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## RESEARCH ARTICLE

### Comorbidities Affect the Recovery Rate of Covid-19 Patients - A Retrospective Study in Lahore, Pakistan

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#### ABSTRACT

Many studies have identified various risk factors associated with Covid-19, for example, individuals with comorbidities are at an increased risk of contracting the disease and developing severe symptoms than those without comorbidities, however, these findings are inconsistent. This study identifies various risk predictors of Covid-19 patients with and without comorbidities. Data of Covid-19 patients was retrieved from Patient Digital Library of Shalamar Hospital, Lahore and encompassed patients' gender, age, symptoms and severity besides other vitals. Data of total 1,639 patients who were admitted at Pulmonology Unit of Shalamar Hospital was examined. Out of this, 180 Covid-19 patients were recruited for final analyses as they were fully in accordance with the eligibility criteria framed for this study. Of these, 137 were suffering from comorbidities and the analysis revealed that these comorbidities had significant effect on the end result of the Covid-19 illness ( $P=0.002$ ) i.e. the mortality rate among the patients with comorbidities was found to be 33.6% ( $n=46$ ) and that of patients with no comorbidities was 9.3% ( $n=4$ ). Likewise, the recovery rate of patients without comorbidities was significantly high (90.7%,  $n=39$ ). However, interestingly, presence or absence of comorbidities had no significant impact on severity of the disease. Moreover,  $O_2$  saturation  $< 90\%$  is predicted as a risk factor of severity whereas age  $> 59$ , presence of comorbidities and severe symptoms are found to be the risk predictors for the outcome of the disease being recovered or expired.

**Key Words:** Comorbidities; Covid-19; Risk Factors; Recovery rate

## 1. Introduction

Coronavirus disease (Covid-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a pandemic that was initially identified in Wuhan, China, on 31st Dec 2019 and spread quickly, making its way to over 180 countries.<sup>1</sup> Initially, WHO declared it a Public Health Emergency of International Concern (PHEIC) on 30th Jan 2020 and later it was declared as a pandemic on 11th Mar 2020. Covid-19 manifestations include a spectrum of illnesses, ranging from asymptomatic infection to severe pneumonia, adult/acute respiratory distress syndrome (ARDS) and even death.<sup>2</sup> As reported by the WHO, there have been 578,142,444 confirmed cases of Covid-19 worldwide, including 6,405,080 deaths by August 04, 2022.<sup>3</sup> The first case of Covid-19 in Pakistan was reported on 26<sup>th</sup> February, 2020 and since then there have been a surge in the number of patients infected with this deadly virus including 1,556,445 confirmed cases and 30,499 deaths as per the latest details.<sup>4</sup>

Over a span of two years, a large number of studies have been carried out to explore different dimensions of the disease. There are still many limitations to our knowledge of who exactly this virus would affect critically.<sup>1</sup> Older adults and people with underlying medical conditions, such as hypertension, cardiac disease, diabetes, kidney diseases and respiratory illnesses have shown worse prognosis.<sup>5-7</sup> Moreover, males are observed to have been affected more by this virus as compared to females.<sup>8-10</sup> A study reported men to be more prone to dying as compared to women when affected by this virus.<sup>11</sup> In relevance to the role of comorbidities in Covid-19, a study found obese patients suffering from this disease to have twofold increased risk of ICU admission or death as compared to normal-weight patients.<sup>2</sup> According to the WHO, seriousness of this disease strongly corresponds to the underlying host conditions including age and overall health.<sup>3</sup> In addition, individuals with other health related issues like liver, kidney and lung diseases also have severe form of the infection.<sup>12,13</sup> According to a study, metabolic-associated fatty liver disease, which affects almost quarter of population of the world, is associated with the severity of Covid-19.<sup>14</sup> Similar results were found with chronic kidney disease and interstitial lung disease as well.<sup>15,16</sup> Although many studies have shown the correlation of underlying comorbidities with severity of Covid-19 infection, yet there are some studies which depicted conflicting results.<sup>17</sup> Similar inconsistent findings are also reported with respect to the mortality rate associated with this disease.<sup>1</sup>

In Pakistan, the incidence of non-communicable chronic diseases is high with 80% of elderly suffering from them<sup>18</sup> which makes them more susceptible to this virus. Identifying the groups of individuals who are at higher risk of getting infected with Covid-19 is important so that medical communities can identify them earlier and treat them accordingly. Moreover, finding the risk factors associated with this disease is also becoming vital because of the increasing number of Covid-19 cases during its fifth wave. Bearing this in mind, this research intends to study the association of presence or absence of comorbid conditions on severity and outcome of Covid-19 patients. Other than comorbidities, age and O<sub>2</sub> saturation are also studied as the potential risk factors for this deadly virus.

