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Physician prescription practice of antibiotics for upper respiratory tract infection at Kilimanjaro Christian Medical Centre Moshi, Tanzania

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Upper respiratory tract infection occurs commonly in both children and adults and is a major cause of morbidity worldwide. Inappropriate antibiotic prescription for upper respiratory tract infections is associated with increasing antibiotic resistance, healthcare costs, adverse events, and poor patient outcomes. The objective of this study was to determine physician prescription practices of antibiotics for upper respiratory tract infections at Kilimanjaro Christian Medical Center hospital in Moshi, Tanzania. This was a retrospective hospital-based cross sectional study which systematically sampled files of patients with diagnosis of upper respiratory tract infection. Information from a total of 300 patients' prescriptions were collected, reviewed and analyzed. The most common infections diagnosis was non-specific upper respiratory tract infections accounting for 102 (34.0%) followed by rhinitis and tonsillitis both accounting for 52 (17.3%) with the least being common cold 22 (7.3%). Antibiotics were prescribed to 200 (66.7%) patients with upper respiratory tract infections. Amoxicillin alone was the most preferred drug for all upper respiratory tract infections 91 (31.5%). In the multivariable logistic regression analysis, patients with cough and running nose (AOR=16.41, 95% CI: 1.95-138.19) had higher odds of being prescribed with antibiotic as compared to those without such symptoms (AOR=1.98, 95% CI: 1.04-3.77), respectively. Antibiotics are being over-prescribed among patients with upper respiratory tract infection. Interventions to reduce the over-prescription and hence overuse of antibiotics for upper respiratory tract infections are urgently needed.

Key words: Antibiotics prescribing, upper respiratory tract infection,Tanzania.

INTRODUCTION

Upper respiratory tract infections (URTIs) is a term used to describe acute infections involving the nasal cavity,

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pharynx and larynx (Mungrue et al., 2009; Yoon et al., 2017). URTIs are classified according to the area of inflammation, which are tonsillitis, pharyngitis, laryngitis, sinusitis, common cold, influenza and otitis media (Centre for Clinical Practice, 2008). Moreover, Otitis media has not been classified as URTIs, although it has been linked with the upper respiratory tract, since it occur as a complication of URTIs hence tends to be identified within URTIs (Chonmaitree et al., 2008).

Most of the URTIs are of viral etiology and these include viruses in the family rhinovirus, coronavirus, parainfluenza, respiratory syncytial virus, adenovirus and influenza (Cotton et al., 2008). Occasionally, bacteria may develop after a viral illness such as a cold or the flu. The significance of pathogenic bacteria in the upper respiratory tract is yet to be characterized (MacIntyre et al., 2017), since positive nasopharyngeal bacterial culture is a weak predictor of URTIs because healthy individuals often carry pathogenic bacteria (Ouédraogo et al., 2014). People are generally thought to be asymptomatic carriers of bacteria (Faden et al., 1997; Givon-lavi et al., 2002; Bogaert et al., 2004). Most episodes of URTIs are typically self-limiting, thus do not require physician visit or antibiotic(s) prescription (Peroš-Golubičić and Tekavec-Trkanjec, 2015; Llor et al., 2017). Acute respiratory infections which are divided into URTI and lower respiratory tract infections, have been established as one of the leading causes of childhood morbidity and mortality in Africa (Symekher et al., 2009). It has been estimated that up to 1.9 million children die each year from acute respiratory with nearly 70% of deaths occurring in Africa and South East Asia (Simoes et al., 2006; Symekher et al., 2009). However, the burden of URTI in most African countries including Tanzania has not been documented.

Despite consistent and continued education among healthcare professionals on antibiotic resistance, antibiotic prescribing rates for URTIs remain high in general practice (Fletcher-Lartey et al., 2016). World Health Organization (WHO) estimated that up to 60% of people with URTIs receive antibiotics inappropriately (Kunda et al., 2015). Inappropriately use of antibiotics contributes to the emergency of antimicrobial resistance (AMR), which is a major public health problem worldwide. Documented factors associated with antibiotic prescription for URTI by physicians include fever (temperature >38°C), fear of complications, inflamed eardrums, cough, and throat irritation as well as primary caregivers' pressure and patients financial gains (Al-Enezi et al., 2011).

