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# **REVIEW** Systematic review and meta-analysis on management of acute urinary retention

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**BACKGROUND:** Acute urinary retention (AUR) is a common urological emergency. In this article, we review the current literature and present a structured summary in management of AUR.

**METHODS:** A systematic review was conducted using the keywords 'acute AND retention AND urin\*' within the title in search engines including Medline, EMBASE and EBM Review. The obtained literature was manually reviewed by the primary author (PDY) and was further refined by confining the subject to management of AUR. Exclusion criteria included paediatric and female population studies, case reports, reviews, surveys, economical assessment and articles on AUR in prostate cancer and post-operative patients.

**RESULTS:** Total of 54 articles met our inclusion and exclusion criteria. The trial without catheter (TWOC) post-immediate catheterisation is widely practiced although there remains a significant variability in terms of type and duration of catheterisation required, use of concurrent medical therapy or post-catheterisation management. Our systematic review and subsequent meta-analysis has shown superiority of  $\alpha_1$ -adrenergic receptor blockers over placebo in achieving successful voiding in patients with AUR. Suprapubic catheter (SPC) is an alternative to urethral catheterisation (indwelling catheter (IDC)) and may provide several advantages. Clean intermittent self-catheterisation may be a safe and useful option for patients with AUR until their definitive management. The overall long-term outcome of in-and-out catheterisation remains promising in selected patients. Surgery is an end point in patients with unsuccessful TWOC as well as in those with significant lower urinary tract symptoms post-successful TWOC.

**CONCLUSIONS:** We recommend use of  $\alpha_1$ -adrenergic receptor blockers before TWOC and discourage emergency operative management. Use of SPC over IDC in AUR is debatable. Duration of catheterisation is controversial but <3 days is a safe option in avoiding catheterisation-related complications. Although TURP remains the current gold standard, there has been an emergence of newer operative management utilising laser techniques.

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# INTRODUCTION

Acute urinary retention (AUR) is a common urological emergency associated with inability to empty the bladder to completion.<sup>1</sup> It is a complex presentation that may represent various pathological processes and more than 10% of men in their 70's and a third in their 80's are expected to be affected by this condition within 5 years.<sup>2</sup>

AUR results from both acute and chronic illnesses including iatrogenic causes such as medications and surgical interventions.<sup>3</sup> In most cases, it is difficult to identify the triggering event and AUR is attributed to BPH. Irrespective of the cause, AUR has a debilitating impact on both the patient's quality of life and the health system. It has been shown that patients with AUR present to emergency with higher pain scores, which are almost comparable to renal colic (7.7 vs 8.3).<sup>4</sup> There is also a substantial economical impact beyond their initial presentation.<sup>4</sup>

Recent epidemiological data report increasing presentations with AUR. An analysis of 3.7 million American patients presenting to a Californian emergency departments between 2007 and 2010 showed a 36% increase over this period.<sup>5</sup> This contrasts to an earlier study from the Hospital Episode Statistics database in

England, which showed decreasing trend for primary AUR by 7% between 1998 and 2003. $^{6}$ 

The resurgence of AUR is an inevitable major public health issue in the western world with increased life expectancy leading to more hospital presentations of the elderly population.<sup>7</sup> There has been an associated increase in the volume of literature published on the management of AUR with ongoing expansion of research activities. We have reviewed the current literature and present a structured summary on the management of AUR.

### MATERIALS AND METHODS

A systematic review was conducted using the keywords 'acute AND retention AND urin\*' within the title in search engines including Medline, EMBASE and EBM Review. Studies from the non-English language literature were included; however, studies on paediatric and female populations were excluded. This search was further refined by confining the subject to management of AUR. The obtained literature was manually reviewed by the primary author (PDY) and case reports/series, reviews, surveys, economical assessment and articles on AUR in prostate cancer patients and post-operative patients were excluded from our

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review as we aimed to focus on the immediate management of AUR. A further reference search was performed if the articles were meta-analysis articles to cite the original articles. All references to levels of evidence reflect those defined by the Oxford Centre for Evidence-based Medicine.<sup>8</sup>

Where adequate numbers of control trials were available, meta-analysis was performed on specific management options. Intention to treat model was used and *P*-value of < 0.05 was considered as significant.

