# Benzoyl Peroxide is Cost-Effective for Preventing Infection by *Cutibacterium Acnes* in Arthroscopic Rotator Cuff Repair



Pearce W. Lane, B.S., B. Gage Griswold, M.D., Daniel W. Paré, B.S., Brandon D. Bushnell, M.D., M.B.A., and Stephen A. Parada, M.D.

Purpose: To evaluate the cost-effectiveness of benzoyl peroxide (BPO) in decreasing postoperative infections through a mathematical model in the setting of arthroscopic rotator cuff repair (RCR). Methods: A break-even equation compared the costs associated with perioperative BPO use and postoperative infection following an arthroscopic RCR. The postoperative infection rate used for calculations was 0.28%, a value established in current literature. The break-even analysis produced a new infection rate, which defined how much BPO is needed to reduce the known infection rate in order for its prophylactic use to be cost-effective. The institution's business office assessed the minimum itemized costs associated with the standard-of-care treatment of postoperative RCR infection. Sensitivity analysis was conducted to demonstrate how variability in the costs of BPO, in infection rates and in the cost of infection treatment affected the absolute risk reduction (ARR) and number needed to treat (NNT). Results: Financial review yielded a minimum institutional cost of treating a postoperative infection following arthroscopic RCR of \$24,991.31. Using the break-even formula to calculate the ARR at which the overhead costs of BPO and the treatment of infection were equal, BPO was economically viable if it decreased infection rate by 0.000734% (NNT = 1,361.92). This value was low because of the order of magnitude of difference between the costs of infection prevention when compared to the costs of treating postoperative infections. **Conclusions:** This break-even analysis model suggests that the use of preoperative BPO in the setting of arthroscopic RCR is cost-effective for prevention of infection with *Cutibacterium acnes*, given the high cost of treating the infection versus the low cost of the solution. **Clinical Relevance:** The economic feasibility of preoperative use of BPO in the setting of arthroscopic RCR could alter the standard of care.

**P**ostoperative infection in the setting of arthroscopic shoulder surgery is rare; however, it is very costly for both the patient and the health care system. The reported incidence of infection following arthroscopic shoulder surgery in the PearlDiver Patient Record Database of 165,820 patients was 0.27%. The study

2666-061X/201887 https://doi.org/10.1016/j.asmr.2021.03.021 further specified the incidence of infection after arthroscopic rotator cuff repair (RCR) to be 0.29%.<sup>1</sup> Pauzenberger et al. similarly found an indicidence of 0.28% in a population of more than 3,000 patients.<sup>2</sup>

Cutibacterium acnes (C. acnes) is a problematic organism in shoulder surgery because it can be responsible for postoperative infections even after arthroscopic procedures. C. acnes (formerly known as Propionibacterium acnes) is a non-spore-forming, anaerobic, gram-positive rod of the normal cutaneous flora, especially in areas rich with pilosebaceous glands such as the shoulder.<sup>3-7</sup> Case reports have demonstrated significant pathology of the joint following infection, some requiring arthroplasty. Additionally, patients have experienced complications resulting from the medical treatment of the infection, including deep venous thrombosis and secondary wound-site infections.<sup>8</sup> A recent study found that 20% of patients required more than a single reoperation.<sup>9</sup> Each complication presents additional cost to the institution and the patient.

From the Medical College of Georgia, Augusta University, Augusta, Georgia, U.S.A. (P.W.L., D.W.P.), Department of Orthopaedics, Augusta University Medical Center, Augusta, Georgia, U.S.A. (B.G.G., B.D.B., S.A.P.), and Harbin Clinic Orthopaedics and Sports Medicine, Rome, Georgia, U.S.A. (B.D.B.).

The authors report no conflicts of interest in the authorship and publication of this article. Full ICMJE author disclosure forms are available for this article online, as supplementary material.

Received November 20, 2020; accepted March 27, 2021.

