

Research Article

Topical antiseptic at time of transrectal ultrasound prostate biopsy is associated with fewer severe clinical infections and improves antibiotic stewardship



Shayann Ramedani^a, Joseph Y. Clark^b, John J. Knoedler^b, Susan MacDonald^b,
Matthew G. Kaag^b, Suzanne B. Merrill^b, Jay D. Raman^{b,*}

^a Penn State College of Medicine, USA

^b Penn State Health Milton S. Hershey Medical Center, USA

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ABSTRACT

Background: The 2017 AUA White Paper on prevention of prostate needle biopsy (PNB) complications highlights an algorithm for reducing procedural related infections. The incorporation of topical rectal antiseptic (TRS) at time of transrectal PNB is listed as one such modality. We present data on over 1000 transrectal PNB procedures to determine the impact of TRS on 1) infectious complications and 2) use of augmented procedural antibiotics.

Methods: The records of 1181 transrectal PNB procedures performed over a 10-year period were reviewed. In 2013, TRS with either 10% povidone iodine or 4% chlorhexidine was more regularly incorporated into PNB procedures. Clinical and procedural factors were analyzed for association with post-procedure infections. Infectious complications outcomes were compared in patients receiving TRS (n = 566) versus those who had not (n = 615).

Results: A total of 990 men underwent 1181 transrectal PNB procedures. Median age of the cohort was 63 years with a median PSA of 7 ng/dL. Of them, 86% of the men were Caucasian, 28% had undergone at least one prior biopsy, 14% were diabetic, and 6% had prior hospitalization within 6 months of the procedure. Five hundred sixty-six patients (48%) received TRS at time of biopsy. Perioperative IV adjunctive antibiotics were used less frequently in patients receiving TRS (13.4% vs. 28.6%, p < 0.001). Furthermore, patients receiving TRS experienced lower rates of clinical infections (1.2% vs. 2.4%, p = 0.14), as well as lower likelihood of severe infections evidenced by decreased rates of hospital admission (0.5% vs. 2.3%, p = 0.013). Rectal vault bacteriology obtained before and after TRS was available in 180 men noting a 98.1% decrease in colony counts after local treatment.

Conclusions: TRS at time of transrectal PNB was associated with decreased use of IV procedural antibiotics as well as decreased severity of infections post-biopsy. This simple technique enhances antibiotic stewardship while simultaneously improving quality outcomes of the procedure.

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1. Introduction

In 2019, over 190,000 men were diagnosed with prostate cancer.¹ Although noninvasive modalities have continued to improve the diagnostic process, prostate needle biopsy (most commonly via the transrectal approach) remains the referent standard for rendering a cancer diagnosis.² Additionally, transrectal ultrasound-

guided prostate needle biopsy (TRUS PNB) with tissue sampling is a critical component for men with prostate cancer on an active surveillance regimen.² Therefore, it is paramount to optimize the safety profile of this procedure.

Infectious complications following TRUS PNB have increased over time with the primary culprit being colonization of the rectal vault with quinolone resistant gram-negative organisms.³ A variety of strategies can be employed to combat this increased risk including the use of rectal swab cultures to identify resistant organisms as well as augmented antibiotic regimens at time of biopsy.⁴ Both approaches have ample data highlighting effectiveness

* Corresponding author. Penn State Health Milton S. Hershey Medical Center, BMR Building c4830F, Hershey, 17033, PA, USA.

E-mail address: jraman@pennstatehealth.psu.edu (J.D. Raman).

therefore underscoring their potential role in clinical practice.⁴ The 2017 AUA White Paper on PNB complications additionally suggests alternate techniques such as rectal preparation or needle cleansing that can be used at time of procedure to further decrease the risk of infection.²

Povidone iodine (PI) and chlorhexidine are commonly used topical antiseptics that significantly reduce microorganism colony counts when applied to a surgical site. Prior work has highlighted that PI administered to the rectal vault at time of TRUS PNB decreases bacterial colony counts by over 97% with resultant decrease in procedural infectious complications.⁵ Two prior randomized trials as well as a systematic review further underscore the potential benefit without demonstrable adverse side effects from this therapy.^{6–8} The impact of PI topical rectal antiseptic on antibiotic stewardship and severity of infections, however, is less well defined.

