Physiologically driven, altitude-adaptive model for the interpretation of pediatric oxygen saturation at altitudes above 2000 m a.s.l.

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ABSTRACT

Background: Hypoxemia is a critical condition that relates to respiratory disease. The use of pulse oximeters for measuring peripheral oxygen saturation (SpO_2) to guide oxygen therapy and treat hypoxemia is largely established for children living at low altitudes. However, at higher altitudes above 2000 m a.s.l., no clear abnormal SpO_2 thresholds and recommendations for oxygen delivery are available.

Objective: Our aim was to provide a plausible model for the calculation of abnormal SpO_2 thresholds for altitudes between 0 m a.s.l. and 4000 m a.s.l. that takes into account physiological adaptation to these altitudes.

Methods: We analysed the altitude sensitivity of oxygen transport parameters, and we created an altitude-adaptive SpO_2 model based on the oxygen cascade. We derived an altitude-adaptive abnormal SpO_2 threshold from known changes in the abnormal range. We compared our model and threshold with a previously proposed statistically derived model to two empirical datasets containing pulse oximetry data that were recorded from Peruvian children living at altitudes up to 4500 m a.s.l.

Results: Our altitude-adaptive SpO_2 model describes the empirical pulse oximetry data, and provides an altitude-adaptive threshold that conservatively estimates abnormal SpO_2.

Conclusion: We propose a digital model to calculate the abnormal SpO_2 threshold for children living at altitude. Since the model takes into account realistic physiological changes, the output of the model is easily reproducible. Such a model could be used in decision support systems to help practitioners adjust oxygen administration for children living at altitudes above 2000 m a.s.l..

Keywords: Hypoxemia, Altitude, Oxygen Saturation, Children health.

INTRODUCTION

Acute lower respiratory infections (ALRI) are a major health burden in low- and middle-income countries. Childhood pneumonia accounts for 14 % of all deaths in children under five years worldwide[1], of which 95 % occur in low resource settings [2]. A common condition observed in ALRI is hypoxemia, an abnormally low level of oxygen partial pressure in the arterial blood (SaO_2) [3] that can lead to dyspnoea and cyanosis. A rapid and non-invasive estimation of hypoxemia can be obtained through pulse oximetry that measures peripheral oxygen saturation (SpO_2). Pulse oximetry has become a suitable technology for application in low resource settings due to the simplicity of use and non-invasiveness of the device [4], [5]. The use of pulse oximeters in clinical applications has shown to drastically reduce death rates and improve child health in general [6]. However, in the countries where these powerful measuremsupplement devices are needed most, health personnel have only slowly started to gain access.

The interpretation of pulse oximetry readings of SpO_2 values for hypoxemia is challenging, especially for health personnel not familiar with respiratory physiology. Furthermore, the accuracy of certified pulse oximeters is approximately ± 2 % (brand and probe dependent), which can easily be overlooked. The World Health Organization (WHO) recommends the administration of oxygen when SpO_2 drops below or is equal to 90 %[7]. This fixed threshold oversimplifies hypoxemia treatment [6]. Additionally, the threshold does not indicate when to stop treatment and disregards the local context. Namely, in many rural areas, oxygen is a rare and precious resource if available at all, and therefore administered only restrictively. Furthermore, altitude has a direct influence on SpO_2 as the air pressure decreases and consequently, the alveolar oxygen partial pressure decreases with increasing altitude [3]. Thus, the treatment of ALRI, i.e. administration of oxygen, might be affected at higher altitudes and the recommended therapeutic thresholds at sea level may not be applicable.

Knowledge regarding SpO_2 distribution across altitudes in healthy and sick children is still limited. While reference values for healthy children living up to 5100 m a.s.l. have been reported over the past 25 years [8]–[13], the distribution of SpO_2 values for sick children is less clear. Furthermore, previous studies have not been able to conclusively answer at which SpO_2 levels oxygen should be administered at altitude or in limited settings. With pulse oximeters increasingly being used as monitors for ALRI diagnosis and treatment, additional research is urgently needed to provide a reliable description of the SpO_2 distribution at altitude, and to develop guidelines of oxygen administration for hypoxemic children living in these settings.

