

Evaluation of a needle disinfectant technique to reduce infection-related hospitalization following transrectal prostate biopsy

Gregory B. Auffenberg, MD, MS^a; Ji Qi, MS^a; Yuqing Gao, MS^a; David C. Miller MD, MPH^a; Zaojun Ye, MS^a; Andrew Brachulis^a; Susan Linsell MHSA^a; Tejal N. Gandhi MD^b; David Kraklau MD^c; James E. Montie MD^a; and Khurshid R. Ghani MBChB, MS^{a*}, for the Michigan Urological Surgery Improvement Collaborative

^a Department of Urology, University of Michigan, Ann Arbor, MI; ^b Division of Infectious Diseases, Department of Medicine, University of Michigan, Ann Arbor, MI ; ^c Lakeside Urology, St. Joseph, MI

* Correspondence:

Khurshid R. Ghani MBChB, MS
Department of Urology, University of Michigan
2800 Plymouth Rd. NCRC Bldg. 16
Ann Arbor, MI 48109
Email: kghani@med.umich.edu
Phone: 734-615-4034
Fax: 734-232-2400

Author email addresses:

Auffenberg: gauffen@med.umich.edu

Qi: qiji@med.umich.edu

Gao: yuqgao@yahoo.com

Miller: dcmiller@med.umich.edu

Ye: zye@med.umich.edu

Brachulis: abrachul@med.umich.edu

Linsell: slinsell@med.umich.edu

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1111/bju.13982](https://doi.org/10.1111/bju.13982)

This article is protected by copyright. All rights reserved

Gandhi: tgandhi@med.umich.edu

Kraklau: dkraklau@lakelandhealth.org

Montie: jmontie@med.umich.edu

Keywords: cancer, prostate; prostate biopsy; infection; quality improvement

ABSTRACT WORD COUNT: 258

MANUSCRIPT WORD COUNT: 2,903

Author Manuscript

DR. GREGORY B AUFFENBERG (Orcid ID : 0000-0003-4798-7781)

Article type : Original Article

Abstract

Objectives – To determine whether a needle disinfectant technique during transrectal prostate biopsy is associated with lower rates of infection-related hospitalization.

Subjects and Methods- We conducted a retrospective analysis of all transrectal prostate biopsies performed across the Michigan Urological Surgery Improvement Collaborative (MUSIC) from January 2012 through March 2015. Natural variation in technique allowed us to evaluate for differences in infection-related hospitalizations based on whether or not a needle disinfectant technique was utilized. The disinfectant technique was an intra-procedural step to cleanse the biopsy needle with antibacterial solution after each core was sampled (i.e., 10% formalin or 70% isopropyl alcohol). After grouping biopsies according to whether or not the procedure included a needle disinfectant step, we compared the rate of infection-related hospitalizations within 30 days of biopsy. Generalized estimating equation (GEE) models were fit to adjust for potential confounders.

Results- During the evaluated period, 17,954 biopsies were performed with 5,321 (29.6%) including a disinfectant technique. The observed rate of infection-related hospitalization was lower when a disinfectant technique was utilized at biopsy (0.60% vs. 0.90% without disinfectant technique, $p=0.04$). After accounting for differences between groups the adjusted hospitalization rate in the disinfectant group was 0.85% (vs. 1.12%), (adjusted OR 0.76, 95% CI 0.50 -1.15, $p=0.19$).

Conclusions – In this observational analysis, hospitalizations for infectious complications were less common when the procedure included a needle disinfection technique. However, after

adjusting for potential confounders the impact of needle disinfection was not statistically significant. Prospective evaluation is warranted to determine if this step provides a scalable and effective method to minimize infectious complications.

Introduction

Infectious complications from transrectal prostate biopsies are estimated to occur after 5-7% of biopsies and can lead to significant morbidity and substantial cost.¹ Although less common, more severe infections requiring hospitalization occur after 1 to 3% of biopsies and are associated with even greater human and financial costs.¹ Fluoroquinolone resistance has been shown to be a contributing factor to these infections and modifications to prophylactic pathways including rectal culture-directed antibiotics and addition of non-fluoroquinolone augmented prophylactic regimens have led to decreases in infectious complications.²⁻⁴ These strategies represent important quality initiatives that have improved patient care. However, implementation challenges, risks of further resistance, and antibiotic side-effects¹ may leave room for even greater improvement.

