetic homology among viruses from patients with common procedure dates. In this facility, the nuclear medicine technologists routinely drew a flush from multidose vials of saline solution using the same needle and syringe that had been used to administer radiopharmaceutical doses. Even though the multipatient use of vials was not observed, it was shown that it had occurred in the past. There was no evidence of transmission via contamination of radiopharmaceuticals at the nuclear pharmacy. The North Carolina Department of Health and Human Services concluded that transmission of HCV occurred because of unsafe injection practices during myocardial profusion imaging. It appears that this occurrence may be related to unsafe injection practices rather than safe injection practices using single-dose vials for multiple patients.

A hepatitis B outbreak associated with a hematology-oncology office practice in New Jersey was reported in 2009 (83). Counsel on state and territorial epidemiologists of New Jersey performed an onsite inspection and environmental assessment, staff interviews, records review, and observation of staff practices, following 2 reports of acute HBV infection after receiving chemotherapy at the same physician's office. Investigators identified multiple breaches in infection control, including deficient policies and procedures, improper hand hygiene, medication preparation in a blood processing area, common use saline bags, and reuse of single-dose vials. Out of 2,700 patients notified, 29 outbreak associated HBV cases were identified. Consequently, the office practice was closed and the physician's license was suspended. Based on multiple unsafe injection practices, it is impossible to derive a causal relationship to single-dose vials utilized with safe injection practices.

Some states also appear to have more hepatitis outbreaks than others. The CDC attributed these factors to some states being more advanced in identifying, investigating, and reporting bloodborne pathogen outbreaks than others, which may make them appear to have more outbreaks. Further, the underestimation is based on a study by the IOM which showed that about 65% to 75% of individuals infected with hepatitis are unaware that they are infected (343). First, many people infected with hepatitis are not aware that they have been infected until they have symptoms of cirrhosis or liver cancer many years later. Second, when symptoms do occur, it may be too late to determine the exact in-

cidence that caused the infection. However, clinicians generally are required to report cases of acute hepatitis B and C infections to their state or local health departments, though this varies by state. Health departments also acknowledge that tracking an infection to a specific health care facility can be difficult because treatment in a health care facility is not generally considered to be an important risk factor for these types of infections (32). Third, the CDC officials also stated that while state and local health departments and even medical staff often may choose to notify the CDC about potential bloodborne pathogen outbreaks, including those possibly related to unsafe practices, there is no requirement for such reporting (344). Consequently, the CDC officials only identify potential bloodborne pathogen outbreaks related to unsafe injection practices when state or local health departments seek their assistance during their investigations of potential outbreaks. Finally, available evidence also indicates, based on the GAO report, that the unsafe injection practices that can cause bloodborne pathogen outbreaks may be prevalent in ASCs, which increases the likelihood that other such outbreaks are occurring undetected in addition to those that have been identified. This is based on a 2008 survey of a randomly selected sample of 68 ASCs in 3 states showed that that about 28% of ASCs were cited for deficiencies related to injection practices or medication handling – primarily for the use of single-dose vials for more than more patient.

According to CDC officials and others the GAO has contacted, while the financial cost to the health care system of bloodborne pathogen outbreaks related to unsafe injection practices can be substantial, there are no comprehensive data on the total costs attributed to such outbreaks. For individuals who are notified that they are at risk of a bloodborne pathogen infection, costs may be incurred for testing (43). The GAO shows an example that in response to a large hepatitis C outbreak in Nevada which required notification of more than 60,000 patients to seek bloodborne pathogen testing, the Southern Nevada Health Department estimated that the laboratory cost for testing all of the potentially exposed patients would be $13.8 million (133). Further, the Southern Nevada Health Department (133) estimated that the cost of treatment for an infected patient would be $30,000. In addition, the GAO estimated that state and local health departments may incur costs for investigating and responding to potential outbreaks, including the cost of notifying and potentially providing bloodborne pathogen testing for patients who may have been exposed to unsafe injection practices.

Based on the same example, the Nevada Health Department estimated that from January 2008 through May 2009, the outbreak investigation and response cost the health department about $830,000 including $255,605 in staff time by health department employees. Further, the costs for clinicians and health care facilities that are directly involved in outbreaks may incur costs associated with lawsuits and settlements. Following a Nebraska outbreak in 2002 (345), the Nebraska Excess Liability Fund, administered by the Nebraska Department of Insurance for medical professional liability coverage, paid nearly $9 million in indemnity costs to settle 83 cases as of December 2010 (346). In addition, clinicians who cause bloodborne pathogen outbreaks through their use of unsafe injection practices may be at risk of losing their medical licenses or facing felony charges related to the outbreak. For example, as the GAO stated, the physician and 2 nurse anesthetists involved in the Nevada outbreak currently are facing state criminal charges tied to the outbreak (347).