# RESULTS

The initial Medline search yielded 43 articles. Further EMBASE and EBM Review search added 11 more articles to our archives when duplicates were excluded (Figure 1). These articles were reviewed including their references to obtain information on management of AUR, which are further categorised and presented below.

#### Aetiology and pathogenesis

The causes of AUR can be largely classified into spontaneous AUR (sAUR) which has no triggering events, and is mostly secondary to the natural history of BPH, and precipitated AUR (pAUR) where there is an identifiable trigger. The Reten-World Study of 6074 men showed that sAUR was the major presentation comprising 70.6% of all casualty presentations with AUR.<sup>9</sup> The differentiation is important clinically as surgical management in pAUR group is much less common.<sup>10,11</sup> Precipitating events of pAUR include recent surgery, medication, alcohol intake, urinary tract infection and faecal impaction. The prevalence of each underlying precipitant varies according to the surveyed region around the world.<sup>9,12</sup>

The exact aetiology of AUR is unclear and is thought to be multi-factorial. It is postulated that a combination of mechanical (BPH, urethral stricture, clot retention) or dynamic obstruction (increased alpha-adrenergic activity, prostatic inflammation), bladder over-distension (immobility, constipation, drugs inhibiting bladder contractility, high alcohol intake) and neuropathic mechanisms (diabetic cystopathy, multiple sclerosis) are attributable for AUR.<sup>1,13,14</sup> The pathogenesis of AUR has been extensively researched and number of mechanisms such as prostatic infarction, abnormal alpha adrenergic activity, decrease in the

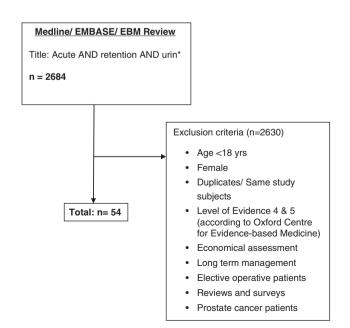


Figure 1. Search strategy.

stromal-epithelial ratio, disruption of neurotransmitter modulation and prostatic inflammation have all been implicated.<sup>1,14</sup>

# Immediate management and trial without catheter

The immediate management of AUR is bladder decompression by catheterisation followed by post-catheterisation management, which may include surgery. The international trend on immediate management of AUR by trial without catheter (TWOC) post-immediate catheterisation is widely practiced, evidenced by multiple cross-sectional studies and surveys worldwide.<sup>9,12,15,16</sup> However, there remains a significant variability within and among countries in the optimal management of AUR in terms of type and duration of catheterisation required, use of concurrent medical therapy or post-catheterisation management.<sup>10</sup>

A French cross-sectional study of 2618 men showed men with no significant post-void residual volume (< 50 ml), less severe lower urinary tract symptoms and no previous episodes of AUR were more likely to undergo a successful TWOC.<sup>3</sup> Men presenting with sAUR were less likely to undergo a TWOC as compared to those with pAUR (66 vs 89%).<sup>3</sup> The former group was also more likely to proceed with elective (22.1%) or immediate (7.5%) BPHrelated surgery as compared with those presenting with pAUR (7.1 and 1.1%, respectively; P < 0.001).<sup>3</sup> A lower success rate of TWOC is seen in older patients of age >70 years, those with an enlarged prostate (>50 ml), higher PSA (>3 ng/ml) and large drained volume at time of catheterisation (>1 l).<sup>12</sup> These results are supported by a separate prospective study by Mahadik and colleagues, who confirmed a significant association between TWOC outcome and age (P=0.0053), and prostate volume on ultrasound (P=0.0427).

The duration of catheterisation before TWOC is controversial. There were five separate studies identified in our review discussing the duration of catheterisation (Table 1). All five studies were not able to show a consistent relationship between successful voiding and duration before TWOC. Two studies showed decreased success of TWOC in longer durations although statistically not significant, especially if they were receiving alpha 1-adrenoceptor blockers (α-blockers).<sup>3,12</sup> In contrast, a multinational study suggested that catheterisation for >3 days was associated with a slightly greater success rate of TWOC (61 vs 64%, P = 0.03 in univariate analysis).<sup>9</sup> Two other randomised control trials (RCTs) supported prolonged catheterisation.<sup>17,18</sup> Taube et al's study was limited to duration less than 3 days hence it is difficult to compare with other studies.<sup>18</sup> Prolonged catheterisation for >3 days was also associated with greater complications and prolonged hospitalisation as compared with patients who were catheterised for 3 days or less (33.8 vs 19.7%, P < 0.001).