An ideal quality improvement strategy to reduce prostate biopsy related infections would be effective, inexpensive, easy to implement, and safe while not augmenting antibiotic resistance. Non-antibiotic strategies of varied efficacy, such as rectal preparation and transperineal biopsy, have been previously investigated but have not been widely adopted.^{5,6} More recently, the role of intra-procedural needle disinfection using 10% formalin during prostate biopsy has been evaluated as a means to potentially reduce intra-prostatic bacterial inoculation and thus diminish the risks of post-biopsy urinary tract infection and/or sepsis.⁷ This single-center study did not demonstrate a statistically significant benefit to needle disinfection, however, the simplicity of this intervention is compelling and warrants further investigation.

In this context, we evaluated the impact of an intra-procedural needle disinfectant step on the rate of infection-related hospitalization within 30 days of transrectal prostate biopsy for patients managed in the diverse academic and community practices comprising the Michigan Urological Surgery Improvement Collaborative (MUSIC). Understanding whether the addition of intra-procedural needle disinfection to transrectal prostate biopsy reduces infection-related complications will help urologists working to optimize the safety of prostate biopsy.

Subjects and Methods

Data Source

MUSIC was established in 2011 in partnership with Blue Cross Blue Shield of Michigan. The quality improvement collaborative currently comprises 43 urology practices with more than 240 urologists, which represents nearly 90% of the urologists in the state. For all prostate biopsies performed across the collaborative, trained data abstractors review all clinical documentation related to a prostate biopsy and follow-up and prospectively enter into a web-based clinical registry a standardized set of demographic and clinicopathologic data pertaining to biopsy findings and complications occurring within 30 days. Prior reports have described MUSIC's data quality-control activities, including annual data audits at each practice and validation analyses based on insurance claims.^{4,8} Each MUSIC practice obtained an exemption or approval for collaborative participation from a local institutional review board.

Patients and comparison groups

The cohort for this analysis included all ultrasound-guided transrectal prostate biopsies performed in participating MUSIC practices from January 2012 through March 2015. During the period evaluated, natural variation across providers and practices determined whether a disinfectant step was used or not during a given procedure. After the MUSIC coordinating center verified each urologist's technique, biopsies were grouped according to whether or not a disinfectant technique was used.

Needle disinfectant techniques

Urologists that used a needle disinfectant technique employed one of two strategies for needle disinfection referred to hereafter as the formalin technique or the alcohol technique. In the formalin technique, after each core is obtained with a standard spring-loaded biopsy needle, the external sheath is withdrawn to expose the core. The needle is then submerged in a sterile specimen cup containing 10% formalin and swirled to dislodge the core and bathe the needle in the disinfectant solution (Figure 1). Some urologists rinsed the needle in a cup of sterile saline before using it to obtain the next specimen. The alcohol technique involves 70% isopropyl alcohol as the disinfectant solution, which is used to soak a Telfa sponge. After each core is obtained the external sheath is drawn back to expose the core, the needle is wiped on the alcohol soaked sponge to dislodge the core and also disinfect the needle tip (Figure 2).

Outcome

The primary outcome measure compared across groups was the rate of hospital admission within 30 days of biopsy for a primary diagnosis of urinary tract infection, fever, or sepsis.

Statistical Analyses

We performed univariate comparisons of demographic and baseline clinical information for the disinfectant versus non-disinfectant groups. Student's t-tests were used to compare continuous measures, while Chi-squared tests were used for categorical outcomes. After comparing the observed rate of hospitalization across groups, we employed common statistical methods^{9,10} to fit a generalized estimating equation (GEE) model with logit link to assess the independent association between use of a disinfectant technique and post-biopsy infection-related hospitalization. The model adjusted for patient age, presence of diabetes, history of prior biopsy, and whether a biopsy occurred before or after our statewide intervention aimed at addressing fluoroquinolone resistance with either culture-directed or augmented antibiotic prophylaxis.⁴ The model accounted for within-patient correlation for patients with more than one biopsy in the dataset.