In this work, we introduce an altitude-adaptive SpO_2 model, and an altitude-adaptive abnormal SpO_2 threshold for hypoxemia. We describe normal and abnormal SpO_2 values of children living at altitudes up to 4000 m a.s.l. to provide new decision support tools for health workers operating in low resource settings and to improve clinical management of hypoxemia in children with ALRI. We aim to provide a better understanding of normal and abnormal SpO_2 values at altitudes above 2000 m a.s.l. for healthy and sick children, while analysing the change of physiological parameters with increasing altitude in rural Andean Peru.

Related Work

The literature presents two modelling approaches that describe the relationship between SpO_2 and altitude.

Subhi and et al. developed a statistical model of the SpO_2 distribution across altitudes that is based on empirical observations from healthy children, and from this model derived an altitude-adaptive threshold for hypoxemia [14]. Data were obtained through a literature review of studies performed between 0 and 4018 m a.s.l.. A linear random effects meta-regression was performed to predict mean and 2.5^{th} centile SpO_2 with an exponential equation. The systematic review with derived modeling could not control numerous influencing factors such as choice of oximeter technology, heterogeneous ethnicity and age range of studied subjects, or the measurement protocols. Subhi et al. proposed also an altitude-adjusted hypoxemia threshold at the 2.5^{th} centile model of

healthy children's SpO_2 at each altitude, contrasting the WHO's suggestion of oxygen administration. It is unclear why this specific, statistically derived threshold was chosen.

Our group developed a digitised model that described the pathway of oxygen throughout the cardio-respiratory body compartments [15]. It implemented the oxygen cascade introduced by West [3]. The model used well-established physiological equations to explain how the partial oxygen pressure and oxygen concentrations are interrelated between alveolar and peripheral blood (see supplementary material). The oxygen cascade describes the oxygen loss from the pressure of inspired air to the resulting measurements of SpO_2 by a pulse oximeter. Therefore, the model was based on physiological parameters and integrated uncertainties due to pulse oximeter inaccuracies. A shortcoming of the model was that it assumed many physiological parameters to be constant and therefore did not consider acclimatisation. Consequently, it could not correctly describe SpO_2 measured at higher altitudes, especially in acclimatised subjects such as permanent residents. This model did not foresee the calculation of hypoxemia thresholds.

In a very recent prospective study, Rojas-Camayo et al. recorded SpO_2 from 6289 subjects in the Peruvian Andes across 15 altitudes (154 m – 5100 m a.s.l.) [13]. They reported the 2.5^{th}, 10^{th}, 25^{th}, 50^{th}, 75^{th}, 90^{th} and 97.5^{th} centile of the data, but neither did provide a descriptive model thereof, nor suggested an abnormal threshold.

MODELLING

Altitude-adaptive SpO_2 model

We propose to model the response of SpO_2 to altitude using the oxygen cascade. We modified the previously established digital model of the oxygen cascade [15] to include physiological adaptation to high altitudes. The oxygen cascade, originally developed for adults, could easily be adapted to a pediatric model as there are no indications that the underlying physics of gas exchange are any different in children [16]. We identified relationships between altitude acclimatization and the parameters of the oxygen cascade, such as air pressure, haemoglobin concentration (cHb), alveolar partial pressure of carbon dioxide ($pACO_2$), the respiratory quotient (RQ), and virtual shunt (VS). We derived normal values for cHb, RQ and VS for two altitudes (0 m and 4500 m a.s.l.) from the literature [3], [17], [18], and linearly interpolated the parameters between these two altitudes. A linear interpolation was chosen because a sensitivity analysis revealed only small changes upon variation of these parameters (see supplementary material). In contrast, $pACO_2$ was directly derived from values reported by Rahn and Otis [19], as it was clear that changes in this parameter would not be linear. The oxygen cascade enabled us to not only estimate the expected SpO_2 for a certain altitude but also to estimate healthy ranges. Furthermore, we could incorporate the technical tolerances that account for the accuracy of pulse oximeters (i.e. ± 2 %) determined according to device standards [19] into the model, as shown in Karlen et al. [15].

