Colin J Crooks^{1,3,4} Joe West^{2,3,4,6} Joanne R Morling^{2,3} Mark Simmonds⁴ Irene Juurlink⁴ Simon Cruickshank⁴ Steve Briggs⁴ Susan Hammond-Pears^{4,6} Dominick Shaw ^{4,5} Timothy R Card^{2,3,4} Andrew W Fogarty^{2,3,4}

- 1. Nottingham Digestive Diseases Centre, School of Medicine, University of Nottingham, NG7 2UH
- 2. Lifespan and Population Health, School of Medicine, University of Nottingham, NG5 1PB.
- 3. NIHR Nottingham Biomedical Research Centre (BRC), Nottingham University Hospitals NHS Trust and the University of Nottingham, NG7 2UH
- 4. Nottingham University Hospitals NHS Trust, NG7 2UH
- 5. Division of Respiratory Medicine, School of Medicine, University of Nottingham, NG5 1PB
- 6. East Midlands Academic Health Science Network, University of Nottingham, Nottingham, NG7 2TU

Corresponding Author: <u>andrew.fogarty@nottingham.ac.uk</u> Word count: 1099 words

Dear Editor,

End stage chronic lung diseases often require long-term oxygen therapy (LTOT), which can reduce mortality and palliate symptoms ¹. The need for LTOT is determined by the Pa0₂ (partial pressure of arterial oxygen) measured by arterial blood gas analysis (ABG), but blood oxygen saturation measured by pulse oximetry (SpO₂) is more convenient and is often used to identify which patients require an ABG. It is now apparent that pulse oximetry measurements are less accurate than previously appreciated, especially in patients with arterial oxygen saturations of less than 92% ². Hence, these pulse oximetry measurements potentially inform the clinicians' decisions to consider when to request an arterial blood gas, particular for patients who are monitored in the community, where arterial blood gases are not routinely available.

We used paired data from oxygen saturations (SpO₂) measured by pulse oximetry, and the PaO₂ from concurrent arterial blood gases, to assess how accurate pulse oximetry was at identifying eligibility for LTOT, based on a PaO₂ of 7.3kPa or less ¹.

The study design uses routinely collected electronic data for patients admitted to Nottingham University Hospitals NHS trust between 1 February 2020 and 31 December 2021 with SARS-CoV-2 ³. Bedside pulse oximetry measurements were recorded electronically (<u>http://nervecentresoftware.com/</u>), and arterial blood gas pulse oximetry measurements were automatically uploaded from the point of care machines. Oximetry measurements within Intensive Care Units (ICUs) were not included in this study as these were not available electronically. Paired measurements of oxygen saturations from pulse oximetry and partial pressure of oxygen from arterial blood gases within a time period of 30 minutes were identified. Patients with an arterial blood gas showing a saturation of 70% or less were excluded from the analysis. As blood pressure can modify the pulse oximetry signal ⁴, patients with a systolic blood pressure of 100mmHg or less were excluded from the analysis as were patients with a haemoglobin measurement of less than 100g/L ⁵.

We measured the true positive rates of identifying patients with a blood gas oxygen pressure ≤7.3kPa at each percentage increment of oxygen saturation between 88 and 95%. We then modelled the association between arterial oxygen pressure and pulse oximetry estimated oxygen saturation by plotting the pulse oximetry saturation against arterial blood gas oxygen partial pressure, fitting a smooth curve using a general additive spline model, and used this model to predict the pulse oximetry oxygen saturation level for an arterial blood gas pressure of oxygen equalling 7.3kPa. The analysis used R (version 4.3.1).

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Governance approval was provided by an NUH Clinical audit (21-294C) and IRAS (REC: 20/WM/0142, amendment No. SA02 20/07/21).

4784 paired arterial blood gas (PaO₂) and pulse oximetry measurements (SpO₂) were available from 3371 patients. 2656 (56%) were male and the mean age was 66.2 years (standard deviation 16.9 years). Ethnicities were recorded as White 3498 (73%), Asian 214 (4%), Black 182 (4%), Other 115 (2%) and Not Recorded 775 (16%).

The proportion of patients with a PaO₂ of \leq 7.3 KPa at each level of oxygen saturation (i.e. would potentially benefit from LTOT/true positives) is shown in the Table. When stratified by pulse oximetry the proportion of true positives reduced from 52% (SpO₂ < 88%) to 11% (SpO₂ >95%).