Two sub-group analyses were performed. In the first sub-analysis, we fit a separate GEE model to a sub-cohort of biopsies where greater information about other infectious risk-factors was available. At the time of these procedures, a questionnaire was completed detailing whether a patient received antibiotics in the 6 months prior to biopsy, had traveled internationally in the past 6 months, or was taking immunosuppressive medications. Each of these factors was added as dichotomous co-variate in a GEE model that also included all co-variables for the base model used in the primary analysis, and we again evaluated for an independent relationship between the disinfectant technique and infection-related hospitalization after adjusting for these other factors. In a second sub-group analysis, the observed rate of infection-related hospitalization was compared across study groups for the subsets of biopsies performed before and after the aforementioned statewide antibiotic intervention that has significantly reduced infection rates across MUSIC.⁴ All statistical testing was performed using commercially available software (SAS v.9.4, SAS Institute, Cary, NC) at the 5% significance level.

Results

Across 41 practices and 233 urologists, 16,920 patients underwent 17,954 transrectal biopsies during the study period. The majority of biopsies were performed without a disinfectant

technique (12,633, 70.4%). Among the biopsies performed with a disinfectant technique, the formalin technique was used for 4,870/5,321 (91.5%). The alcohol technique was used in the remaining 451 (8.5%) biopsies.

Demographic information for the study groups is reported in Table 1. Mean age was similar (64.1 years vs 64.4, $p=0.08$; for no disinfectant and disinfectant groups, respectively). Men in the needle disinfectant group were less likely to have received a prior biopsy (Table 1). Relative to biopsies performed without a disinfectant technique, a greater proportion of the biopsies using a disinfectant technique were performed after the collaborative-wide effort to reduce biopsy-related infections with use of either culture-directed or augmented antibiotic prophylaxis (87.6% versus 63.3%; $p < 0.001$).

Infection-related hospitalizations were less common after biopsies that included a needle disinfectant technique (32 admissions (0.60%) vs. 114 admissions (0.90% of biopsies without disinfectant); odds ratio (OR) = 0.67; $p=0.040$) (Figure 3a). There were no admissions reported for the 451 biopsies performed using 70% isopropyl alcohol as a disinfectant. There were no deaths in either group, or any reported adverse events related to the use of needle disinfectant.

Table 2 reports findings from our multivariable analyses. Men with diabetes and those undergoing biopsy prior to MUSIC's antibiotic intervention were more likely to be hospitalized for an infection after biopsy. After adjusting for the covariates in table 2, there was no longer a statistically significant difference in hospitalization rates across study groups (adjusted OR 0.76, 95% CI 0.50-1.15, $p=0.19$) (Figure 3b).

In the first sub-group analysis there were 8,382 biopsies included. After adjusting for the factors included in the primary analysis as well as for use of antibiotics during the 6 months prior to biopsy, recent international travel, and whether a patient was taking immunosuppressants at the time of biopsy, there was not a statistically significant difference in hospitalization rates attributable to use of a needle disinfectant technique (adjusted OR =0.86; 95% CI 0.47 -1.58; $p=0.64$, reference= no use of disinfectant). None of the added risk factors was a significant predictor of hospitalization in this sub-cohort (adjusted odds ratio for hospitalization associated with 1) using antibiotics in 6 months before biopsy = 1.20; 95% CI 0.67-2.17; $p=0.54$; 2) recent international travel = 1.72; 95% CI 0.81 – 3.67; $p=0.16$; 3) use of immunosuppressants at time of biopsy = 1.77; 95% CI 0.55-5.71; $p=0.33$).