## 2. Methodology

### 2.1. Study Design, Setting and Participants

This was a retrospective study conducted at the Department of Research & Innovation, Shalamar Institute of Health Sciences in Lahore, Pakistan. Self-designed questionnaire based study proforma was used to record the data of patients. Medical records of patients admitted at the Department of Pulmonology of Shalamar Hospital, Lahore within the time period of 1<sup>st</sup> May 2020 to 31<sup>st</sup> October 2021 were thoroughly checked. The Covid-19 patients of both genders and above the age of 18 were included in the study and all the Covid-19 patients taking any anti-viral or who had incomplete data were excluded.

### 2.2. Data Extraction

The Patient Digital Library of Shalamar Hospital was approached to retrieve data for patient's age, gender, symptoms, severity and O<sub>2</sub> saturation. Moreover, whether the patient received treatment at home or at Hospital was also noted. In addition, the outcome of the disease was recorded as either recovered or expired. The Covid-19 patients who were discharged on request were excluded from final analysis because their outcome was unknown. Severity of Covid-19 illness in patients was based on the clinical symptoms and their need for oxygen and ventilation as well. The patients who had sore throat, cough, runny nose, diarrhea, muscular pain, fever, fatigue, loss of taste, loss of smell, headache, malaise, vomiting, shortness of breath and oxygen saturation  $\geq 90\%$  were considered to have less severe illness. Whereas the patients with shortness of breath, liver dysfunction, septic shock, O<sub>2</sub> saturation less than 90%, respiratory frequency of more than 30 breaths/minute and lung infiltrate  $> 50\%$  were categorized as severe.

### 2.3. Data Analysis

The IBM SPSS Statistics 20 was used for the analysis of data. The association between variables was tested by Chi-square test and regression analysis was performed through binary logistic regression. Goodness of fit was estimated through Hosmer-Lemeshow test. Moreover, P value less than 0.05 was considered statistically significant.

### 2.4. Ethical Considerations

Prior conducting the study, ethical approval was obtained from Institutional Review Board of Shalamar Medical & Dental College, Lahore (IRB-0320). All patients' records obtained were password protected and kept under proper lock. Only the members of the research team had access to the data.

### 3. Results

According to the data collected from Patient Digital Library of Shalamar Hospital, 1,639 patients were found admitted at the Pulmonology unit of Shalamar Hospital within the period of May 2020 to October 2021. Out of these, 180 patients met the inclusion criteria of this study comprising 54.4% males (n=98) and 45.6% females (n=82). Amongst these, 137 were suffering from different comorbidities like diabetes, hypertension, cardiac disease, lung disease, liver disease etc whereas 43 patients had no comorbidity at all. The mean age of all these patients was  $59 \pm 14.88$  (Mean  $\pm$  SD) with 63.9% and 36.1% having severe and less severe illness respectively. Of these, 130 got recovered and remaining patients died of the illness. Other than shortlisted Covid-19 patients, there were 54 more confirmed Covid-19 patients who were discharged on request due to financial constraints or other unknown reasons. Because their outcome was not known, they were excluded from final analysis.

The comorbidities that were found to be most prevalent among these Covid-19 patients were hypertension (73.7%, n=101) and diabetes (67.9%, n=93) followed by cardiac disease

(31.4%, n=43). Other comorbidities which were present in < 2% of patients included hyperlipidemia, guillain-barre syndrome, arthritis, oral candidiasis, hyponatremia, hyperkalemia, thrombocytopenia and anemia. In addition, 2-6% of the patients had obesity, neurological issues, hypothyroidism and auditory processing disorder, whereas 10-20% of the patients were suffering from certain diseases of lung, kidney and liver.