Address correspondence to Pearce W. Lane, B.S., 1120 15th Street, Augusta, Georgia, U.S.A. E-mail: pearcewlane@gmail.com

<sup>© 2021</sup> THE AUTHORS. Published by Elsevier Inc. on behalf of the Arthroscopy Association of North America. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

$$IR_{f} = \frac{(IR_{i} \times C_{t}) - C_{d}}{C_{t}} \begin{cases} Where: \\ R_{t} = Final (break-even) infection rate \\ R_{t} = Initial (current) infection rate \\ C_{t} = Cost to treat infection \\ C_{b} = Cost of decolonization of skin \end{cases}$$

**Fig 1.** Break-even equation used to calculate the financial efficacy of BPO.

Standard perioperative skin preparation with chlorhexidine gluconate (CHG) has proven to be ineffective in decolonizing *C. acnes* from the shoulder region due to the organism's ability to reside within dermal sebaceous glands and hair follicles.<sup>10,11</sup> Benzoyl peroxide (BPO) has been shown to be more effective in reducing the bioburden of *C. acnes* on skin both at the beginning and at the conclusion of shoulder surgery.<sup>12,13</sup> This may result in a hypothetical lower risk of postoperative infection.

A recent study substantiated the financial benefit of BPO in shoulder arthroplasty. The authors found BPO to be cost-effective if it prevented infection in at least 1 of 4,348 shoulder arthroplasties, which equated to an absolute risk reduction (ARR) of 0.023%.<sup>14</sup>

The purpose of this study was to evaluate the costeffectiveness of using BPO to decrease postoperative infections. We used a mathematical model in the setting of arthroscopic RCR, hypothesizing that the preoperative use of BPO would be financially cost-effective in decreasing postoperative infections following arthroscopic RCR.

#### Methods

A break-even infection rate analysis was calculated by using the institutional costs (provided by the business office at the authors' hospital) associated with treating a postoperative infection following an arthroscopic RCR. Hatch et al. originally developed an equation to determine the economic viability of insituting a new protocol with an associated increased cost.<sup>15</sup> This analysis employs an equation to determine the final infection rate required for a new protocol to be economically viable, given the initial infection rate, the total cost of treating an infection and the cost of an infection-prevention strategy (Fig 1).<sup>16</sup> Calculating the difference between the initial and final infection rates yields ARR, which is the percent by which a protocol must reduce the infection rate to justify economically its use as a prophylactic measure. The number needed to treat (NNT) was calculated from the inverse of ARR. The NNT in this study indicates the minimum number of patients who must be treated to prevent 1 infection for the indication to be fiscally responsible. This study did not require Institutional Review Board approval.

The costs of skin-preparation solutions, the costs of treating postoperative infections and infection rates themselves are variable. These variables are dependent on the source of data or institution and are likely to evolve over time. With this in mind, a sensitivity analysis was performed in which the break-even infection rate was calculated over a range of costs and infection rates to ensure that the findings could be applied in assorted settings.

The estimated incidence of infection was obtained from 2 different studies. Pauzenberger, et al. reviewed the cases of 3,294 arthroscopic RCRs and demonstrated an overall infection rate of 0.85%; however, this number included many patients who did not receive preoperative antibiotics. The patient population that did not receive preoperative antibiotics had a significantly higher infection rate (1.54% vs 0.28%).<sup>2</sup> Another large study, by Yeranosian and colleagues, found the incidence of postoperative infection after arthroscopic RCR to be 0.29%, although the authors did not specificy whether or not preoperative antibiotics were dministered.<sup>1</sup> Felsch et al. observed a similar incidence in 2020.<sup>17</sup> With 2 highly powered studies demonstrating similar incidence of infection, an incidence rate of 0.28% was selected for our calculations.

The product costs of BPO and the cost of treating an infected arthroscopic RCR were obtained from the institution's purchasing records. The cost of a benzoyl peroxide 5% gel 60-gram tube was \$18.35, whereas chlorhexidine gluconate 2% 120 milliliter solution costs \$2.66 per container. The expected cost for hospital admission, a single irrigation and debridement procedure along with antibiotic treatment for an infected arthroscopic RCR at the authors' institution was found to be \$24,991.31 (Table 1).

#### Results

Using the break-even formula, CHG was found to be economically viable if it decreased the infection rate by 0.000106% (NNT = 9,395.23) (Table 2). The cost of BPO was found to be economically beneficial if it decreased the infection rate by 0.000734% (NNT =1,361.92). This demonstrates that BPO provides an economic benefit if it

**Table 1.** Average Cost of Managing an Arthroscopy RCR

 Infection at Our Institution

Intervention	Cost (\$) Per Unit	Units Required	Total cost (\$)
Hospital admission for	20930.00	1	20930.00
irrigation and debridement			
ID Consult	116.85	1	116.85
Cultures		1	0.00
Hospital stay, 2-3 days	1075.08	3	3225.24
PICC line placement	145.23	1	145.23
Penicillin (3 mil units q4	2.50	224	560.00
hrs) $\times$ 2 weeks			
Doxycycline (100 mg BID) $\times$ 2	1.00	14	14.00
weeks			
Total			24991.31

ID, infectious disease; PICC, peripherally-inserted central catheter.