A second sub-group analysis of the 5,299 biopsies performed prior to the MUSIC antibiotic intervention demonstrated no significant difference in observed hospitalization rates when 661 disinfectant biopsies (5 hospitalizations; rate=0.76%) were compared to 4,638 performed without disinfectant (56 hospitalizations; rate =1.21%, p=0.31) (Figure 4). Similarly, there was no difference in rate of infection-related hospitalization when comparing 4,660 disinfectant biopsies (27 hospitalizations; rate = 0.58%) to 7,995 biopsies performed without disinfectant (58 hospitalizations; rate= 0.73%; p=0.33) after the collaborative-wide antibiotic intervention (Figure 4).

Discussion

In our evaluation of nearly 18,000 transrectal prostate biopsies performed in Michigan, approximately 30% of biopsies utilized a needle disinfectant technique. Among this large sample of patients from academic and community urology practices, the observed rate of infection-related hospitalization within 30 days of biopsy was lower among biopsies where a disinfectant technique was utilized. However, after accounting for potential confounders, adjusted hospitalization rates no longer differed across study groups. A sub-group analysis of the biopsies performed before implementation of a statewide antibiotic intervention demonstrated that there was no significant difference in hospitalization rates during that time period. Similarly, when examining biopsies performed after the antibiotic intervention, hospitalization rates did not differ significantly.

Our findings build on a single-center investigation that introduced the concept of the formalin disinfectant technique.⁷ Issa and colleagues reported a 0.30% rate of urinary infection or sepsis in 1,642 prostate biopsies performed with a 10% formalin needle disinfection step. Despite a very low rate of infection, the authors did not find a statistically significant reduction in infections when disinfectant biopsies were compared to a cohort of 990 biopsies performed in the same center without needle disinfection (infection rate=0.80%; p=0.13). To further evaluate a mechanistic explanation for a protective effect of formalin, in vitro experimentation has also been used to demonstrate that treating MacConkey agar dishes with 10% formalin for 10 seconds prevents growth of fluoroquinolone resistant E. Coli in the culture media and further, that needle-tips from transrectal biopsies where a needle disinfectant technique is used do not demonstrate bacterial growth.⁷ In the present analysis, we observed a lower rate of hospitalization when

biopsies included a disinfectant technique (0.60% versus 0.90%, $p=0.04$), however given the observational nature of our investigation it was necessary to evaluate for alternative explanations for our findings. As noted, MUSIC led a statewide antibiotic initiative associated with notable reductions in infection rates during the time period evaluated in the current analysis.⁴ Given the impact of the antibiotic initiative on the outcome of interest, it was important to account for this and other important co-variables in evaluating the disinfectant technique. After accounting for these factors, there was not a statistically significant difference in hospitalization attributable to the disinfectant technique.

The included sub-analyses were performed to provide more detail on the impact of needle disinfection while accounting for the collaborative-wide antibiotic intervention in a different way. In looking at only the biopsies performed before the changes to antibiotic prophylaxis, the absolute difference in hospitalization rates was larger than when looking at the entire cohort (1.21% for biopsies that did not use disinfectant versus 0.76% for those that did). Statistical significance may have been precluded due to the small number of events in both groups and the relatively limited number of biopsies (661) performed with disinfectant prior to the antibiotic intervention. Following our antibiotic intervention, we found the rate of infection-related hospitalization dropped to 0.73% among biopsies performed without a disinfectant technique. Despite a larger cohort of disinfectant biopsies in this period, the observed rate of hospitalization (0.58%) was not significantly lower when compared to biopsies performed without disinfectant. We hypothesize that the impact of disinfectant may be masked in the period following the antibiotic intervention given the substantially lower rate of infection in the non-disinfectant group. Disinfectant techniques may have protective effects; however, we are not able to demonstrate this in a statistically significant manner given the relative rarity of events and the confounding influence of our antibiotic statewide guideline intervention.