Guidelines by Centre of Disease Control (CDC) do not recommend antibiotic prescribing in non-specific URTIs because antibiotics neither enhance illness resolution nor prevent complications (CDC, 2017). One study showed that only 12% of physician would request laboratory tests such as culture and sensitivity before prescribing antibiotics, and 88% of the physician considered laboratory investigations as unnecessary (Mohan et al., 2004). Misdiagnosis and improper diagnosis leads to incorrect antibiotics prescription and so increases AMR in many parts of the world (Haque, 2017). For better treatment outcome, healthcare workers are encouraged to request for microbiological testing prior to start of antibiotics for a more rational antibiotic use in both children and adults (Levy-Hara et al., 2011; Chaw et al., 2018).

Several studies have shown the rate of antibiotic prescriptions in relation to the diagnosis of URTIs made which was high and inappropriate (Teng et al., 2004; Gwimile et al., 2012; Kunda et al., 2015). Inappropriate antibiotic prescription for URTI is a global public health problem, therefore URTIs are important for strategies aimed at reducing excess antibiotic use because antibiotics are frequently prescribed in these illnesses that are predominantly of viral etiology (Easton and Saxena, 2010; Kunda et al., 2015; Fletcher-Lartey et al., 2016; Zhang et al., 2017).

Although prescribing patterns generally differ between countries due to the national guidelines and drugs available, very little is known about antibiotics prescribing practices in Tanzania and specifically at Kilimanjaro Christian Medical Centre (KCMC). Despite the fact that awareness of the consequences of antibiotic misuse is increasing among population (Mbwambo et al., 2017), as well as among healthcare providers (Lyimo et al., 2018), in the northern part of Tanzania, overprescribing of antibiotics is still being practiced at high rate even before availability of laboratory results are made available (Chilongola et al., 2015; Kajeguka et al., 2017). Therefore, this study aimed at assessing physician prescription practice on antibiotics for URTIs.

METHODS

Study design and area

This was a retrospective hospital-based cross sectional study carried out from April 2017 to July 2017 at KCMC hospital in Moshi, Kilimanjaro region, Tanzania. Physicians' antibiotic prescriptions from January 2015 to June 2017 were included. KCMC is a consultant referral hospital with 630 inpatient beds serving several regions in northern part of Tanzania. The study was conducted in three departments; which are Pediatric, Internal medicine and Outpatient department (OPD).

Sample size determination and sampling

The following formula was used to obtain the required sample size:

$N = [Z^2 P (1-P)] / (d^2)$,

where N is the required sample, Z is the confidence level at 95% (1.96), P is the prevalence of 0.78, and d is the margin of error at 5% (0.05).

Table 1. General characteristics of study participants (N=300).

Variable		Measure
Age in years, Mean ± SD		2.02 ± 1.03
Age categories (in years)	<15	126 (42.0)
	15-35	84 (28.0)
	36-45	25 (8.3)
	>45	65 (21.7)
Sex	Male	92 (30.7)
	Female	208 (69.3)
Ward/Department	Pediatric	62 (20.7)
	Internal medicine	42 (14.0)
	Outpatient Department	196 (65.3)

The prevalence of antibiotics prescription on URTI was 78% (Kunda et al., 2015). A maximum of 300 patient files were systematically sampled. Records with missing data on URTIs were excluded.

Data collection methods and tools

All prescriptions of patient with the diagnosis of URTI from physician in selected departments/wards at KCMC hospital were included. Data was extracted from patient's medical records (files). The following data were recorded; age, sex, diagnosis given, if laboratory test were requested, if antibiotic was prescribed, type of antibiotic prescribed, number of antibiotics prescribed and type of URTIs. Signs and symptoms that prompted antibiotic prescription were recorded, such as fever (Temperature >38°C), chest pain, cough, running nose, exudates in throats, inflamed ear and difficulty in breathing.

Data analysis

Data were analyzed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp, Armonk, NY, USA). Descriptive statistics was used to summarize data. Differences between categorical data were calculated using Pearson's Chi-square test (χ^2). Factors that were found to have a level of significance of $p \leq 0.05$ were then entered into the final model of the multivariable logistic regression analysis, which was used to compute adjusted odds ratio (AOR) and 95% confidence intervals (95% CI) to assess the independent associations of these variables with outcome of interest (antibiotic prescription). A $p<0.05$ was significant.