History taking and examination of the patient remain critical. This should be followed by immediate bladder decompression by catheterisation to relieve their discomfort. A digital rectal examination is performed to determine BPH or prostatic carcinoma. Urinalysis and cultures to exclude evidence of infection or haematuria are a crucial part of the assessment. Adjunct information to identify the cause of retention and to begin appropriate treatments should be sought. Drained volume post-catheterisation, renal ultrasound and blood tests including renal function and inflammatory markers can help to predict the severity of AUR and subsequent management. If causes are still unclear, then CT scans, functional investigations such as urodynamic studies, MRI scanning to rule out neurological pathology or cystoscopy to rule out structural abnormalities such as strictures can follow to identify the patient's pathology.<sup>19</sup>

The patient will require admission if there are evidence of urosepsis, gross haematuria, significant residual volume of >1 l or acute renal impairment.<sup>19</sup> Significant post-catheterisation diuresis will require intravenous fluid support and any patients with atypical symptoms such as severe abdominal pain or neurological

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Study (year)	Subjects	Duration	Successful voiding (%)	Complication (%)	Miscellaneous
Park et al. <sup>12</sup>	262	< 5 days	81	NA	
		> 5  days	77		
		LE: IIb	NA		
Fitzpatrick et al. <sup>9</sup>	6074	< 3 days	61	19.7	Multivariate analysis: duration statistically not significant Includes Desgrandchamps <i>et al.</i> 's population <sup>3</sup>
		>3 days	64	33.8	
		LE: Ila	P = 0.03	P < 0.001	
Desgrandchamps <i>et al.</i> <sup>3</sup>	2618	< 3 days	59.5	2.2	Significant less hospital stay in $<$ 3 days group
		> 3 days	40.5	6.5	
		LE: IIb	NA	P < 0.001	
Djavan <i>et al.</i> <sup>17</sup>	114	0 days	44	NA	Larger (>1.2 L) retained volumes likely to benefit from prolonged catheterisation
		2 days	51		
		7 days	62		
		LE: Íb	NA		
Taube <i>et al</i> . <sup>18</sup>	60	0 days	27.8	NA	Larger (>900 ml) retained volumes likely to fail TWOC
		1 days	20.0		
		2 days	36.4		
		LE: Ib	NA		

symptoms should be admitted for further investigations. Those with disabilities or social issues where managing urethral catheterisation at home is a challenge also warrant admission.<sup>19</sup>

Use of suprapubic catheter, clean intermittent self-catheterisation and in-and-out catheterisation

Suprapubic catheter (SPC) is an alternative to urethral catheterisation and may provide several advantages over its urethral counterpart. Horgan *et al.*<sup>20</sup> reported in his case–control trial of 86 patients (LE: IIIb), a lower rate of urinary tract infection and lower incidence of urethral stricture at 3 years follow-up with SPC when compared with urethral catheterisation.<sup>20</sup> SPC also has the theoretical advantage of avoiding damage to the urethra and bladder neck. There is also the added benefit of permitting a trial of void by spigotting the catheter before removal avoiding the need for re-catheterisation.<sup>9</sup>

There are significant risks associated with insertion of SPC. Some studies have reported a 2.5% risk of bowel injury and a 1.8% 30-day mortality rate.<sup>21</sup> Those having undergone previous lower abdominal surgery or having neurological diseases have been identified to be at increased risk of complications.<sup>21</sup> Higher rates of haematuria are also reported following SPC when compared with urethral catheterisation.<sup>3</sup> The British Association of Urological Surgeons' SPC practice guidelines recommend SPC insertion either using an open technique or with the adjunct of imaging to exclude the presence of bowel loops in the intended catheter track if such risks are present.<sup>22</sup> This has lead to the trend of SPC insertion being performed only by an experienced medical practitioner and therefore preferential use of urethral catheterisation over SPC in emergency departments.<sup>13</sup>