Prior to consideration of increased adoption or further investigation, potential safety concerns of needle disinfection should be considered. Formalin is an aqueous solution of formaldehyde—recognized by the World Health Organization and Environmental Protection Agency (EPA) as a chemical irritant and possible carcinogen.^{11,12} The average formaldehyde exposure from a standard 12-core biopsy with a disinfectant technique has been estimated at 3.9 mg.⁷ This is significantly lower than the maximum exposure threshold set by the EPA at

0.2mg/kg/day (e.g., 70 kg person maximum daily exposure threshold=14 mg).¹¹ Formaldehyde exposure is common in normal human living environments, and the exposure from a single prostate biopsy is in range with the degree of exposure humans experience from common sources on a daily basis (Supplemental Table). Although, our investigation did not directly evaluate exposure or safety, the published data suggests the potential for harmful effects from a formalin disinfectant technique would be remote. Incorporating a saline rinse after formalin disinfection may further reduce the load inoculated to the prostate, and is used as an adjunct by some urologists in MUSIC. Similarly, it is unlikely that isopropyl alcohol is of substantial concern for patient safety. Isopropyl alcohol is a common over-the-counter disinfectant with a proven safety record when used in small volumes, and according to the Centers for Disease Control it is not a human carcinogen.¹³ Across our collaborative there have been no reports of biopsy complications or unintended events, such as granulomatous prostatitis or impaired pathological assessment, that could be linked to the utilization of a disinfectant technique.

Our findings should be considered in the setting of several limitations. First, this is an observational analysis where disinfectant technique was not strictly standardized (e.g., dwell time in disinfectant solutions was per clinician routine and may vary across providers) and, as detailed, an antibiotic-based quality improvement initiative was implemented during the evaluated time period. Further it is possible other co-variables (e.g., antibiotic type) that we are not able to account for may influence the outcome as well. Although, a randomized controlled trial would be beneficial for demonstrating whether the disinfectant technique is protective it would need to be a large trial given the rarity of infection-related hospitalizations after prostate biopsy (e.g., assuming a hospitalization rate of 1.2% in the control group, and the disinfectant technique could reduce the event rate by 0.5%, it would require nearly 6,000 patients in each group to detect the effect of disinfectant with a power of 0.8). In the context of limited resources, we felt an observational analysis would be an important first-step in determining whether further consideration of disinfectant techniques is warranted. Second, physician self-report with regard to disinfectant utilization was used to group biopsies into the study groups. The MUSIC coordinating center verified behavior for each urologist. Although there is possibility of mis-grouping of some of the biopsies, we anticipate the impact of mis-grouping would be small.

These limitations notwithstanding and in the context of concerns about both rising antibiotic resistance and the safety of extended fluoroquinolone therapy,¹⁴ there are important implications to this work. Avoiding infectious hospitalization, the associated morbidity, and costs via a simple, low-risk modification to biopsy procedures represents a potential for improvement with minimal downside. Furthermore, as needle disinfection does not increase antibiotic utilization; it may represent an important adjunct or alternative to the antibiotic-based quality improvement strategies that continue to carry the potential for worsening antibiotic resistance despite laudable reductions in post-biopsy infections demonstrated within our collaborative⁴ and elsewhere.³ This, to our knowledge, represents the largest evaluation of the needle disinfectant technique to date. In the absence of a statistically significant difference in adjusted hospitalization rates, we cannot state that needle disinfection should be a new standard, but feel it may remain prudent to incorporate needle disinfection into biopsy regimens given the potential for benefit with little to no risk. Further, we feel this investigation provides evidence regarding the necessity of a prospective study of this technique in order to limit confounding and more definitively determine if there is a benefit to needle disinfection.

Moving forward, we have planned further prospective investigation of this technique within MUSIC where several pilot sites have changed practice to adopt a disinfectant technique. Analysis of outcomes before and after this change within pilot sites will afford us further information on the impact of needle disinfection. We are also interested in the sub-population of biopsies being performed with isopropyl alcohol as a disinfectant. Given patients in this group had no infectious hospitalizations during the study, we continue to monitor the impact of this method to determine if it is possibly superior to the formalin technique.

In conclusion, men undergoing transrectal prostate biopsy within MUSIC were less commonly hospitalized for infectious complications within 30 days of biopsy when their procedure included a needle disinfectant technique using either 10% formalin or 70% isopropyl alcohol. Despite differences in observed hospitalization rates, multi-variable analyses revealed no significant difference in hospitalization rates attributable to the use of a needle disinfectant after accounting for potential confounders. Despite these findings, needle disinfection may remain a scalable, low-risk intervention to reduce infectious complications following prostate biopsy that warrants further investigation.