RESULTS

Demographics characteristics and URTIs diagnosed

A total of 300 patient files were reviewed. The mean age in years (±Standard deviation) was 2.02 ± 1.03, with those aged 15 years and below constituting the highest proportion 126 (42.0%) followed by those aged 16 to 35 years 84 (28.0%). Two hundred and eight participants (69.3%) were female. Most of the participants were from OPD 196 (65.3%), followed by pediatric 62 (20.7%) and internal medicine 42 (14.0%) (Table 1). The most common URTIs diagnosed were non-specific URTIs 102 (34.0%) followed by rhinitis and tonsillitis, both 52 (17.3%). The least diagnosis assigned was common cold 22 (7.3%) (Figure 1).

Antibiotics prescribing pattern for URTIs

Two hundred patients with URTI (66.7%) received atleast one antibiotic (Any antibiotic); with the highest in pharyngitis 47 (100%), followed by non-specific URTIs 82 (80.4%) and rhinitis 38 (73.1%) (Table 2). Amoxicillin alone was the most frequently prescribed antibiotic for common cold 16 (72.7%). Ampicillin was frequently prescribed for otitis media 7 (28.0%), followed by tonsillitis 14 (26.9), and pharyngitis 11 (23.4%). Ampiclox was commonly prescribed for otitis media 10 (40.0%) (Table 2).

Signs and symptoms that influenced antibiotic prescription for URTIs

Multiple responses were allowed in this variable. Cough 236 (32.1%), running nose 114 (19.4%), fever (temperature >38°C) 115 (15.6%), exudates in throats 84 (11.4%), chest pain 70 (9.5%), difficulty in breathing 38 (5.2%), and inflamed ear 26 (3.5%) constituted the most common clinical presentations which affected the physician's decision to prescribe antibiotics for URTIs

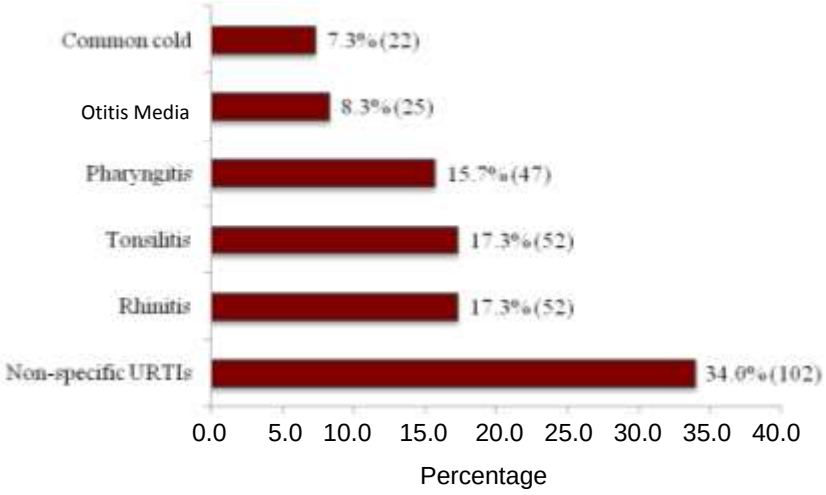

Figure 1. Type of URTIs diagnoses (N=300).

(Figure 2).

The multivariable logistic regression analysis revealed that five independent variables had a significant influence on the antibiotic prescription. In the adjusted analysis (additional adjustment such as sex and age) patients who had fever, chest pain and difficulty in breathing had reduced odds of being prescribed with antibiotic as compared to those without such symptoms (AOR=0.02, 95% CI: 0.008-0.09), (AOR=0.29, 95% CI: 0.12-0.74) and (AOR=0.25, 95% CI: 0.07-0.85), respectively. Moreover, patients who had cough and running nose had higher odds of being prescribed with antibiotic as compared to those without such symptoms (AOR=16.41, 95% CI: 1.95-138.19) and (AOR=1.98, 95% CI: 1.04-3.77), respectively (Table 3).