Altitude-adaptive abnormal SpO_2 threshold

Analogously, we derived an altitude-dependent threshold for abnormal SpO_2. Hypoxemia is defined as reduced arterial partial pressure of oxygen (paO_2), which results in a decrease of SpO_2 and VS [3]. Therefore, we used typical values measureable under hypoxemia to adjust the healthy limits. At sea level, we considered a patient to have hypoxemia if the paO_2 level is below 80 mmHg [17], [21]. We were unable to retrieve any data from the literature that would describe physiological changes in paO_2 and alveolar partial pressure of oxygen (pAO_2) during hypoxemia at altitudes above sea level. Therefore, we calculated the percentage difference between healthy subjects and patients at sea level, assuming VS to increase above 10 % and SpO_2 to decrease below 95 % [18]. We then derived pAO_2 under the assumption that the percentage change between healthy subjects and patients is constant throughout all altitudes with no changes in cHb, $pACO_2$, and RQ. Potential variation due to pulse oximeter technology was then added to the threshold.

MATERIALS AND METHODS

We retrospectively evaluated our novel altitude-adaptive SpO_2 model against multiple datasets and models. We compared our model to pulse oximeter recordings obtained during a randomised controlled trial performed in children living in the northern Andes of Peru. In addition, we introduced a recently published dataset to the comparison and depicted them together with an alternative model that was rooted in statistical modelling.

Study design and data collection

Our data collection was embedded within a randomised controlled trial by the Swiss- Peruvian Health Research Platform set in the Cajamarca region of the northern highlands of Peru, located in the provinces of San Marcos and Cajabamba. Our study harnessed the operational and logistical local setup of this trial, which assessed the efficacy of an Integrated Home-environmental Intervention Package (IHIP-2) to improve child respiratory, enteric, and early child development outcomes [22].

After institutional review board approval from the University Peruana Cayetano Heredia (UPCH clearance number 268-12-15), 320 families with at least one child aged between 6 and 36 months in 102 rural communities were recruited, and informed written consent was obtained from the children's guardians. Over the course of just over a year (6 weeks pilot trial, followed by 54 weeks of main trial), field workers (FWs) visited each child at home to perform a mobile health assessment once a week. FWs had experience from earlier research projects in collecting basic vital signs and symptoms [23], [24], received five additional days of educational training for the collection of morbidity data, and underwent one month of practical training before the study started (pilot). FWs were equipped with a TAB 2 A7-10 tablet (Lenovo Group Ltd, Beijing, CN). The tablet had a custom mHealth app installed that was developed using the *lambdanative* framework[25]. It recorded a photoplethysmogram (PPG) and derived SpO_2 and heart rate (HR) using an USB connected iSpO_2 Rx pulse oximeter (Masimo International, Neuchatel, CH) with a universal Y-probe. Simultaneously, respiratory rate was recorded using the RRate app module [26]. In addition, the app acquired location and altitude using the embedded global positioning system (GPS) sensor. Information about the visit such as child ID and child agitation during the measurements was reported using a questionnaire. All electronically collected data was uploaded from the app directly into an online research database [27]. Health seeking behaviour and other relevant endpoints were reported in a paper-based, validated questionnaire [24], quality checked, and digitised at the end of the study.

Post processing

The IHIP-2 vital signs data obtained from the pulse oximeter were post processed to guarantee high data quality. The PPG, SpO_2, HR, and perfusion index (PI) time series from the main trial period were imported into Matlab (R2017b, MathWorks Inc., Natick, USA) where a signal quality index (SQI) for the PPG was calculated [28]. Only recordings with high SQI were used to extract SpO_2 segments. Segments with a SpO_2 value of 0 and above 100 were excluded. Recordings were excluded if a single segment duration was shorter than 12 s or, if multiple segments were available, shorter than 15 s. We excluded the recordings if the range of combined SpO_2 segments was too high (95^{th} - 5^{th} centile > 5 %). Moreover, we excluded those recordings where the range of the HR was ≥ 20 bpm and mean PI was ≤ 0.8. For the remaining segments, we reported the median SpO_2 over the combined segments. Additionally, we verified the consistency of the altitude provided by the GPS. Since each child was scheduled to be measured at the same altitude, we evaluated the median altitude of all measurements for each child. We excluded recordings that contained no GPS information and outliers that were more than three scaled median absolute deviations away from the median. The median altitude per child was reported.