A feasibility trial (LE: IIIb) of clean intermittent self-catheterisation after a short period of indwelling catheter (IDC) (mean = 2.6 days) on 50 patients had a higher success of voiding compared with the IDC group (56 vs 25%).<sup>23</sup> The author notes study's limitation on lack of randomisation has lead to clean intermittent self-catheterisation group being much younger and having smaller prostates where they are more expected to have a successful TWOC.<sup>23</sup> Nonetheless, the article shows some evidence that clean intermittent self-catheterisation may be a safe and useful option for patients with AUR until their definitive management (e.g., surgery).

In-and-out catheterisation is a TWOC strategy for treatment in AUR management also being trialled around the world.

Retrospective analysis of 515 AUR patients (LE: IIb) managed with in-and-out catheterisation and IDC showed comparable success rate of TWOC (25.1 vs 30.3%) with post-residual volume being the most important predictor for failure.<sup>24</sup> The most frequent complication of intermittent catheterisation is urinary tract infection.<sup>25</sup> The overall long-term outcome remains promising in selected patients.

# Alpha 1-adrenoceptor blockers

The rationale for using  $\alpha$ -blockers before a TWOC is based on the pathophysiology of BPH-related AUR secondary to sudden stimulation of  $\alpha_1$ -adrenergic receptors, which result in prostatic smooth muscle contraction and hence an increase in bladder outlet resistance.<sup>26</sup> By decreasing the sympathetic tone by blocking the receptor, bladder outlet resistance is reduced, followed by successful TWOC.

A Cochrane review of five RCTs showed statistically significant benefit of  $\alpha$ -blockers compared with placebo in contributing to successful TWOC.<sup>27</sup> Tamsulosin (400 mcg daily), alfuzosin (10 mg daily) and newer selective  $\alpha$ -blockers such as silodisin (8 mg daily) and doxazosin (4 mg daily) have been shown to be effective in successful TWOC.<sup>28–40</sup> In a French cross-sectional study of 2618 men, 79% of subjects were treated with  $\alpha$ -blockers during the time of catheter insertion and the TWOC success rate was significantly higher in men who received medical therapy before TWOC (53.0 vs 39.6%).<sup>3</sup> Similar findings are reported by Reten-World Study Group where prevalent use of  $\alpha$ -blockers (86%) worldwide is noted with the result doubling success rate of TWOC.<sup>9</sup>

Our systematic review was able to identify 13 RCTs (LE: lb) and subsequent meta-analysis has shown superiority of  $\alpha$ -blockers over placebo in achieving successful voiding in patients with AUR (Table 2, Figure 2).

# 5-Alpha reductase inhibitors

5-Alpha reductase inhibitors are often used in primary prevention of AUR in patients with BPH. In contrast to its long-term benefits, there are no immediate effects on increasing success rates of TWOC and therefore is not indicated in the immediate management of AUR. Nonetheless, it has been shown to modify disease progression of BPH and to reduce recurrence of AUR as well as lower urinary tract symptoms after 3–6 months of therapy.<sup>41–43</sup>

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Study (year)	Agent	Subjects (n)	Duration of catheter	Successful voiding (%)		Р
				a-Blocker	Placebo	
Kumar et al. <sup>28</sup>	Silodosin (8 mg OD)	60	3 days	76.7	36.7	0.002
Tiong <i>et al.</i> <sup>31</sup>	Alfuzosin (10 mg OD)	67	2 days	60	34	0.036
McNeill et al. <sup>29</sup>	Alfuzosin (10 mg OD)	357	3 days	61.9	47.9	0.012
Shah <i>et al.</i> <sup>32</sup>	Alfuzosin SR (5 mg BD)	62	Min 3 doses or 36 h	50.0	57.1	NA
McNeill <i>et al</i> . <sup>33</sup>	Alfuzosin SR (5 mg BD)	81	24 h	55.0	29.3	0.03
Maldonado-Avila et al. <sup>34</sup>	Alfuzosin (10 mg OD)	90	4 days	35.2	26.3	0.662
	Tamsulosin (400 mcg OD)			43.2		
Agrawal <i>et al.</i> 35	Alfuzosin (10 mg OD)	150	3 days	66	36	NA
-	Tamsulosin (400 mcg OD)			70		
Lucas et al. <sup>30</sup>	Tamsulosin (400 mcg OD)	149	Up to 8 doses	45.3	24.3	0.011
Hua et al. <sup>36</sup>	Tamsulosin (400 mcg OD)	72	3 days	61	28	< 0.01
Al-Hashimi <i>et al</i> . <sup>37</sup>	Alfuzosin (10 mg OD)	245	3 days	62.3	32.7	0.000
Prieto <i>et al.</i> <sup>38</sup>	Doxazosin (4 mg OD)	47	30 days	56.5	54.2	0.87
Lorente <i>et al.</i> <sup>39</sup>	Doxazosin (4 mg OD)	40	7 days	60	25	0.02
Perepanova <i>et al.</i> 40	Doxazosin (4–8 mg OD)	36	Up to 3 days	63.3	16.7	NA