Ethnicity was an important modifier of the measurement difference of pulse oximeters in the spline model (likelihood ratio test including ethnicity in model, p = 0.003). Using separate models for each ethnicity to predict an arterial oxygen partial pressure of 7.3kPa; White patients had a predicted pulse oximetry saturation of 90.3% (95% confidence intervals CI: 89.8% to 90.7%), with corresponding values for Asian patients of 93.1% (95% CI: 92.2% to 94.0%), and for Black patients of 92.9% (95% CI: 91.4% to 94.5%).

This analysis demonstrates that in a large population of 3371 unselected patients, oxygen saturations derived from pulse oximetry cannot reliably identify patients who are eligible for LTOT, with approximately 15% of patients with an apparently healthy pulse oximeter oxygen saturation of 92%, having an arterial partial pressure of less than or equal to 7.3 kPa. This measurement error is higher in patients with non-white skin.

The strengths of this analysis are the availability of large numbers of paired pulse oximetry and arterial blood gas measurements across a range of severities of respiratory failure. We were able to generate estimates of patients who would have been denied LTOT stratified by pulse oximeter saturation, and further model the impact of ethnicity on this process. It builds upon a small study of 212 patients with COPD that reported that 5% of patients with a Sp02 of 92% or more would be denied LTOT using this criterion⁶.

The limitations of the analysis include generalisability, as our data are from patients with Covid-19 infection. However, we excluded patients with very severe respiratory failure, hypotension and anaemia mimicking a population with respiratory failure who may be eligible for LTOT. Although in the early stages of the Covid-19 pandemic, there were concerns that Covid-19 infection resulted in

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differing responses to hypoxia than other diseases, subsequent analysis demonstrated that 'silent hypoxaemia' was not a distinct clinical entity in this patient group ⁷.

A significant implication of this analysis is that pulse oximetry has little or no added value in informing LTOT consideration in patients with respiratory disease. Although this is highlighted in the British Thoracic Society guidelines from 2015, which state that '*Patients potentially requiring LTOT should not be assessed using pulse oximetry alone*'¹, it seems likely that the ubiquitous use of pulse oximetry measurements in healthcare will result in these measurements becoming one of the main factors involved in considering testing for LTOT eligibility. This measurement error may be larger in patients with non-white skin ⁸. Differences in measurement error of oxygen saturations derived from pulse oximeters may already contribute to delays in delivering acute medical to patients with non-white skin tones ⁹ and may also delay consideration of LTOT in these patient groups ¹⁰.

In conclusion, this analysis using real-world data of the measurement error of Sp02 demonstrates that using this measure alone to identify patients who are eligible for LTOT will miss many suitable individuals, and this is likely to be higher in non-White populations. The National Institute of Clinical Excellence in the United Kingdom recommends that people with stable COPD and a persistent resting stable oxygen saturation of 92% or less have their arterial blood gases measured to assess whether they need LTOT ¹¹. This threshold would not identify approximately 11% of patients. These data are consistent with the suggestion by Sudat *et al* that current guidelines for the usage of pulse oximeters should be 'revisited, investigated, and revised' ¹².

Author contributions

AF and DS developed the hypothesis. JW, TC, CC, SB, JM, IJ, MS, SC, SH-P developed the database. CC did the statistical analysis. The first draft of the manuscript was written by AF and edited by all of the manuscript's authors.

Competing interests: The authors have no competing interests to declare.

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Table. Proportion of samples with arterial oxygen pressure <= 7.3 KPa at different oxygen saturations measured by pulse oximetry and by arterial blood gas

	Pulse oximetry saturations			Arterial blood gas saturations		
Oxygen Saturation	N	Number paO2 ≤ 7.3	Percentage paO2 ≤ 7.3	N	Number paO2 ≤ 7.3	Percentage paO2 ≤ 7.3
<88	431	226	52.40%	806	699	86.70%
88	227	95	41.90%	164	88	53.70%
89	167	53	31.70%	172	59	34.30%
90	284	83	29.20%	236	41	17.40%
91	245	42	17.10%	294	15	5.10%
92	448	66	14.70%	348	<10	-
93	347	48	13.80%	410	<10	-
94	548	72	13.10%	413	<10	-
95	447	46	10.30%	434	<10	-
>95	1640	176	10.70%	1507	<10	-

Patient population of arterial blood gas samples with a paired pulse oximetry measurement within 30 minutes, arterial haemoglobin \geq 10g/L, systolic blood pressure \geq 100mmHg, and arterial oxygen saturation \geq 70%.

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