Acknowledgements

The authors acknowledge the significant contributions of the clinical champions, urologists, administrators and data abstractors in each participating Michigan Urological Surgery Improvement Collaborative (MUSIC) practice (details around specific participating urologists and practices can be found at www.musicurology.com), as well as members of the MUSIC Coordinating Center at the University of Michigan. In addition, we would like to acknowledge the support provided by David Share, MD, MPH; Tom Leyden, MBA; Rozanne Darland, BSBA; David Bye II, MBA; and the Value Partnerships program at BCBSM.

Funding/Support: Support for MUSIC is provided by Blue Cross and Blue Shield of Michigan (BCBSM) as part of the BCBSM Value Partnerships program. This work was also funded by grant 1T32-CA180984 (GBA) from the National Cancer Institute.

Role of the Funder/Sponsor: Neither BCBSM nor the National Cancer Institute had a role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

References

1. Liss M, Ehdai B, Loeb S, et al: The prevention and treatment of the more common complications related to prostate biopsy update, American Urological Association Paper. Available at: <https://www.auanet.org/common/pdf/education/clinical-guidance/AUA-PNB-White-Paper.pdf>. 2016
2. Feliciano J, Teper E, Ferrandino M, et al: The incidence of fluoroquinolone resistant infections after prostate biopsy--are fluoroquinolones still effective prophylaxis? J Urol 179:952-5; discussion 955, 2008
3. Taylor AK, Zembower TR, Nadler RB, et al: Targeted antimicrobial prophylaxis using rectal swab cultures in men undergoing transrectal ultrasound guided prostate biopsy is associated with reduced incidence of postoperative infectious complications and cost of care. J Urol 187:1275-9, 2012
4. Womble PR, Linsell SM, Gao Y, et al: A Statewide Intervention to Reduce Hospitalizations after Prostate Biopsy. J Urol 194:403-9, 2015

5. Park DS, Oh JJ, Lee JH, et al: Simple use of the suppository type povidone-iodine can prevent infectious complications in transrectal ultrasound-guided prostate biopsy. *Adv Urol*:750598, 2009
6. Symons JL, Huo A, Yuen CL, et al: Outcomes of transperineal template-guided prostate biopsy in 409 patients. *BJU Int* 112:585-93, 2013
7. Issa MM, Al-Qassab UA, Hall J, et al: Formalin disinfection of biopsy needle minimizes the risk of sepsis following prostate biopsy. *J Urol* 190:1769-75, 2013
8. Womble PR, Montie JE, Ye Z, et al: Contemporary use of initial active surveillance among men in Michigan with low-risk prostate cancer. *Eur Urol* 67:44-50, 2015
9. Zeger SL, Liang KY, Albert PS: Models for longitudinal data: a generalized estimating equation approach. *Biometrics* 44:1049-60, 1988
10. Hanley JA, Negassa A, Edwardes MD, et al: Statistical analysis of correlated data using generalized estimating equations: an orientation. *Am J Epidemiol* 157:364-75, 2003
11. United States Environmental Protection Agency: 2012 Edition of the Drinking Water Standards and Health Advisories. EPA Publication 822-S-12-001. April 2012. Available at: <https://www.epa.gov/sites/production/files/2015-09/documents/dwstandards2012.pdf>
12. World Health Organization: Air Quality Guidelines-Second Edition. Chapter 5.8 – Formaldehyde. 2001. Available at: http://www.euro.who.int/_data/assets/pdf_file/0014/123062/AQG2ndEd_5_8Formaldehyde.pdf
13. The National Institute for Occupational Safety and Health (NIOSH): International Chemical Safety Cards: Isopropyl Alcohol. Edition: July 22, 2015. Available at: <https://www.cdc.gov/niosh/ipcsneng/neng0554.html>
14. United States Food and Drug Administration: FDA Drug Safety Communication -FDA updates warnings for oral and injectable fluoroquinolone antibiotics due to disabling side effects. Published: May 12, 2016. Available at: <https://www.fda.gov/Drugs/DrugSafety/ucm511530.htm>