	BPO			CHG		
Rate Of Infection (%)	Break-even (%)	ARR (%)	NNT	Break-even (%)	ARR (%)	NNT
0.05	0.049265745	0.000734255	1361.924251	0.049893563	0.000106437	9395.22932
0.15	0.149265745	0.000734255	1361.924251	0.149893563	0.000106437	9395.22932
0.28	0.279265745	0.000734255	1361.924251	0.279893563	0.000106437	9395.22932
0.35	0.349265745	0.000734255	1361.924251	0.349893563	0.000106437	9395.22932
0.45	0.449265745	0.000734255	1361.924251	0.449893563	0.000106437	9395.22932

Table 2. Maintaining Cost of BPO and the Cost of Treating Infection While Varying Initial Infection Rates

ARR, absolute risk reduction; BPO, benzoyl peroxide; CHG, chlorhexidine gluconate; NNT, number needed to treat.

Presume a cost of CHG \$2.66, BPO \$18.35 and treatment cost of \$24,991.31.

Boldface denotes the infection rate used.

prevents at least 1 infection of 1,361.92 arthroscopic RCR surgeries (NNT), whereas the use of CHG is justified if it prevents 1 infection of 9,395.23 arthroscopic RCR cases (NNT). The necessary ARR is constant when considering higher infection rates while holding constant the cost of the skin decolonization protocols and those of treating the infection. Table 3 demonstrates a decreasing ARR necessary to break even for both CHG and BPO, increasing costs associated with treating with postoperative infection. An ARR of 0.001835 (NNT = 544.96) is required to break even if postoperative infection treatment costs \$10,000, but only an ARR of 0.00046 (NNT = 2,179.84) is necessary if the treatment costs \$40,000.

#### Discussion

The findings of this study support the economic advantage of BPO in the perioperative setting because of the significant difference in the cost to treat a post-operative infection compared to the minimal cost of the solution. *C. acnes* presents an unlikely but potentially devastating risk of postoperative infection following an arthroscopic RCR. Despite an infection rate of only an estimated 0.28%, the risk necessitates diligent prevention.

Although the NNT values seem disparate, the low ARR values resulted from the order of magnitude difference between the costs of this preoperative infection prevention compared to the cost of treating a post-operative infection (Table 2). This vast difference in costs requires so little improvement in infection rates to

break even that seemingly large changes in initial infection rates yield virtually equivalent results. Given that the cost of treating a postoperative infection after an arthroscopic RCR may vary across institutions and treatment protocols, a constant rate of infection and cost of skin decolonization demonstrates an inverse relationship between economic viability of BPO and the cost of treating postoperative infection (Table 3).

Surgical debridement and long-term antibiotics are typically the mainstay of treatment for postoperative infection following arthroscopic RCR.<sup>6</sup> Multiple debridements may be required to eradicate the infection, which will often impact the patient's outcome significantly.<sup>8,18</sup> Kwon et al. demonstrated an average number of 2.6 surgical debridements per patient with postoperative infection following arthroscopic RCR. The patients involved completed University of California, Los Angeles, shoulder-scoring system questionnaires, which revealed that more than half of the cohort was dissatisfied with the postoperative outcome.<sup>18</sup>

*C. acnes* is also known to be present as normal skin flora of the shoulder and can remain present after standard surgical preparation.<sup>11</sup> Chuang et al. found that patients undergoing arthroscopic shoulder surgery still had a high incidence of *C. acnes*-positive superficial and deep cultures (72.5% and 19.6%), even after a standard skin preparation with 4% chlorhexidine and 2% chlorhexidine gluconate/70% isopropyl alcohol.<sup>7</sup>

Several studies have demonstrated the usefulness of preoperative BPO in various shoulder procedures. In a

Table 3. Maintaining the Cost of BPO and Initial Infection Rate Constant While Varying the Cost of Treating Infection

	Benzoyl Peroxide			Chlorhexidine Gluconate			
Cost (\$)	Break-even (%)	ARR (%)	NNT	Break-even (%)	ARR (%)	NNT	
10,000	0.278165	0.001835	544.9591281	0.278165	0.001835	544.9591281	
20,000	0.2790825	0.0009175	1089.918256	0.2790825	0.0009175	1089.918256	
24,991.31	0.279265745	0.000734255	1361.924251	0.279265745	0.000734255	1361.924251	
30,000	0.279388333	0.000611667	1634.877384	0.279388333	0.000611667	1634.877384	
35,000	0.279475714	0.000524286	1907.356948	0.279475714	0.000524286	1907.356948	
40,000	0.27954125	0.00045875	2179.836512	0.27954125	0.00045875	2179.836512	

Presumes that the cost of chlorhexidine gluconate is \$2.66 and the cost of benzoyl peroxide is \$18.35; there is an initial infection rate of 0.28%. ARR, absolute risk reduction.