Regarding the severity levels of Covid-19, they were categorized into 2 subcategories i.e. less severe and severe. Most of the patients (63.9%, n=115) admitted had severe form of the illness with symptoms like shortness of breath, myocardial injury, lung infiltrate of >50%, respiratory frequency of >30 breaths/minute, O<sub>2</sub> saturation of <90% and liver dysfunction. Some other symptoms included palpitations, epigastric pain, loose motion, hemoptysis, myalgia, syncope, altered state of consciousness and pulmonary edema. Less severe symptoms included sore throat, cough, runny nose, diarrhea, muscular pain, fever, fatigue, loss of taste and smell, headache, malaise, vomiting, erythematous rash and saturation of oxygen  $\geq 90\%$ .

The Covid-19 patients recruited in this study were further categorized into two sets, one had patients with comorbidities (n=137) and the second had patients with no comorbidity at all (n=43). In the first set, 56.2% (n=77) patients had up to 2 comorbidities and 43.8% (n=60) had more than 2 comorbidities. The mean age of patients with comorbidities was  $63 \pm 12.4$  (Mean  $\pm$  SD) and of patients with no comorbidities was  $47 \pm 15.99$  (Mean  $\pm$  SD). Of all the patients under analysis, 175 patients (97.2%) were treated at Hospital and 5 (2.8%) patients were given treatment at home. Those patients who were treated at Hospital remained there for approximately 6.5 days. Figure 1 shows the overall distribution of the Covid-19 patients with respect to gender, mean age, severity of the disease, their treatment place and number of days admitted in Hospital.

All Patients	Patients with Comorbidities	Patients without Comorbidities
Total: 180 M: 98 (54.4%) F: 82 (45.6%)	Total: 137 M: 72 (52.6%) F: 65 (47.4%)	Total: 43 M: 26 (60.5%) F: 17 (39.5%)
Mean age±SD 59 ± 14.88	Mean age±SD 63 ± 12.4	Mean age±SD 47 ± 15.99
Severe: 115 (63.9%) Less severe: 65 (36.1%)	Severe: 92 (67.2%) Less severe: 45 (32.8%)	Severe: 23 (53.5%) Less severe: 20 (46.5%)
Treated at: Hospital:175 (97.2%) Home: 5 (2.8%)	Treated at: Hospital: 133 (97.1%) Home: 4 (2.9%)	Treated at: Hospital: 42 (97.7%) Home: 1 (2.3%)
Average days admitted at Hospital: 6.5 days	Average days admitted at Hospital: 7 days	Average days admitted at Hospital: 5 days

**Figure 1.** Summary of Covid-19 patients admitted at the Shalamar Hospital from 1<sup>st</sup> May 2020 to 31<sup>st</sup> October 2021

For statistical analysis, data was divided into 3 groups. The Group 1 comprised data of all the Covid-19 patients whereas Group 2 and 3 had data of patients with comorbidities and patients without comorbidities respectively. The data was analyzed with respect to the association of age, gender, O<sub>2</sub> saturation and comorbidities with the severity and outcome of the disease. The analysis of all groups revealed significant association of O<sub>2</sub> saturation with both severity and outcome of the disease ( $P<0.05$ ). Moreover, significant association of these variables was also found with the age of Group 1 and 3 ( $P<0.05$ ). Likewise, in Group 1, comorbidities were found to have significant effect

on the end result of the Covid-19 illness ( $P=0.002$ ) i.e. the mortality rate among the patients with comorbidities was found to be 33.6% ( $n=46$ ) and that of patients with no comorbidities was 9.3% ( $n=4$ ). Similarly, the recovery rate of patients without comorbidities was significantly high (90.7%,  $n=39$ ) as compared to those with comorbidities (66.4%,  $n=91$ ). On the other hand, severity of the disease was not found to have any significant impact of either presence or absence of comorbidities. Similarly, no substantial impact of gender on severity and outcome of Covid-19 was observed in this study. The results of all groups are summarized in Tables 1-3.