Legends:

Figure 1. Demonstration of the Formalin disinfectant technique

Figure 2. Demonstration of the Alcohol disinfectant technique. (Needle is wiped against a Telfa sponge soaked in 70% Isopropyl alcohol to dislodge sampled prostate core)

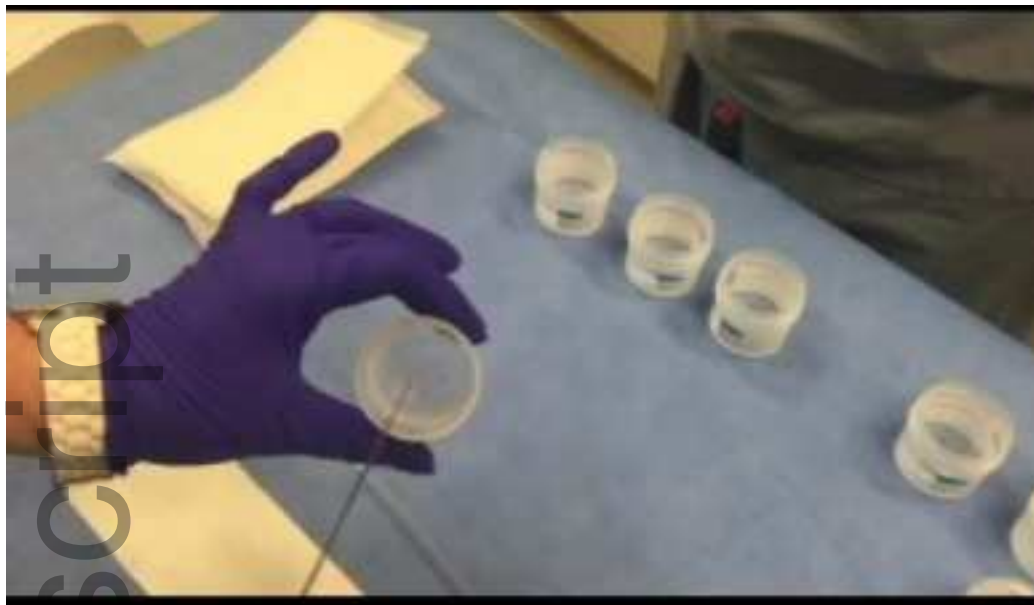
Table 1. Characteristics of patients undergoing transrectal prostate biopsy with or without a needle disinfectant technique. Student's t-test used to compare continuous measures and Chi-squared test for categorical measures. SD= standard deviation

Figure 3. Comparison of the rate of infection related hospitalization following prostate biopsy a) observed rate b) risk adjusted* rate (*adjusted for age, presence of diabetes, history of prior biopsy, and timing of biopsy related to collaborative-wide antibiotic initiative) Chi-squared test used to compare differences across groups

Table 2. Results of multi-variable regression analysis to predict probability of hospitalization after prostate biopsy

Figure 4. Comparison of the observed rate of infection-related hospitalization for biopsies performed prior to and after collaborative-wide antibiotic intervention. Chi-squared test used to compare differences across groups.

Supplemental Table. Quantity of human formaldehyde exposure from common environmental sources.