Boldface values denote cost at our institution.

double-blinded, randomized trial of patients undergoing primary or revision arthroplasty or arthroscopic shoulder surgery, Kolakowski et al. compared the positive culture rate with the use of BPO versus CHG, using the contralateral shoulder as a negative control. This study instructed participants to perform 3-minute shoulder washes with the assigned solution on preoperative days -2 and -1 as well as on the morning of surgery. Samples collected prior to the procedure demonstrated fewer positive cultures in participants who washed with BPO, and no changes were seen with the CHG group compared to the controls.<sup>12</sup> In another study evaluating BPO in arthroscopic procedures, Sabetta et al. demonstrated that the use of a BPO skin preparation reduces the number of 1 or more positive cultures with C. acnes after undergoing arthroscopic shoulder surgery. The authors found that preoperative BPO washes, beginning 48 hours prior to surgery, reduced the rate of cultures positive for C. acnes by approximately 50%.<sup>13</sup>

The benefit of hydrogen peroxide, which is the active ingredient in BPO, in addition to standard preoperative preparations has also been evaluated. Chalmers et al. demonstrated that hydrogen peroxide was associated with a significant decrease in the number of patients with triple-positive cultures as compared to the controls, but there was no significant difference in the percentage of patients with 1, 2 or more positive skin, dermal or joint cultures with the addition of hydrogen peroxide.<sup>19</sup> Yamakado's study suggests no significant reduction of *C. acnes* with the use of hydrogen peroxide.<sup>20</sup> The results demonstrate that although a hydrogen peroxide solution is likely to be beneficial in reducing the bacterial burden, it is not a replacement for BPO.

### Limitations

There are several limitations in this study. The primary limitation is the use of mathematical modeling to generate a break-even cost analysis. A randomized controlled trial in which the authors controlled for BPO application techniques and compliance in order to evaluate the clinical outcomes in the setting of arthroscopic RCR would identify the precise financial benefit of BPO. Another limitation is that the model used cost data specific to the authors' institution. It is likely that the costs associated with the treatment of postoperative complications vary widely across regions and are likely to evolve over time.

# Conclusions

This break-even analysis model suggests that the use of preoperative BPO in the setting of arthroscopic RCR is cost effective for the prevention of infection with *C. acnes,* given the high cost of treating the infection versus the low cost of the solution.