**Table 1.** Association of age, gender, O<sub>2</sub> saturation and comorbidities with severity and outcome in Group 1 having all Covid-19 Patients

Variables		Age				Gender				O <sub>2</sub> Saturation				Comorbidities			
		≤ 59		> 59		Male		Female		< 90		≥ 90		Absent		Present	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Severity	Less severe	29	36.7	36	35.6	33	33.7	32	39	4	6.2	61	53	20	46.5	45	32.8
	Severe	50	63.3	65	64.4	65	66.3	50	61	61	93.8	54	47	23	30.8	92	67.2
	P- value	0.883				0.457				0.000				0.104			
Outcome	Recovered	65	82.3	65	64.4	71	72.4	59	72	35	53.8	95	82.6	39	90.7	91	66.4
	Expired	14	17.7	36	35.6	27	27.6	23	28	30	46.2	20	17.4	4	9.3	46	33.6
	P- value	0.008				0.941				0.000				0.002			

**Table 2.** Association of age, gender, O<sub>2</sub> saturation and comorbidities with severity and outcome in Group 2 having Covid-19 Patients with comorbidities

Variables		Age				Gender				O <sub>2</sub> Saturation				Comorbidities			
		≤ 63		> 63		Male		Female		< 90		≥ 90		≤ 2		> 2	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Severity	Less severe	19	26.4	26	40	22	30.6	23	35.4	3	5.6	42	50.6	26	33.8	19	31.7
	Severe	53	73.6	39	60	50	69.4	42	64.6	51	94.4	41	49.4	51	66.2	41	68.3
	P- value	0.09				0.548				0.000				0.795			
Outcome	Recovered	49	68.1	42	64.6	48	66.7	43	66.2	27	50	64	77.1	48	62.3	43	71.7
	Expired	23	31.9	23	35.4	24	33.3	22	33.8	27	50	19	22.9	29	37.7	17	28.3
	P- value	0.67				0.949				0.001				0.251			

**Table 3.** Association of age, gender and O<sub>2</sub> saturation with severity and outcome in Group 3 having Covid-19 Patients without comorbidities

Variables		Age				Gender				O <sub>2</sub> Saturation			
		≤ 47		> 47		Male		Female		< 90		≥ 90	
		n	%	n	%	n	%	n	%	n	%	n	%
Severity	Less severe	13	61.9	7	31.8	11	42.3	9	52.9	1	9.1	19	59.4
	Severe	8	38.1	15	68.2	15	57.7	8	47.1	10	90.9	13	40.6
	P- value	0.048				0.494				0.004			
Outcome	Recovered	21	100	18	81.8	23	88.5	16	94.1	8	72.7	31	96.9
	Expired	0	0	4	18.2	3	11.5	1	5.9	3	27.3	1	3.1
	P- value	0.04				0.532				0.017			

In this study, binary logistic regression was performed to predict the risk factors for severity and outcome of the Covid-19 illness in all the groups. With respect to the severity of the disease, the regression analysis of Group 1 revealed that Covid-19 patients with O<sub>2</sub> saturation < 90% will have 23.61 times more chances of getting severe symptoms of the disease as compared to those with ≥ 90% of O<sub>2</sub> level (CI: 5.42-102.85). Similarly, analysis of Group 2 and 3 showed that O<sub>2</sub> saturation < 90% in patients with and without comorbidities have 43.17 (CI: 5.67-328.77) and 15.26 (CI: 1.59-145.96) times chances of getting severe form of the Covid-19 illness. With respect to the end result of this disease, age, presence of comorbidities and severe form of the illness are all found to be the risk predictors for the mortality rate of the patients suffering from Covid-19. Group 1

analysis depicted that Covid-19 patients with less severe symptoms and age ≤ 59 will have 0.16 (0.06-0.41) and 0.43 (CI: 0.202-0.94) times chances of getting recovered in comparison with the patients above this age. Likewise, patients with comorbidities will have 0.28 times (CI: 0.08-0.87) chances of recovery from this disease. Similar to the analysis of Group 1, severity of the disease is predicted to be the risk factor for its outcome i.e. severe patients of Covid-19 will have 0.302 (CI: 0.105-0.87) times chances of dying of the illness as compared to those patients who will have less severe form of the disease. Moreover, in the patients with O<sub>2</sub> level ≥ 90% will have 2.96 times (CI: 1.25-6.93) chances of getting recovered as compared to those with O<sub>2</sub> saturation less than 90%. These results are summarized in Table 4.