Therefore, to better address this question, we reviewed a cohort of approximately 1200 TRUS PNB procedures to determine the impact of incorporating topical rectal antiseptic on 1) antibiotic stewardship; and 2) incidence and severity of infections post-procedure.

2. Material and methods

The charts of 990 consecutive men who underwent 1181 TRUS PNB from January 2008 to July 2018 were reviewed for post-biopsy complications. IRB approval was obtained for the patient's charts utilized in this study. All patients received one to three doses of preprocedure oral antibiotics (quinolone or trimethoprim/sulfamethoxazole). Periprocedural intravenous or parenteral agents (most commonly aminoglycosides or extended generation cephalosporins) were administered based on individual urologist preference. Rectal cultures were not used in our clinical practice over this time interval.

Biopsy procedures were either performed by faculty or by a resident under direct supervision by faculty according to institutional supervision requirements. A topical rectal antiseptic (TRS) preparation using 10% povidone-iodine (starting March 2012) or chlorhexidine 4% without alcohol (starting August 2015) was incorporated into biopsy procedures at the discretion of the treating urologist. Overall, in this 10-year study period, 566 patients received TRS at TRUS PNB compared to 615 who did not. Povidone-iodine 10% (N = 355) or chlorhexidine solution 4% without alcohol (N = 211) was used as topical antiseptic agent (Fig. 1). For patients treated with a topical rectal antiseptic, a gynecologic swab painted the perianal area and thereafter the rectal vault by techniques previously described in text⁵ and in video.⁹ TRUS PNB was

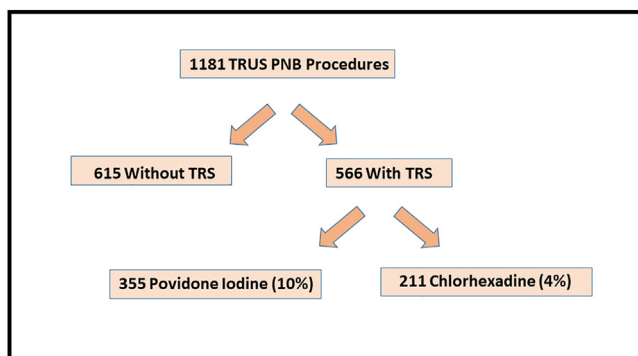


Fig. 1. Patient treatment cohorts.

performed by standard techniques after letting the prep dry for 2–3 minutes.

Baseline demographic information was collected regarding age, race, PSA, prior history of prostatitis, diabetes, immunosuppression, and history of prior prostate biopsy. Additional variables annotated were recent hospitalization or antibiotic use in the prior 6 months prior, number of cores obtained at biopsy, and presence of prostate cancer on biopsy pathology.

Outcomes of interest between the TRS and non-TRS cohorts included use of adjunctive procedural antibiotics, postoperative infection, bacteremia, hospital admission for infection, and ICU admission. These endpoints were determined by patient directed phone calls at 7 and 30 days after biopsy by a designated nurse and clinical research assistant as well as by office records at first post-biopsy visit. Statistical analysis was performed with SPSS version 27.0 with significance set at a p value ≤ 0.05 .

3. Results

A total of 990 men underwent 1181 transrectal PNB procedures over the study interval. Table 1 highlights the cohort characteristics stratified by receipt of procedural TRS. In summary, median age of the men was 63 years with a median PSA of 7 ng/dL. Eighty-six percent of the men were Caucasian, 28% had undergone at least one prior biopsy, 14% were diabetic, 3% were immunosuppressed, and 2% reported a history of prostatitis. Thirteen percent of men indicated exposure to antibiotics within 6 months of biopsy and 6% were hospitalized within 6 months prior to the procedure. There were some baseline differences in the cohort with respect to prior biopsy, hospitalization, and antibiotic exposure in the prior 6 months. There were no differences in the number of biopsy cores obtained between the two groups.

