## Do the Results of the OXYGEN Trial Change if Analyzed as &Idquo;As-Treated?": A Secondary Analysis of the OXYGEN Trial

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The OXYGEN trial evaluated if elevated levels of perioperative oxygen reduce the risk of surgical site infections (SSI) after fixation of tibial pilon, tibial plateau, and calcaneus fractures. An "intention-to-treat" approach was used for the primary analysis, however, control group adherence to the assigned protocol was 83%. It is possible the study results may differ by re-analyzing using an "as treated" approach?

## METHODS:

The original study randomized patients to receive 80% FiO2 (treatment) or 30% FiO2 (control) in the operating room and up to 2 hours in the recovery room. The primary outcome was a composite of either deep (treated with surgery) or superficial (treated with antibiotics alone) SSI within 182 days of definitive fixation. Secondary outcomes were deep and superficial surgical site infections within 90, 182, and 365 days of definitive fixation.

Adherence was defined using two different criteria. Criterion 1 required at least 80% of the surgery time less than or equal to 40% FiO2 for the control group or greater than or equal to 70% FiO2 for the treatment group. Criterion 2 required at least 80% of surgery time to fall within 20 - 40% (control) or 70 - 90% FiO2 (treatment). Weighted Kaplan-Meier was used to estimate the probability of the primary and secondary outcomes as-treated. RESULTS:

A total of 1231 patients ages 18 - 80 enrolled with tibial plateau, tibial pilon, or calcaneus fractures thought to be at elevated risk of infection.

Under Criterion 1, the primary outcome occurred in 7% (38/523) and 10% (49/471) of patients in the treatment and control groups, respectively (P=0.10). Deep infection occurred in 30 (6%) treatment and 30 (6.4%) control group patients (P=0.75). Superficial infection occurred in 9 (2%) treatment group patients and 20 (4%) control group patients (RR, 0.41; P=0.03).

Using Criterion 2, the primary outcome occurred in 7% (36/498) of treatment and 10% (48/468) of control patients (P=0.12). Deep infection occurred in 28 (5%) treatment and 29 (6%) control group patients (P=0.81). Superficial infection occurred in 9 (2%) treatment and 20 (4.3%) control group patients (RR=0.43; P=0.03). DISCUSSION AND CONCLUSION:

When re-analyzing based on which patients actually received high or control levels of oxygen, the results are generally consistent with the original "intent to treat" analysis. Specifically, high perioperative oxygen still lowered the risk of superficial SSI but did not affect deep infections in tibial plateau, pilon, and calcaneus fractures. However, the composite outcome of any infection showed a similar trend but was no longer statistically significant. This might be due to the decreased precision of the smaller sample size or a selection bias of sicker patients requiring high oxygen in the control group. This analysis should reassure patients and clinicians that the findings of the trial appear to be robust to the analysis method.