DISCUSSION

The objective of the present study was to assess physician prescription practice on antibiotics for URTIs in order to have baseline information on antibiotic use and thereafter make recommendations to stake holders. It has been documented that most URTIs are of viral origin in 80% of cases (Kunda et al., 2015), however, physicians in many settings frequently prescribe antibiotics for these illnesses and contributing to increasing antibiotic over-prescribing is a problem in many settings (Easton and Saxena, 2010; Kunda et al., 2015; Fletcher-Lartey et al., 2016; Zhang et al., 2017) and the present results show that Tanzania is not an exception.

In this study, it was found that a significant number of patients with URTIs were prescribed with at least one antibiotic (66.7%). This prevalence was notably high and if not prevented it will continue to escalate the problem of antibiotic resistance. The present study, reports a relatively lower prevalence as compared to a studies by Gwimile et al. (2012) with a prevalence of 84.9%, a study in Namibia, with a prevalence of 78% among adults and children (Kunda et al., 2015) and in Malaysia, a prevalence of 68.4% (Teng et al., 2004). The reason for lower prevalence could be because of the availability of supportive environments such as laboratory facilities and effective hospital policies that influence antibiotic prescribing behaviors (Lyimo et al., 2018).

The most common URTIs diagnosed was non-specific URTIs (34.0%) followed by rhinitis and tonsillitis both 17.3%. This result was lower than studies conducted in Windhoek, Namibia and North Trinidad where it was 45and 54.5%, respectively (Mungrue et al., 2009; Kunda et al., 2015). This study shows that amoxicillin alone was the preferred drug for almost all URTIs. The same scenario was reported in Trinidad whereby amoxicillin alone or with clavulanate was the most frequently prescribed antibiotic for all URTIs (Mohan et al., 2004). This is of concern because prescribing antibiotics for these conditions in adults and children does not have any therapeutic benefits, but only increases the risk of developing antibiotic resistance. In addition, antibiotics do not warrant a better outcome in terms of cure or persistence of symptoms in patients who receive antibiotics compared to those who do not (Snellman et al., 2013).

Regarding signs and symptoms that influenced physician's decision to prescribe antibiotics for URTIs, fever (temperature >38°C), chest pain, cough, running nose and difficulty in breathing were the factors mostly affecting physician's decision to prescribe antibiotics. In this study, patients with fever, chest pain and difficulty in

Table 2. Antibiotics prescribed for URTIs.