As shown in the ASC study (43), 46% of ASCs mishandled blood glucose monitoring equipment, 28% failed to adhere to recommended practices regarding reprocessing of equipment, 28% used single-dose medication vials for more than one patient, and approximately 18% had lapses identified in 3 or more of the infection control categories. It is rather surprising since they know that they are being inspected. Two-thirds of the centers continue to have lapses. Results also suggest that the audit is likely to enhance surveyor attention to infection control, resulting in an increased number of facility citations related to infection control and medication handling compared with national numbers from the previous year. However, no infections were reported in this study or from the centers which were involved in this study. Lapses with single-dose vials were similar to a lack of adherence to reprocessing of equipment. Further, this was a great opportunity for surveyors to culture the injection samples but they have not done so. The issue of costs can go in both directions; increasing regulations without evidence increases costs, which may not assist in reducing costs due to exposures. The costs of implementing of single-dose vials appropriately with radiation protection gloves will skyrocket, which may amount to $1 to $2 billion a year for interventional techniques.

In 2009, CMS substantially expanded its oversight of unsafe injection practices in ASCs by increasing both

the intensity of its examination of safe injection and other infection control practices and the number of on-site surveys conducted in ASCs to determine compliance with CMS health and safety standards (27,32). Within these health and safety standards, those relating to infection control specifically require ASCs to maintain an infection control and prevention program designed to minimize the occurrences of HAIs, such as bloodborne pathogen infections resulting from unsafe injection practices, and have a qualified professional direct this program (46). Safe injection practices are included under several of CMS's broader health and safety standards, which also address a number of other topics related to infection control and medication administration (347).

CMS also directed the surveyors to use a tracer methodology in conjunction with the worksheet, which according to CMS officials, involves observing a patient at the beginning and end of a procedure or through his or her entire procedure. In addition, for fiscal years 2011 and 2012, CMS expects that state survey agencies will survey at least 25% of unaccredited ASCs each year, an increase from its expectation that at least 10% of unaccredited ASCs would be surveyed annually in fiscal year 2009, and 5% in fiscal year 2008. This is secondary to CMS making available $10 million in additional funds to state survey agencies to survey unaccredited ASCs, and in fiscal year 2010, CMS expected the survey agencies to survey at least 33% of unaccredited ASCs. CMS plans to officially analyze the data; as of May 2012, CMS officials expected to have this analysis completed in July 2012 in reference to surveys and infection control issues. Further, CMS officials said that the agency decided to stop collecting data directly from surveyor worksheets after fiscal year 2011; however, the GAO recommended that this be continued and HHS agreed (32).

The GAO report shows many issues related to the information provided by the CDC without direct collection of the information or direct analysis of the data. It is notable that the GAO has not used all the studies reported in the CDC's latest report (133). Eleven of the 16 studies reported by the CDC were not included in the GAO report even though the total included in the GAO report was 18. The present analysis includes all the studies, once again confirming that there is no direct causal relationship to single-dose vials being responsible for bloodborne pathogen outbreaks or infections when appropriate sterile measures are utilized. There are multiple limitations to various evaluations, including the present evaluation, due to limited data. All the studies, including the present one, have included reviewed outbreaks based on investigations by the CDC or state and local health officials meeting inclusion criteria of at least 2 patients.

In 2006, the national viral hepatitis survival data revealed that 50% of patients with acute HBV and HCV infection were reported not to have accompanying risk factor data (348). Among patients for whom risk factors data were reported, 56% with acute HBV infection and 32% with acute HCV infection could not specify a known risk factor for their infection such as injection drug use, sexual or household contact with another infected person, occupational exposure to blood, or needlestick injury (348). Thus, viral hepatitis surveillance reports from health departments may contain HBV and HCV infections that were unknowingly acquired in health care settings. Consequently, these points underscore the inadequacy of current surveillance for bloodborne pathogen outbreaks in the United States to detect health care related infections. Thus, Thompson et al (22) noted that their report should be considered the "tip of the iceberg." By the same token, the expenses related to unproven measures without implementing appropriate measures to provide cost-effective drugs for single doses is enormous and the interventional pain management descriptions itself may be the "tip of the iceberg."