	Alpha-blo	ckers	Placel	00		Risk Ratio		R	isk Ratio		
Study or Subgroup	Events	Tota	Events	Tota	Weight	M-H, Fixed, 95% CI	Year	М-Н,	Fixed, 95% Cl		
McNeill 1999	22	40	12	41	4.8%	1.88 [1.08, 3.26]	1999			_	
Perepanova 2001	19	30	1	6	0.7%	3.80 [0.62, 23.21]	2001	-	_		$\rightarrow$
Shah 2002	17	34	16	28	7.2%	0.88 (0.55, 1.39)	2002	-			
Hua 2003	22	36	10	36	4.1%	2.20 [1.22, 3.96]	2003			_	
McNeill 2004	146	236	58	121	31.3%	1.29 [1.05, 1.59]	2004				
Lucas 2005	34	75	18	74	7.4%	1.86 [1.16, 2.99]	2005			-	
Lorente 2005	12	20	5	20	2.0%	2.40 [1.04, 5.55]	2005				
Hashimi 2007	71	114	36	110	15.0%	1.90 [1.40, 2.58]	2007				
Prieto 2008	13	23	13	24	5.2%	1.04 [0.62, 1.74]	2008	-	<u> </u>		
Agrawal 2009	68	100	18	50	9.8%	1.89 [1.27, 2.80]	2009				
Tiong 2009	21	35	11	32	4.7%	1.75 [1.01, 3.02]	2009			-	
Kumar 2013	23	30	11	30	4.5%	2.09 [1.26, 3.48]	2013		—	_	
Maldonado-Avila 2013	28	71	5	19	3.2%	1.50 [0.67, 3.35]	2013		<u> </u>	-	
Total (95% CI)		844		591	100.0%	1.61 [1.43, 1.82]			•		
Total events	496		214								
Heterogeneity: Chi <sup>2</sup> = 19	.99, df = 12	(P = 0.07	7); l <sup>2</sup> = 40 <sup>4</sup>	%			F				
Test for overall effect: Z							0.1	0.2 0.5	1 2	5	10
								Favours placeb	o Favoursalj	oha-bloc	kers

Figure 2. Forest plot illustrating superiority of alpha blockers over placebo in achieving successful voiding in patients with acute urinary retention.

# Surgical intervention

There is a role for surgical intervention in patients with unsuccessful TWOC as well as in those with significant lower urinary tract symptoms post-successful TWOC. TURP patients have significantly lower rates of subsequent urinary retention<sup>44</sup> and it is generally considered to be the end point for AUR. Those patients with a large prostate size (> 50 ml) and a high serum PSA level during AUR (>10 mcg/L) are more likely to undergo future surgical intervention.<sup>45</sup> A prospective study of 40 conservatively managed AUR patients followed up to 24 months showed that only 22 (55%) voided spontaneously after TWOC and remained to do so.<sup>46</sup> PLESS study found that 67% of patients who suffered from sAUR eventually underwent BPH-related surgery, as compared with 35% of patients presenting with pAUR over a 4-year interval.43 Previous studies have reported only 23-28% of men with AUR will void successfully after a TWOC and have no need for a prostatectomy in the short to medium term.<sup>18,47</sup> Lo et al.<sup>45</sup> showed that although  $\alpha$ -blockers increased the success rate of TWOC, approximately half of the patients required additional intervention within 5 years. Similar findings are reported by the ALFAUR study, of those commenced on alfuzosin 10 mg once daily after AUR, 17.1% of patients still required surgical treatment within 6 months.  $^{\rm 29}$ 