Antibiotic		URTIs [n(%)]						
		Pharyngitis	Rhinitis	Tonsillitis	Common cold	Otitis media	Non-specific URTIs	Total
Amoxicillin	No	24 (51.1)	32 (61.5)	36 (69.2)	6 (27.7)	23 (92.0)	84 (82.4)	206 (68.7)
	Yes	23 (48.9)	20 (38.5)	16 (30.8)	16 (72.7)	2 (8.0)	18 (17.6)	94 (31.3)
Ampicillin	No	36 (76.6)	49 (94.2)	38 (73.1)	22 (100)	18 (72.0)	101 (99.0)	264 (88.0)
	Yes	11 (23.4)	3 (5.8)	14 (26.9)	0 (0.0)	7 (28.0)	1 (1.0)	36 (12.0)
Co-amoxiclav	No	38 (80.9)	51 (98.1)	48 (92.3)	22 (100)	23 (92.0)	100 (980)	264 (88.0)
	Yes	9 (19.1)	1 (1.9)	4 (7.7)	0 (0.0)	2 (8.0)	2 (2.0)	36 (12.0)
Cloxacillin	No	46 (97.9)	52 (100)	52 (100)	22 (100)	21 (84.0)	100 (980)	282 (94.0)
	Yes	1 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)	4 (16.0)	2 (2.0)	18 (6.0)
Ceftriaxone	No	46 (97.9)	52 (100)	43 (82.7)	22 (100)	16 (64.0)	101 (99.0)	293 (97.7)
	Yes	1 (2.1)	0 (0.0)	9 (17.0)	0 (0.0)	9 (36.0)	1 (1.0)	7 (2.3)
Clarithromycin	No	43 (91.5)	50 (96.2)	46 (88.5)	22 (100)	25 (100)	102 (100)	280 (93.3)
	Yes	4 (8.5)	2 (3.8)	6 (11.5)	0 (0.0)	0 (0.0)	0 (0)	20 (6.7)
Ampiclox	No	43 (91.5)	52 (100)	47 (90.4)	21 (95.5)	15 (60.0)	100 (980)	289 (96.3)
	Yes	4 (8.5)	0 (0.0)	5 (9.6)	1 (4.5)	10 (40.0)	2 (2.0)	11 (3.7)
Chloramphenicol	No	4 5(95.7)	52 (100)	48 (92.3)	22 (100)	24 (96.0)	102 (100)	278(92.7)
	Yes	2 (4.3)	0 (0.0)	4 (7.7)	0 (0.0)	1 (4.0)	0 (0)	22(7.3)
Penicillin G	No	47 (100)	52 (100)	48 (92.3)	22 (100)	25 (100)	102 (100)	293 (97.7)
	Yes	0 (0.0)	0 (0.0)	4 (7.7)	0 (0.0)	0 (0.0)	0 (0)	7 (2.3)
Gentamicin	No	47(100)	52 (100)	52 (100)	22 (100)	21 (84.0)	102 (100)	296 (98.7)
	Yes	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (16.0)	0 (0)	4(1.3)
Doxycycline	No	46 (97.9)	47 (90.4)	51 (98.1)	20 (90.9)	25 (100)	99 (97.1)	288 (96.0)
	Yes	1 (2.1)	5 (9.6)	1 (1.9)	2 (9.1)	0 (0.0)	3 (2.9)	12 (4.0)
Azithromycin	No	47 (100)	52 (100)	50 (96.2)	22 (100)	21 (84.0)	102 (100)	294 (98.0)
	Yes	0 (0.0)	0 (0.0)	2 (3.8)	0 (0.0)	4 (16.0)	0 (0)	6 (2.0)
Any Antibiotic	No	0 (0.0)	14 (26.9)	23 (45.1)	9 (40.9)	9 (36.0)	20 (19.2)	100 (33.3)
	Yes	47 (100)	38 (73.1)	28 (54.9)	13 (59.1)	16 (64.0)	82 (80.4)	200 (66.7)

breathing were less likely to be prescribed with antibiotics. In other settings, patients with fever and cough were reported to be prescribed with antibiotics assuming that they were more severely ill (Akkerman et al., 2005). In areas like Tanzania where malaria is common, symptoms of fever and cough may also be shared with those of malaria. In such scenario, it is likely that clients who presented with these symptoms may have been prescribed with antimalarial, and this has been evidenced in different studies conducted in Kilimanjaro region, Northern Tanzania (Hertz et al., 2012; Crump et al., 2013; Kajeguka et al., 2016, 2017).

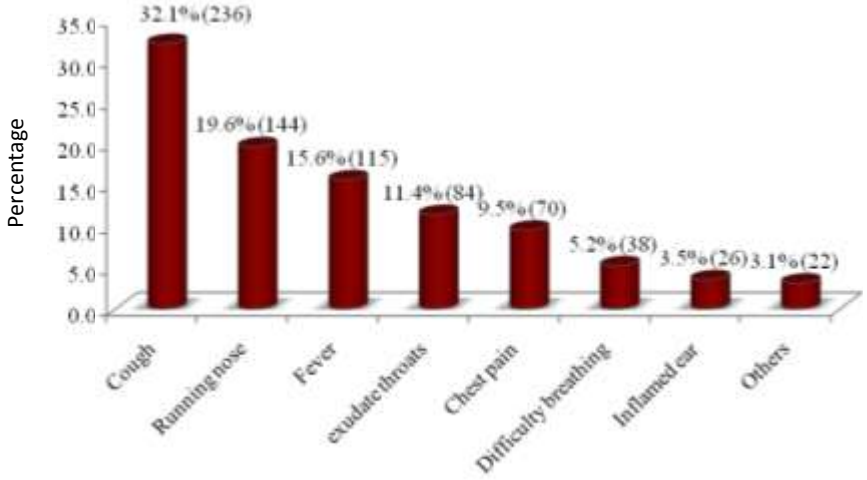

Figure 2. Signs and symptoms prompted antibiotic prescription (n=736, multiple responses were allowed).