Table 2 summarizes data pertaining to procedural antibiotic prophylaxis and infections. Perioperative IV adjunctive antibiotics were used in 21% of cases albeit less frequently in patients receiving TRS (13.4% vs. 28.6%, $p < 0.001$). Overall, 1.9% of men experienced a clinical infection, 1.4% required hospital admission for this infection, 0.5% ICU admission, and 0.4% had evidence of culture positive bacteremia. Patients receiving TRS experienced lower rates of clinical infections (1.2% vs. 2.4%, $p = 0.14$), as well as likelihood of severe infections evidenced by decreased rates of hospital admission (0.5% vs. 2.3%, $p = 0.013$). When stratifying by type of TRS, we observed clinical infections and hospital admissions in 4/355 (1.1%) and 2/355 (0.6%) patients treated with povidone-iodine versus 3/211 (1.4%) and 1/211 (0.5%) patients treated with chlorhexidine.

Table 3 highlights logistic regression evaluating variables associated with clinical infections and hospital admissions. The use of topical rectal antiseptic was associated with a decreased likelihood of clinical infections (OR 0.79, $p = 0.04$), while antibiotic exposure within the previous 6 months was associated with a higher post-biopsy infection rate (odds ratio [OR] 3.22, $p = 0.005$). The remaining variables of interest were not associated with infectious complications following TRUS PNB. When considering hospital admissions, TRS was associated with fewer admissions after TRUS PNB (OR 0.59, $p = 0.005$), while hospitalization (OR 2.87, $p = 0.001$) and prior antibiotic use in the previous 6 months (OR 3.06, $p < 0.001$) were associated with admission to the hospital postprocedure.

Table 1 highlighted some baseline differences between the two cohorts. Most notably, antibiotic exposure over the prior 6 months varied between the groups and was found to be significantly associated with a three-fold greater risk of post-biopsy infection. To better determine the impact of TRS in a “cleaner” model, we re-performed the multivariate logistic regression after exclusion of the 149 patients with prior antibiotic exposure (57 TRS, 92 no TRS).

Table 1
Clinical and demographic characteristics of 990 men undergoing 1181 TRUS PNB procedures.

Variable	Total procedures (n = 1181)	Rectal antiseptic (n = 566)	No rectal antiseptic (n = 615)	p value
Age (median, range)	63 (43 – 92)	63 (43 – 86)	64 (45 – 92)	0.78
Caucasian race (No., %)	1013 (85.8)	480 (84.8)	533 (86.7)	0.41
Diabetes (No., %)	163 (13.8)	87 (15.4)	76 (12.4)	0.15
Hx Prostatitis (No., %)	27 (2.3)	15 (2.7)	12 (2.0)	0.44
Immunosuppression (No., %)	38 (3.2)	18 (3.2)	20 (3.3)	1.00
PSA level (median, range)	7 (1 – 882)	7 (1 – 358)	6 (1 – 882)	0.83
Prior biopsy (No., %)	326 (27.6)	134 (23.7)	192 (31.2)	0.004
Hospitalization prior 6 mos (No., %)	73 (6.2)	23 (4.1)	50 (8.1)	0.004
Abx exposure prior 6 mos (No., %)	149 (12.6)	57 (10.1)	92 (15.0)	0.01
Biopsy cores (median, range)	12 (3 – 48)	12 (1 – 60)	12 (3 – 48)	1.00

Hx, history; PSA, prostate-specific antigen; Abx, antibiotics.

Table 4 summarizes this revised model whereby the use of TRS continues to be associated with fewer biopsy infections (OR 0.86, $p = 0.04$) while hospitalization in the prior 6 months (OR 1.99, $p = 0.01$) now becomes significant.

Rectal vault microbiology data were available in 180 men. Mean colony counts decreased by 98.1% from 2.8×10^5 CFU/mL to 5.3×10^3 CFU/mL ($p < 0.001$) following administration of TRS.

4. Discussion

The goal of prostate needle biopsy is tissue sampling to render a diagnosis while limiting risks of the procedure including (but not limited to) infection, bleeding, and urinary retention. Infection risks remain the greatest concern following TRUS PNB particularly with the increased incidence of quinolone-resistant organisms colonizing the rectal vault.¹⁰ The 2017 AUA White Paper on complications of prostate needle biopsy offers a reasonable algorithm to tackle this problem with rectal antiseptic treatment being one proposed intervention.