The decision to offer prostatectomy should be undertaken on the basis of persistent symptoms or decreased quality of life rather than the diagnosis of AUR alone. Recent UK studies have shown that immediate surgical management after AUR was associated with greater risks.<sup>7,48</sup> Surgical intervention especially in the failed TWOC group and in older patients, in the presence of a urinary catheter, leads to an increased risk of sepsis, which potentially contributes to the observed increase in operative morbidity.<sup>15</sup> The UK National Prostatectomy Audit (LE: IIb) showed that compared with elective surgery for obstructive symptoms alone, emergency surgery following AUR with a catheter *in situ* resulted in a 3.0-fold increase in the risk of post-operative death at 30 days, a 2.5-fold increase in the risk of requiring a transfusion, a 2.0-fold increase in the risk of operative complications and a 1.6-fold increase in postoperative complications.<sup>48</sup>

Although TURP remains the current gold standard, there has been an emergence of newer technology using laser techniques. We have identified five papers discussing management of AUR using laser which presents varying results. The CLasP randomised trial (LE: Ib) comparing TURP with Nd:YAG laser assisted prostatectomy in 148 men showed significantly higher treatment



Use of SPC over IDC in AUR	lla and IIIb (heterogeneous)	Option
Duration of catheterisation ( $<$ 3 days)	Ib and IIa (heterogeneous)	Option
Use of α-adrenergic receptor blockers before TWOC	la	Standard
Emergency operative management should be avoided	lla	Recommendation
Factors influencing TWOC: larger prostate size (>50 ml), older age (>70 years),	lb	

Abbreviations: AUR, acute urinary retention; IDC, indwelling catheter; IPSS, International Prostate Symptom Score; SPC, suprapubic catheter; TWOC, trial without catheter.

failure rate for the laser than the TURP group (9.5 vs 1.4%, P = 0.029).<sup>49</sup> Holmium: YAG Laser Resection of Prostate technique showed mean postoperative catheterisation time of 1.5 days and only 3 men (8.3%) required a catheter for more than 48 h (LE: IV).<sup>50</sup> Thulium laser resection for AUR is also supported by a Chinese prospective case series (LE: IV) with relatively low perioperative adverse events and recatheterisation rate of 3.8%.<sup>51</sup> An Australian group showed that PVP (photoselective vaporisation of the prostate) is an efficacious and safe treatment modality for AUR (LE: IIb).<sup>52</sup> Chinese group also demonstrated this in their 42 post-PVP patients with only two patients experiencing recurrent urinary retention (LE: IIb).<sup>53</sup>

#### Miscellaneous

More research is being performed to combine agents for the management of AUR. For instance, combination of tamsulosin and ketoconazole was tested in a recent RCT (LE: lb), where patients with AUR due to BPH had more successful TWOC after 7 days of combination therapy compared with control group of tamsulosin therapy alone (77.35 vs 58.84%, n = 106, P = 0.01).<sup>54</sup>

The use of transurethral microwave thermotherapy has been advocated in one study as a useful option for the patient with AUR who is not a suitable candidate for surgery with 94% (29/31) of patients regaining their voiding abilities by 4 weeks (LE: IV).<sup>55</sup> Use of a bio-absorbable braided urethral stents is also being piloted in regard to its efficacy and safety and has yielded promising results when combined with dutasteride (LE: IV).<sup>56</sup> All subjects (n = 10) were able to void short term and 50% of subjects were still able to spontaneously void at 3 months.<sup>56</sup>

# CONCLUSION

We recommend following on the management of AUR based on our systematic review and meta-analysis of the literature (Table 3.) From our review, it was evident that there is high variability in the management of AUR worldwide, especially in early management. There is a need for further standardisation and guidelines to harmonise the management of AUR. Further research is hence warranted for development of economical, efficient and evidencebased practice in management of AUR for the patients as well as the health system.

### **CONFLICT OF INTEREST**

The authors declare no conflict of interest.

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