**Table 4.** Risk Predictors for Severity and Outcome in Covid-19 Patients

		Severity		Outcome	
		OR (95% CI)	P-value	OR (95% CI)	P-value
<b>Group 1</b>	Gender	0.91 (0.203-0.945)	0.186	0.95 (0.46-1.96)	0.897
	Age	1.51 (0.68-3.32)	0.31	0.43 (0.202-0.94)	<b>0.034</b>
	O <sub>2</sub> Saturation	23.61 (5.42-102.85)	<b>0.000</b>	0.54 (0.104-0.93)	0.246
	Comorbidities	0.65 (0.27-1.55)	0.334	0.28 (0.08-0.87)	<b>0.028</b>
	Severity	n/a	n/a	0.16 (0.06-0.41)	<b>0.000</b>
<b>Group 2</b>	Gender	1.11 (0.49-2.51)	0.8	0.84 (0.39-1.83)	0.662
	Age	1.61 (0.71-3.65)	0.256	0.63 (0.28-1.39)	0.248
	O <sub>2</sub> Saturation	43.17 (5.67-328.77)	<b>0.000</b>	2.96 (1.25-6.93)	<b>0.013</b>
	Comorbidities	0.76 (0.33-1.72)	0.506	1.503 (0.68-3.303)	0.31
	Severity	n/a	n/a	0.302 (0.105-0.87)	<b>0.027</b>
<b>Group 3</b>	Gender	1.41 (0.23-6.56)	0.667	0.66 (0.21-1.50)	0.25
	Age	0.33 (0.08-1.45)	0.142	0.21 (0.156-0.99)	0.526
	O <sub>2</sub> Saturation	15.26 (1.59-145.96)	<b>0.018</b>	1.36 (0.58-0.94)	0.123
	Severity	n/a	n/a	0.14 (0.10-0.85)	0.21

#### 4. Discussion

This is one of the few studies being conducted in Pakistan which describes the impact of low O<sub>2</sub> saturation, presence of comorbidities and higher age on the recovery rate among Covid-19 patients. Out of 1,639 patients admitted in the defined period, 180 patients were in accordance with the inclusion criteria framed for this study; hence their data was extracted for final analysis. The mean age of the patients observed from their data was found to be 59 ± 14.88 (Mean ± SD) with maximum patients suffering from severe form of the illness. Similar to many other studies<sup>19-22</sup>, in this study, more

males than females were found admitted in the Hospital with this life threatening illness. Males and females differ not only in their susceptibility but also in their response to the viral infections<sup>23</sup>. This difference might be due to the greater immune response in females as compared to males.<sup>24-26</sup> However, some studies have also shown contrasting gender distribution with respect to the incidence of Covid-19.<sup>11,27</sup>

Severity of Covid-19 was categorized as severe and less severe in this study. Common symptoms found among patients with severe illness were O<sub>2</sub> saturation less than 90%, lung infiltrate >50%,

respiratory frequency more than 30 breaths per minute, shortness of breath, myocardial injury and liver dysfunction. Sporadic symptoms observed were pulmonary edema, altered state of consciousness, epigastric pain, loose motion, palpitations, hemoptysis, myalgia and syncope. On the other hand, patients with less severe symptoms experienced oxygen saturation  $\geq 90\%$ , sore throat, cough, runny nose, fever, fatigue, loss of taste and smell, headache, erythematous rash diarrhea, muscular pain, malaise and vomiting. These symptoms were set according to the clinical guidelines defined by the World Health Organization.<sup>28</sup> The results revealed that severe cases of Covid-19 were more prevalent in this study as compared to less severe cases. Similar to other studies<sup>10,29-32</sup>, this is most likely because of the presence of comorbidities in most of the patients i.e. 137 out of 180 Covid-19 patients had more than one comorbidity.