In this study, we review a large cohort of patients undergoing TRUS PNB specifically focusing on the impact of topical rectal antiseptic (introduced in 2012) on infectious complications. Several observations were observed in this work. First, the rate of clinical infections following TRUS PNB decreased following implementation of a procedural rectal antiseptic. Second, the severity of infections declined as well as evidenced by a lower rate of hospital admissions and even more importantly intensive care unit monitoring. Third, the use of adjunctive systemic antibiotics at PNB was lower in the cohort who received topical rectal antiseptic.

The concept of using rectal cleansing mechanisms such as povidone-iodine and chlorhexidine is predicated on decreasing bacterial load through biocidal mechanisms including denaturing the cell wall, proteins, or nucleotides.¹¹ Our current observations are concordant with prior work implicating potential benefit with respect to infections. In 2012, Ghafoori and colleagues performed a randomized prospective study in 280 patients noting the use of a povidone iodine preparation yielded a 2.4 fold decreased risk of infection (95% confidence interval 1.4 – 4.1, $p = 0.001$).⁶ In 2013, AbuGhosh et al. similarly investigated the potential benefit of

povidone-iodine in a randomized prospective study of 865 patients. Here, the authors noted a 42% risk reduction in infections in the rectal antiseptic group (2.6% vs. 4.5%) albeit not statistically significant ($p = 0.15$). Finally, a large systematic review by Pu and colleagues encompassing seven trials and 2049 patients noted that a povidone-iodine rectal preparation significantly reduced the incidence of fevers, bacteriuria, and bacteremia compared with controls.⁸

Unique to this current work is our observation that rectal antiseptic reduces the severity of clinical infections with associated reduction of associated costs. Antibiotic resistance associated with sepsis yields potential annual health care costs of almost 2.9 billion dollars attributable not only to the cost of hospitalization but also potential for ICU care, expensive parenteral therapies, as well as loss of economic potential of the impacted patient. When considering that povidone-iodine costs approximately 10 cents, it is increasingly apparent that the enormous potential for cost savings with a relatively miniscule investment compared to the average ICU stay for sepsis being 70,000 dollars.¹² Furthermore, in a recent review analyzing cumulative costs of prostate biopsy infection, Gross and colleagues identified that average hospitalization ranged from 1.1 to 14 days and the percent admitted to an ICU ranged from 1.1% to 25%.¹³ The estimated cost of sepsis post-prostate biopsy, adjusted for inflation, ranged from \$8,672 to \$19,100 USD. When considering our experience, the use of TRS would have yielded a cumulative cost savings of approximately \$167,000 USD.

The use of rectal antiseptic also improves antibiotic stewardship through reduction of additional procedural augmented treatment. Indeed, antibiotic augmentation is one reasonable approach to combat TRUS PNB infections. However, flaws exist with this strategy when considering long-term implications in patients. Notably, many organisms which are resistant to quinolones are multidrug resistant and therefore additional antibiotic therapy is not necessarily always effective. Furthermore, men undergoing PNB whether it be for diagnosis or surveillance of prostate cancer will often require repeat biopsy procedures in the future.¹⁴ Routine use of augmented antibiotics while helpful in the short term may further compound the issue of resistant organisms thereby limiting the effectiveness of augmentation in the future.¹⁵

Table 2
Infectious complications following TRUS PNB.

Variable	Total procedures (n = 1181)	Rectal antiseptic (n = 566)	No rectal antiseptic (n = 615)	p value
Adjunctive peri-op Abx (No., %)	252 (21.3)	76 (13.4)	176 (28.6)	< 0.001
Clinical infection* (No., %)	22 (1.9)	7 (1.2)	15 (2.4)	0.14
Hospital admission for infection (No., %)	17 (1.4)	3 (0.5)	14 (2.3)	0.013
ICU admission (No., %)	6 (0.5)	1 (0.2)	5 (0.8)	0.22
Bacteremia (No., %)	5 (0.4)	1 (0.2)	4 (0.7)	0.38

Abx, antibiotics; ICU, intensive care unit.

* Defined as documented fever ≥ 38.5 C or culture positivity (urine and/or blood).

Table 3
Logistic regression for variables associated with clinical infections and hospital admission.