Table 3. Signs and symptoms and antibiotic prescribed for URTIs.

Categories		Frequency [n (%)]	COR (95% CI)	AOR (95% CI)	[a] AOR (95% CI)
Fever	Yes No	115 (38.3) 185 (61.7)	0.02 (0.008-0.08)	0.03 (0.009-0.10)	0.02 (0.008-0.09)
Chest pain	Yes No	70 (23.3) 230 (76.7)	0.26 (0.13-0.55)	0.24 (0.10-0.58)	0.29 (0.12-0.74)
Cough	Yes No	236 (78.7) 64 (21.3)	43.96 (5.99-322.39)	12.89 (1.60-103.59)	16.41 (1.95-138.19)
Running nose	Yes No	114 (48.0) 156 (52.0)	2.87 (1.73-4.74)	2.04 (1.08-3.86)	1.98 (1.04-3.77)
Exudates in throat	Yes No	84 (28.0) 216 (72.0)	0.89 (0.53-1.49)	-	-
Inflamed ear	Yes No	26 (8.7) 274 (91.3)	2.76 (0.60-12.72)	-	-
Difficulty in breathing	Yes No	38 (12.7) 262 (87.3)	0.31 (0.14-0.70)	0.28 (0.10-0.74)	0.25 (0.07-0.85)

COR: Crude odds ratio, AOR: adjusted odds ratio. Only variables that were predictors of antibiotic prescription (set in the bivariate analysis to $p<0.05$) were included in multivariate analysis. [a]Includes additional adjustment such as sex and age.

The CDC and WHO recommend a performance of a group A β-hemolytic streptococci test prior to treatment of sore throat with antibiotics (Biezen et al., 2015). Laboratory test (such as culture and sensitivity) was obtained for investigation for about 136 (47.1%) patients diagnosed with URTIs before antibiotic therapy was prescribed. This indicates that most prescribers are still not well aware of the concept and implications of

antibiotic resistance. Therefore, they do not take laboratory tests into consideration when they decide whether or not to prescribe antibiotics for URTIs.

In order to reduce the irrational use of antibiotic prescribing in URTIs, it is of greatest importance that at the health facility level, the health care providers are trained on appropriate antibiotic prescription. This will assist in alleviating antibiotic overprescribing and the consequence of antibiotic resistance. Health workers' continuing education should be strengthened through conferences and seminars. Equally important is the periodic antibiotic use review, which can provide feedback to prescribers in health facilities on antibiotic use expenditure and resistance patterns. Also, there is obvious need for an antibiotic stewardship committee that will follow-up closely and enable care providers to rationally prescribe antibiotics.

Additionally, Tanzanian Ministry of Health, Community Development, Gender, Seniors and Children should consider adopting a strategy of delayed prescription or delayed antibiotic use, which has shown to be effective in reducing antibiotic usage for URTIs (Spurling et al., 2013; Ryves et al., 2016). In a Cochrane Review it has been highlighted that delayed prescribing may be a suitable compromise in place of immediate prescribing to significantly reduce unnecessary antibiotic use and thereby reduce antibiotic resistance while maintaining patient safety and satisfaction levels (Spurling et al., 2017). Moreover, regular training in antibiotic management for healthcare professionals is paramount, also there should be an awareness regarding antibiotics among patients and the community (Mbwambo et al., 2017). Further research is recommended to identify factors contributing to antibiotic over-prescribing in URTIs in Tanzania, which will also identify barriers of compliance to standard treatment guideline.

STRENGTHS AND LIMITATIONS

The study utilized systematic random sampling of prescriptions in KCMC and captured a broad view of antibiotic prescribing for URTIs in this setting. The study was conducted at one health facility. This prevented generalization of the results to the larger population of Tanzania. This study relied on the diagnosis written on the prescription and clinical presentation of the patient not the microbiological culture, which lead to a failure to comment on the appropriateness of the antibiotic prescription in relation to laboratory results.

CONCLUSION

In URTI treatment, use of antibiotic is always an area of concern. An irrational prescription practice of antibiotics is an important public health issue that affects the community. Use of antibiotic for the treatment of URTIs is evidently inappropriate unless the infection was proven to be bacteria.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests

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