## References

- Yeranosian MG, Arshi A, Terrell RD, Wang JC, McAllister DR, Petrigliano FA. Incidence of acute postoperative infections requiring reoperation after arthroscopic shoulder surgery. *Am J Sports Med* 2014;42: 437-441. https://doi.org/10.1177/0363546513510686.
- 2. Pauzenberger L, Grieb A, Hexel M, Laky B, Anderl W, Heuberer P. Infections following arthroscopic rotator cuff repair: Incidence, risk factors, and prophylaxis. *Knee Surg Sports Traumatol Arthrosc* 2017;25:595-601. https://doi.org/10.1007/s00167-016-4202-2.
- 3. Scholz CFP, Kilian M. The natural history of cutaneous propionibacteria, and reclassification of selected species within the genus Propionibacterium to the proposed novel genera Acidipropionibacterium gen. nov., Cutibacterium gen. nov. and Pseudopropionibacterium gen. nov. *Int J Syst Evol Microbiol* 2016;66:4422-4432. https://doi.org/10.1099/ijsem.0.001367.
- Christensen GJ, Bruggemann H. Bacterial skin commensals and their role as host guardians. *Benef Microbes* 2014;5: 201-215. https://doi.org/10.3920/BM2012.0062.
- 5. Patel A, Calfee RP, Plante M, Fischer SA, Green A. Propionibacterium acnes colonization of the human shoulder. *J Shoulder Elbow Surg* 2009;18:897-902. https://doi. org/10.1016/j.jse.2009.01.023.
- Atesok K, MacDonald P, Leiter J, McRae S, Stranges G, Old J. Postoperative deep-shoulder infections following rotator cuff repair. *World J Orthop* 2017;8:612-618. https:// doi.org/10.5312/wjo.v8.i8.612.
- Chuang MJ, Jancosko JJ, Mendoza V, Nottage WM. The incidence of Propionibacterium acnes in shoulder arthroscopy. *Arthroscopy* 2015;31:1702-1707. https://doi. org/10.1016/j.arthro.2015.01.029.
- Athwal GS, Sperling JW, Rispoli DM, Cofield RH. Deep infection after rotator cuff repair. *J Shoulder Elbow Surg* 2007;16:306-311. https://doi.org/10.1016/j.jse.2006.05. 013.
- Frank JK, Nadiotis N, Heuberer PR, Laky B, Anderl W, Pauzenberger L. Mid- to long-term outcomes after deep infections after arthroscopic rotator cuff repair. *Arthrosc Sports Med Rehabil* 2020;2:e315-e320. https://doi.org/10. 1016/j.asmr.2020.03.004.
- Sethi PM, Sabetta JR, Stuek SJ, et al. Presence of Propionibacterium acnes in primary shoulder arthroscopy: Results of aspiration and tissue cultures. *J Shoulder Elbow Surg* 2015;24:796-803. https://doi.org/10.1016/j.jse.2014. 09.042.
- 11. Lee MJ, Pottinger PS, Butler-Wu S, Bumgarner RE, Russ SM, Matsen FA 3rd. Propionibacterium persists in the skin despite standard surgical preparation. *J Bone Joint Surg Am* 2014;96:1447-1450. https://doi.org/10.2106/ JBJS.M.01474.
- Kolakowski L, Lai JK, Duvall GT, et al. Neer Award 2018: Benzoyl peroxide effectively decreases preoperative *Cuti-bacterium acnes* shoulder burden: A prospective randomized controlled trial. *J Shoulder Elbow Surg* 2018;27: 1539-1544. https://doi.org/10.1016/j.jse.2018.06.012.
- 13. Sabetta JR, Rana VP, Vadasdi KB, et al. Efficacy of topical benzoyl peroxide on the reduction of *Propionibacterium acnes* during shoulder surgery. J Shoulder Elbow Surg

2015;24:995-1004. https://doi.org/10.1016/j.jse.2015.04. 003.

- 14. Menendez ME, Moverman MA, Puzzitiello RN, Pagani NR, Namdari S. A break-even analysis of benzoyl peroxide and hydrogen peroxide for infection prevention in shoulder arthroplasty. *J Shoulder Elbow Surg* 2020;29:2185-2189. https://doi.org/10.1016/j.jse.2020. 06.019.
- Hatch MD, Daniels SD, Glerum KM, Higgins LD. The costeffectiveness of vancomycin for preventing infections after shoulder arthroplasty: A break-even analysis. *J Shoulder Elbow Surg* 2017;26:472-477. https://doi.org/10.1016/j.jse. 2016.07.071.
- Kirchner GJ, Ghazaryan H, Lieber AM, Sunkerneni AR, McKinnon BJ. Cost-effectiveness of preoperative *Staphylococcus aureus* screening and decolonization in cochlear implantation. *OTO Open* 2019;3:2473974X19866391. https:// doi.org/10.1177/2473974X19866391.

- 17. Felsch Q, Mai V, Durchholz H, et al. Complications within 6 months after arthroscopic rotator cuff repair: Registrybased evaluation according to a core event set and severity grading. *Arthroscopy* 2021;37:50-58. https://doi. org/10.1016/j.arthro.2020.08.010.
- Kwon YW, Kalainov DM, Rose HA, Bisson LJ, Weiland AJ. Management of early deep infection after rotator cuff repair surgery. *J Shoulder Elbow Surg* 2005;14: 1-5. https://doi.org/10.1016/j.jse.2004.04.010.
- Chalmers PN, Beck L, Stertz I, Tashjian RZ. Hydrogen peroxide skin preparation reduces *Cutibacterium acnes* in shoulder arthroplasty: A prospective, blinded, controlled trial. *J Shoulder Elbow Surg* 2019;28:1554-1561. https:// doi.org/10.1016/j.jse.2019.03.038.
- Yamakado K. Hydrogen peroxide does not significantly reduce *Cutibacterium acnes* suture contamination in arthroscopic rotator cuff repair. *Arthroscopy* 2020;37: 1134-1140. https://doi.org/10.1016/j.arthro.2020.12.186.