Variable	Clinical infections			Hospital admission		
	OR	95% CI	p value	OR	95% CI	p value
Age (per 5 year increment)	1.10	0.83 – 1.44	0.67	1.07	0.89 – 1.58	0.71
Caucasian race	0.93	0.79 – 1.22	0.49	0.98	0.91 – 1.44	0.62
Diabetes	1.17	0.98 – 1.51	0.22	1.31	0.94 – 1.66	0.26
Hx prostatitis	1.62	1.31 – 1.98	0.17	1.28	1.01 – 1.88	0.21
Immunosuppression	1.77	0.88 – 3.62	0.37	1.89	0.76 – 3.44	0.48
PSA level	1.02	0.69 – 1.61	0.88	0.99	0.64 – 1.69	0.91
Prior biopsy	1.43	1.16 – 1.89	0.26	1.77	1.35 – 1.92	0.19
Topical Rectal antiseptic	0.79	0.51 – 0.93	0.04	0.59	0.43 – 0.76	0.005
Hospitalization prior 6 mos	1.58	1.44 – 2.22	0.09	2.87	1.21 – 5.07	0.001
Abx exposure prior 6 mos	3.22	1.87 – 6.33	0.005	3.06	1.46 – 7.11	< 0.001

CI, confidence interval; OR, odds ratio.

Table 4
Logistic regression for variables associated with clinical infections excluding the 149 patients with prior antibiotic exposure (57 TRS, 92 no TRS).

Variable	Odds ratio	95% confidence interval	p value
Age (per 5 year increment)	1.18	0.91 – 1.75	0.59
Caucasian race	0.94	0.79 – 1.26	0.52
Diabetes	1.04	0.87 – 1.56	0.19
Hx prostatitis	1.28	1.11 – 1.87	0.24
Immunosuppression	1.53	0.61 – 4.01	0.29
PSA level	0.98	0.71 – 1.46	0.92
Prior biopsy	1.37	1.09 – 1.67	0.31
Topical rectal antiseptic	0.86	0.73 – 0.98	0.04
Hospitalization prior 6 mos	1.99	1.67 – 2.88	0.01

We acknowledge some limitations in our work. First, these data originate from a single large academic medical center caring for a rural population of patients and the observations may not be generalizable to a different cohort of patients. Specifically, data do highlight variances in local antibiogram based on local region.¹⁶ Second, the potential exists to miss subclinical infections or those that may have been managed outside of our health system. Third, this experience does not reflect incorporation of a rectal swab protocol which can culture for quinolone resistant gram-negative organisms.¹⁷ Indeed, we began incorporating this strategy (in addition to the use of TRS) in 2018 with initial experience noting an infection rate of 0.6% (data not shown).

Nonetheless, we believe our work confirms prior findings of the benefits of topical rectal antiseptic while exploring novel benefits with regards to infection severity and antibiotic stewardship. We therefore believe that this easily employed procedural element should continue to be employed in practice and should remain as part of the algorithm in future quality initiatives explored in this realm.

5. Conclusion

Topical rectal antiseptic at time of TRUS PNB not only decreases the incidence and severity of clinical infections but also improves antibiotic stewardship by limiting routine systemic therapy. Given the negligible side effect profile, this should become a regular procedural component for patients undergoing TRUS PNB.

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Conflicts of interest

None.