						Table CL Friencey and Procedury Chilome Mouseum	
Dable L Baseline Characteristics of Patients (Modified I	ofention to Treat Population;			Treatment	Cestrel		
	Treatment	Centrel	Characteristic	Group	Greep	Outcome	
Characteristic	Group	Greep		(N = 575)	(N = 561)	Prince senses; region sin infection at 165 days.	
	$\phi N = 5750$	(N = 561)	2 or more	11(2%)	19 (8%)	Terming retirence	
Most age a SD, vr	45.1 ± 14.5	457 a 142	American Society of Assorbiology physical status score			Deep marginal site infloritemat IEO days?	
Make sen*	AUD (TRIV)	200-10773	1	104(185)	80 (14%)	transporting day majori distribution d. HC days*	
Mose body wast index a SDP	286 a 6.1	28.6 a 6.6	x	356(60%)	360 (62%)	Gram requires deep respiral site indication at 100 dept*	
Tobacca use <sup>46</sup>				(25(2)%)	337 (34%)	Superficial complete size industries an ISO day of	
Connect and Original recognition of manufact	207 (36%)	191 (MS)	TV	1.0%	40%	Drush at Not days?	
						Loss of Bods or ampointum at 36th day of	
Former use too use	306 (64%)	365 (65%)	*The values are given as the number and persentage of too			Final Adiasan at No dept*	
Diabetes*	49 (1%)	49 (9%)	*Body mass index data was missing for 2 patients (0%) in	"Dody mass index data was missing for 2 patients (0%) in the treatment group and 4 patients (1%) in the			
Finance type*			control group.			* The values are given as the number and percentage of treatment	
Tibid plateau	249 (42%)	234 (42%)	<sup>6</sup> Two polants (PN) in the testment group and 5 polants (	<sup>6</sup> Two patients (8%) in the leadment group and 5 policets (1%) in the orniral group did not provide tobacco			
Tibial pilos	199 (34%)	297 (59%)	use information.				
Cifcures	(39 (34%)	150 (33%)	*Two putions (0%) in the treatment group and one patient	(9%) in the central group had closed f	indure with		
Finalize severity**			missing Technico Classification.				
Open fracture	88 (15%)	80 (14%)	<sup>4</sup> Fridy server putients (10%) in the treatment group and 42 below Serveits Sourcelds.	policels (2%) in the oreled group was	mining		
Gedile Type			agas arrives armenas.				
1	13 (2%)	5 (1%)					
п	23 (4%)	29 (5%)					
IIIA.	52 (994)	47 (8%)					
Closed Suctors (Tucherus grade 6-2)	489 (195)	434 (77%)					
Closed fraction (Technine grade 3)	46 (875)	45 (85)					
Mean Jojony Severity Some 2 SDF	7.1 ± 8.5	68±7.5					
Number of internal fination stages*							
t.	504 (98%)	542 (97%)					
		1			2		

Characteristic 2 or more	Closep (N = 575)	Group	
2craw	QN=5759		
2 or more	(N = 575) 11 (2%)	(N = 581)	
	11(25)	19 (9%)	
American Society of American loopy physical status score*			
1	104(18%)	80 (14%)	
x	356(60%)	360 (62%	
	(28(21%)	337 (34%	
TV	1 (0%)	4(15)	
ase information.  Two pulsaris (3%) in the bootiness group and one polices (3%) in to missing Turburne Chandibusion.	he control group had closes	fruiter with	
missing Techana Classification.  Fifty server registric (1974) in the treatment orean and 27 registrate.	7%) in the control encourse	no minoine	

	Trubent	Control	Truberd XFe1			
Montes	Onep	Cerup	The Difference	Edward Total	Plate	
	(5 = 579)	(61+500)				
history restricted also inductives at 165 days."	4(95)	800771	JP14225 to 8451	005669330	6.00	
ironalog rationers						
Deep marginal site influsion at 100 days?	30 (8.6%)	27 (5473)	$-0.070 \pm 0.071 \pm 0.071)$	ON (S.N to 1.39)	6.80	
transposites depropriet to advise at 100 dept.	22 (0.8%)	310399	-0.05 (4.25 to 4.95)	071 (040 to 120)		
Cram require down amount six infrational TIC desir	28.50	1(921)	671 (845 to 102)	2.66 (8.27%)		
can alter and advanta money at all	7 (6.7%)		631(4314101)	15.00		
Superficial complete site industries on ESE days*	38 (1.75)	34 (43/5)	210 (470, 640)	041 (030 to 149)	606	
Draft at Not dept*	3 (4.85)	60.231	445 (435, 945)	0.07 (0.14 to 2.24)		
Loss of Both or ampristion at Nifeliger*	2 (4.3%)	6(373)	-0.65	6-61		
Francisco Colonius at 760-digart	7 (12%)	12 (2.7%)	435124144350	0.N (0.22 to 1.41)		
Front Misson a NO April	20.50	510451	435132544460	00210319129		
Kond soom at honeous # Nil day?"	8 (8.8%)	10351	-8.65	644		