Hospitals have been applauded for well-established and updated infection control measures (352,353) and employment of infection control personnel to conduct surveillance, monitor practices, and provide education and training on appropriate infection control practices. Thompson et al (22) and the GAO report (32) also described that specific infection control resources and oversight have traditionally been lacking in non-hospital settings (49,354-357). They state that without better adherence to standard precautions and aseptic technique, the number of persons who become infected or are placed at risk for bloodborne infections in these settings may continue to increase. However, many outbreaks related to hospitals, both inpatient and outpatient settings, may continue to increase. Once again, this may only be the "tip of the iceberg." Further, compounding issues continue to mount both in hospital and nonhospital settings. In fact, a report on the state of pharmacy compounding for purchase products showed that trends in patient incidences involving compounding errors have increased from 30% in 2009 to 33% in 2010 and 34% in 2011, with an increasing

number of hospitals recognizing that they have had a patient incident(s) involving a compounding error over the past 5 years.

Interventional pain management has been growing rapidly (425-434). The United States is facing a major crisis with exploding health care expenditures resulting in numerous regulations. Along with various sectors of health care, increasing expenses are part of interventional pain management. Further, in these debates, the lack of effectiveness of interventional techniques is also discussed; however, multiple well conducted studies and systematic reviews illustrate evidence contrary to such assertions (435-446). However, significant issues related to fraud and abuse in relation to interventional techniques continue (4,5,447,448). Thus, patient safety and incurred expenses are major issues for all health care professionals and regulators. There is also potential for increase in opioid use resulting in abuse and escalating fatalities (28-31,52,94,97,133,147,164,177,280,348,360,361,362,449-453). Thus, appropriate provision of interventional techniques is essential to contain health care costs, excessive opioid use, and abuse, and avoid an epidemic of fatalities.

From 1997 through 2011, it is estimated that a total of 200 million interventional procedures were performed, with only 37 infections during that time. If the infections were to increase 10-fold, it would translate to 1 infection for approximately every 500,000 procedures. However, if the infections are increased by 100 fold, it would translate to one infection for every 50,000 interventional procedures.

This evaluation in reference to interventional techniques and infection control practices shows only limited or poor evidence correlating the use of single-dose vials with appropriate infection control practices and the occurrence of infections. Of all the reports available, there were 11 studies directly related to interventional techniques (54,56,57,79,84,92-94,97,115,162).

Further, the majority of the reports evaluated systematically failed to show an occurrence of infections even though they illustrated many infection control breakdowns. The only infection control reports are related to the postsurveillance reports.

To resolve the issue of single-dose vials in reference to infection outbreaks, the administration and Congress should impose regulations on manufacturers to produce single-dose vials which are cost-effective rather than artificially inflate prices where a 50 mL vial of contrast medium is less expensive than a 10 mL vial.

4.0 Conclusion

This comprehensive review shows the importance of adherence to infection control practices, including handwashing, wearing a mask during interventional procedures, following appropriate sterile precautions at each and every step, environmental infection safety, and finally, vigilance. However, this evaluation fails to show causal relationship with limited evidence connecting single-dose vials to infection outbreaks when appropriate sterile precautions were utilized. To continue to utilize CDC guidelines that a single dose be utilized in a single patient, it is crucial that the Administration and Congress work with manufacturers and produce cost-effective single-dose vials, which do not increase health care costs and curb access to health care.

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Conflict of Interest:

Dr. Falco is a consultant for St. Jude Medical Inc. and Joimax Inc.

Dr. Benyamin is a consultant with Bioness and Nevro, serves on the advisory boards of Vertos Medical and Nuvo Pharma, teaches/lectures for Vertos Medical, Boston Scientific, Neurotherm, and Bioness, and receives research/grants from Alfred Mann Foundation, Teknon Foundation, Spinal Restoration, Inc., Bioness, Boston Scientific, Vertos Medical, Medtronic, Kimberly Clarke, Epimed, BioDelivery Sciences International, Inc., Theravance, Mundipharma Research, Cephalon/Teva, AstraZeneca, and Purdue Pharma, LP.

Dr. Helm is a clinical investigator with Epimed and receives research support from Cephalon/Teva, AstraZeneca, and Purdue Pharma, LP. He has attended an advisory group meeting for Activas.

Dr. Hirsch has received fees from CareFusion in the past 12 months. He participated in an Aetrium focus group and received compensation.

Dr. Caraway is a consultant for Medtronic, Inc., Spinal Modulation, Inc., and Vertos, Inc.

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