References

- Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. *CA: A Cancer J Clin* 2019;69(1):7–34. <https://doi.org/10.3322/caac.21551>.
- Liss MA, Ehdaie B, Loeb S, Meng MV, Raman JD, Spears V, et al. An Update of the American Urological Association White Paper on the Prevention and Treatment of the More Common Complications Related to Prostate Biopsy. *J Urol* 2017;198(2):329–34. <https://doi.org/10.1016/j.juro.2017.01.103>.
- Liss MA, Chang A, Santos R, Nakama-Peeples A, Peterson EM, Osann K, et al. Prevalence and significance of fluoroquinolone resistant *Escherichia coli* in patients undergoing transrectal ultrasound guided prostate needle biopsy. *J Urol* 2011;185(4):1283–8. <https://doi.org/10.1016/j.juro.2010.11.088>.
- Lu DD, Raman JD. Strategies for prevention of ultrasound-guided prostate biopsy infections. *Infection and Drug Resistance* 2016;9:161–9. <https://doi.org/10.2147/IDR.S96163>. Dove Medical Press Ltd.
- Gyorfi JR, Otteni C, Brown K, Patel A, Lehman K, Phillips BE, et al. Peri-procedural povidone-iodine rectal preparation reduces microorganism counts and infectious complications following ultrasound-guided needle biopsy of the prostate. *World J Urol* 2014;32(4):905–9. <https://doi.org/10.1007/s00345-014-1291-8>.
- Ghafoori M, Shakiba M, Seifmanesh H, Hoseini K. RADIOLOGY Iranian Journal of urogenital imaging & contrast media Decrease in Infection Rate Following Use of Povidone-Iodine During Transrectal Ultrasound Guided Biopsy of the Prostate: A Double Blind Randomized Clinical Trial. *Iran J Radiol* 2012;9(2):67–70. <https://doi.org/10.5812/iranjradiol.7561>.
- Abughosh Z, Margolick J, Goldenberg SL, Taylor SA, Afshar K, Bell R, et al. A prospective randomized trial of povidone-iodine prophylactic cleansing of the rectum before transrectal ultrasound guided prostate biopsy. *J Urol* 2013;189(4):1326–31. <https://doi.org/10.1016/j.juro.2012.09.121>.
- Pu C, Bai Y, Yuan H, Li J, Tang Y, Wang J, et al. Reducing the risk of infection for transrectal prostate biopsy with povidone-iodine: a systematic review and meta-analysis. *Int Urol Nephrol* 2014;46(9):1691–8. <https://doi.org/10.1007/s11255-014-0713-2>.
- Raman JD, Lehman KK, Dewan K, Kirimanjeswara G. Povidone iodine rectal preparation at time of prostate needle biopsy is a simple and reproducible means to reduce risk of procedural infection. *JoVE* 2015;2015(103). <https://doi.org/10.3791/52670>.
- Zani EL, Clark OAC, Rodrigues Netto Jr N. Antibiotic prophylaxis for transrectal prostate biopsy. *Cochrane Database Syst Rev* 2011;5. <https://doi.org/10.1002/14651858.cd006576.pub2>.
- Zhao D, Lim CP, Miyayama K, Tanji Y. Iodine from bacterial iodide oxidation by *Roseovarius* spp. inhibits the growth of other bacteria. *Appl Microbiol Biotechnol* 2013;97(5):2173–82. <https://doi.org/10.1007/s00253-012-4043-y>.
- Chin-Yee N, D'Egidio G, Thavorn K, Heyland D, Kyeremanteng K. Cost analysis of the very elderly admitted to intensive care units. *Crit Care* 2017;21(1):109. <https://doi.org/10.1186/s13054-017-1689-y>.
- Gross MD, Alshak MN, Shoag JE, Laviana AA, Gorin MA, Sedrakyan A, et al. Healthcare Costs of Post-Prostate Biopsy Sepsis. *Urology* 2019;133:11–5. <https://doi.org/10.1016/j.urology.2019.06.011>. Elsevier Inc.
- Heidenreich A, Bellmunt J, Bolla M, Joniau S, Mason M, Matveev V, et al. EAU guidelines on prostate cancer. Part 1: Screening, diagnosis, and treatment of clinically localised disease. *Eur Urol* 2011;59(1):61–71. <https://doi.org/10.1016/j.eururo.2010.10.039>.

15. Horcajada JP, Busto M, Grau S, Sorlí L, Terradas R, Salvadó M, et al. High Prevalence of Extended-spectrum Beta-lactamase-producing Enterobacteriaceae in Bacteremia After Transrectal Ultrasound-guided Prostate Biopsy: A Need for Changing Preventive Protocol. *Urology* 2009;74(6):1195–9. <https://doi.org/10.1016/j.urology.2009.06.061>.
16. Yaghi MD, Kehinde EO. Oral antibiotics in trans-rectal prostate biopsy and its efficacy to reduce infectious complications: Systematic review. *Urology Annals* 2015;7(4):417–27. <https://doi.org/10.4103/0974-7796.164860>. Medknow Publications.
17. Cussans A, Somani BK, Basarab A, Dudderidge TJ. The role of targeted prophylactic antimicrobial therapy before transrectal ultrasonography-guided prostate biopsy in reducing infection rates: A systematic review. *BJU Int* 2016;117(5):725–31. <https://doi.org/10.1111/bju.13402>. Blackwell Publishing Ltd.