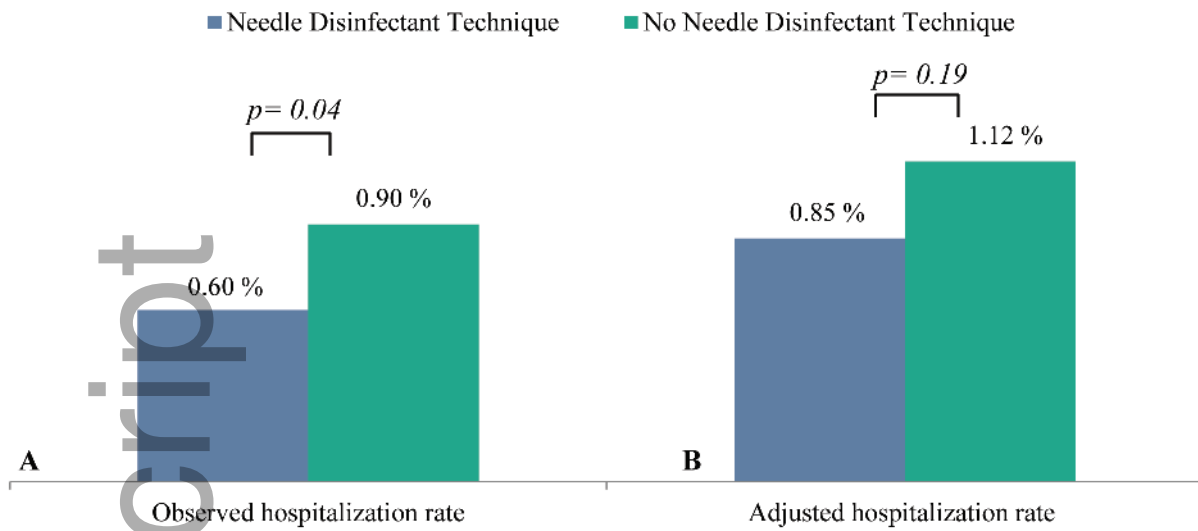


bj_u_13982_f1.jpg

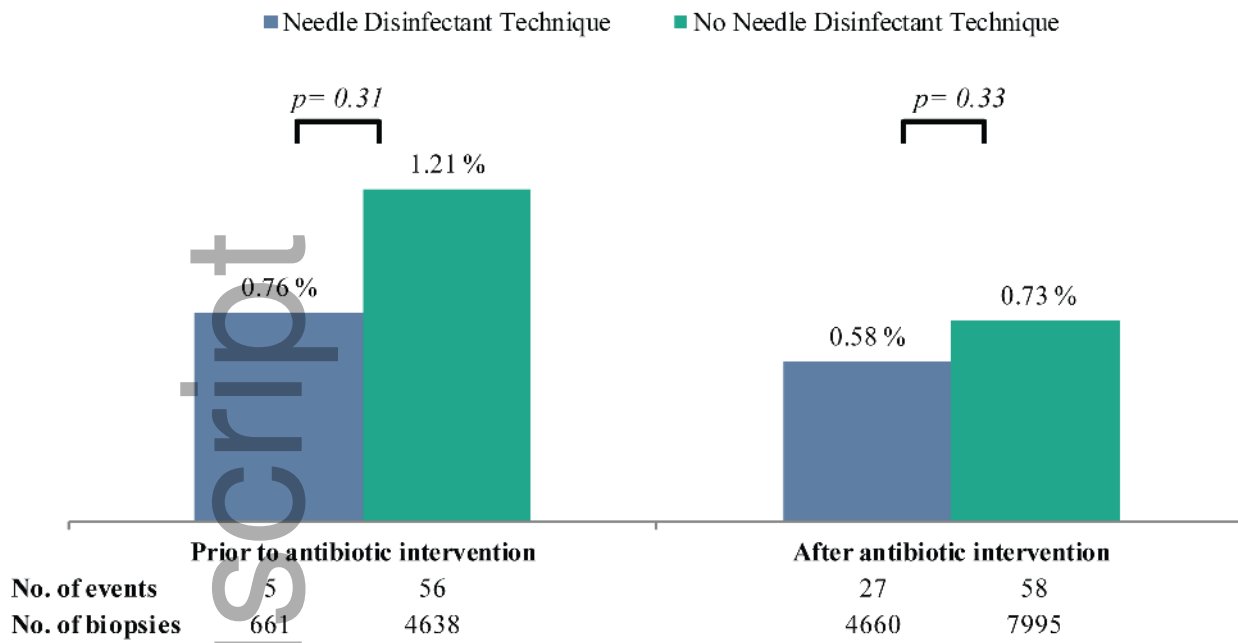
Author Manuscript



bjv_13982_f2.tif



bj_u_13982_f3.tif



bj_u_13982_f4.tif