The most common comorbidities that were present in Covid-19 patients admitted at Shalamar Hospital included hypertension, diabetes and cardiac disease. In accordance with the findings of other studies<sup>1,33-39</sup>, this study also observed hypertension as the most prevalent comorbidity followed by diabetes. Additionally, various diseases of lungs, kidneys and liver were also co-occurring but in not more than 20% of the patients. Amongst these, chronic kidney disease has also been reported by some studies to be associated with increased hospitalization due to Covid-19 infection.<sup>12,13</sup> Moreover, patients with obesity, neurological issues, hypothyroidism and auditory processing disorder were also admitted but they were less than 10% of all the patients. Though, obesity has been reported as the most prevalent comorbidity in other countries including China.<sup>37,40,41</sup> Furthermore, in accordance with other studies<sup>42-46</sup>, there were some other comorbid conditions in the patients of this study which were rarely occurring. For example, guillain-barre syndrome, oral candidiasis, hyponatremia and hyperkalemia were uncommon comorbidities in the subjects of this study. On the other hand, the present study also reported some uncommon comorbid conditions in Covid-19 patients which were found significantly associated with this disease in other populations. These included dyslipidemia, arthritis and thrombocytopenia.<sup>47-51</sup> Besides, like some other studies which reported anemia as a rare comorbidity in their Covid-19 patients, this study also observed anemia as an uncommon disorder.<sup>52,53</sup> Conversely, various studies have observed anemia as a common comorbidity and also reported its significant association with severity of Covid-19.<sup>54-56</sup>

Individuals suffering from one or more underlying health conditions like hypertension and diabetes are at an increased risk of contracting this deadly virus.<sup>1</sup> Similar to the findings of other studies<sup>36,57,58</sup>, comorbidities have been found significantly associated with the outcome of the disease in this study as well. However, unlike other studies which showed strong association between comorbidities and severity of the disease<sup>59-61</sup>, this study did not find any association of presence of comorbidities with severity of Covid-19.

The results of this study revealed strong association of low O<sub>2</sub> saturation i.e.  $< 90\%$  or hypoxia with both the severity and outcome of Covid-19 patients irrespective of presence or absence of comorbidities. This shows that the effect of low O<sub>2</sub> saturation is independent of the underlying health conditions of Covid-19 patients. Likewise, certain studies have also reported that low O<sub>2</sub> levels are significantly associated not only with severity of the disease but also are predictors of mortality in patients suffering from Covid-19.<sup>62-64</sup> Low level of oxygen saturation has also been found to increase the vascular permeability and serum pro-inflammatory cytokines in animal models leading to lung disease.<sup>65</sup>

The patients recruited in this study, either male or female, have no significant difference with respect to the severity or outcome of the illness. As reported by some other studies, both genders in this study were also equally susceptible to the disease, its severity and mortality or recovery from the disease.<sup>66,67</sup> However, other studies showed contrasting results i.e. men were found to have more severe illness as compared to women.<sup>8-10</sup> Moreover the fatality rate was also significantly different in both genders with males at more risk than females.<sup>68,69</sup> This difference is believed to be due to the higher levels of estrogen in female patients of Covid-19 which are responsible for rise in innate and humoral immune responses, which ultimately reduces the risk of severity and mortality in female patients.<sup>70-72</sup>

The analysis of the impact of age on the severity or outcome of the disease in all patients either with comorbidity or not, revealed that age is significantly associated with outcome of the disease as reported by other studies also.<sup>5,73</sup> However, when analyzed in the group of patients with no comorbidities at all, age was found to have strong impact on both severity and outcome of the disease. Older patients have been reported to have severe form of the illness due to weaker immunity.<sup>74-76</sup>

The present study also predicted some risk factors for severity and outcome of the Covid-19 illness. With respect to the severity of the disease, similar

to findings of other studies<sup>64,77,78</sup>, O<sub>2</sub> saturation below 90% is found to be a risk factor for developing severe form of the illness in individuals either suffering from any comorbidities or not. On the other hand, age, comorbidities and severe illness are all found to be the risk predictors for the mortality rate of the patients suffering from this disease. These are also in accordance with the predictions of the risk factors by other studies.<sup>79-83</sup> These results suggest that better management of such risk factors can result in better and early recovery of these patients.

## 5. Conclusion

This study describes the association of multiple factors with the severity and outcome of Covid-19 patients with and without comorbidities. With the 5<sup>th</sup> wave of Covid-19 surging up, it is highly important to understand the risk predictors of the severity and outcome of the disease so that health professionals can treat the patients timely. Furthermore, older patients and those with comorbidities should follow all the protective measures to prevent themselves from worse effects of the disease.

## Conflict of Interest:

The authors declare no conflict of interest.

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