Evaluation

To compare the two models with the available datasets, we visualised the altitude dependence of SpO_2. We applied a locally weighted scatterplot smoothing (lowess) smoother function [29] to all SpO_2-altitude data pairs collected during the IHIP-2 trial. We limited the comparison to the range of available data (2000–4000 m a.s.l.)

to avoid extrapolation errors. Instead of the LMS method used by Rojas-Camayo et al. [13], we reported the centiles of their data with a lowess smoother.

To visualise the difference between the various hypoxemia thresholds that have been proposed, we graphically compared the altitude-adaptive abnormal SpO_2 threshold, the statistical hypoxemia threshold, and the WHO definition for oxygen administration (90%) with the 2.5th centile (lowess smoothed) reported by Rojas-Camayo et al. [13].

RESULTS

We obtained an altitude-adaptive computational model to describe the expected SpO_2 range in healthy children, and to determine a threshold for an abnormal range that would indicate hypoxemia. The mathematical description of the model that accepts altitude as an input parameter can be found in the supplementary material, and the parameters used to define normal and abnormal ranges are available in Table 1. We included 6388 SpO_2 measurements from the IHIP-2 trial that contained both, GPS and PPG data with a good SQI for the analysis. Detailed numbers about the distribution of the children across altitudes can be found in the supplementary material.

*Table 1: Physiological parameters obtained from the literature used to describe the altitude-adaptive SpO_2 model. The healthy ranges (min, max and mean) describe known and expected values in a healthy subject. Parameters that are expected to change under hypoxemic conditions are reported in the last column. We do not differentiate between adults and children. *the data has been derived from healthy ranges at sea level. FiO_2 : Fraction of inspired O_2, P_{atm} : atmospheric pressure, PH_2O : vapour pressure of water.*

Parameter	Unit	Ref.	Healthy ranges						Hypoxemia
			Sea level			4500 m a.s.l.			
			min	mean	max	min	mean	max	
$pACO_2$	mmHg	[17], [19]	35	38	45	24*	29	34*	Assumed to be equal to healthy range
RQ	unitless	[3]		0.8			1		
cHb	g/100 ml	[3], [17]	12	15	17.5	17.5*	20	23*	
VS	%	[3], [18]	0	5	10	0	5	10	≥ 10
pAO_2	mmHg		Derived by the alveolar gas equation, with parameters FiO_2, P_{atm}, PH_2O, $pACO_2$ and RQ						86 % of the mean healthy value*

Our altitude-adaptive model provided a SpO_2 of 98.7 % at sea level with a range between 94.6 % and 100 % (Figure 1 and 2). The SpO_2 decreased with increasing altitude to 90 % at 4000 m a.s.l. with a healthy SpO_2 range from 84 % to 95 %. The two available data sets with empirical SpO_2 values showed highly overlapping curves for the 50th centile (Figure 1). The 2.5th and 97.5th centiles reported by Rojas-Camayo et al. followed the same trend as those acquired in the IHIP-2 trial but had a smaller range. Up to 3200 m a.s.l., the 2.5th to 97.5th centile range of both empirical data sets was well covered by the healthy range of the altitude-adaptive SpO_2 model, whereas at higher altitudes, the 2.5th centile of the IHIP-2 data exceeded the healthy range up to 3% at 4000 m a.s.l.

The two studied models showed very similar trends and values at lower altitudes (from 0 m a.s.l. to 2200 m a.s.l.) with a maximum absolute difference between the two models of less than 0.1 % (Figure 2). At altitudes above

2200 m a.s.l., the statistically obtained model had a negative bias towards lower SpO_2 values with a difference of up to -3.4 % at 4000 m a.s.l. compared to the altitude-adaptive SpO_2 model.

The altitude-adaptive abnormal SpO_2 threshold followed a similar trend as the 2.5th centile of Rojas-Camayo's empirical data with 91.5 % vs 94 % at 2000 m a.s.l. and 82 % vs 84 % at 4000 m a.s.l. (Figure 3). The 2.5th centile threshold explored by Subhi et al. had a SpO_2 threshold of 82.8% at 2000 m a.s.l. and then rapidly diverged towards much lower SpO_2 values for higher altitudes (75.5 % at 4000 m a.s.l.).

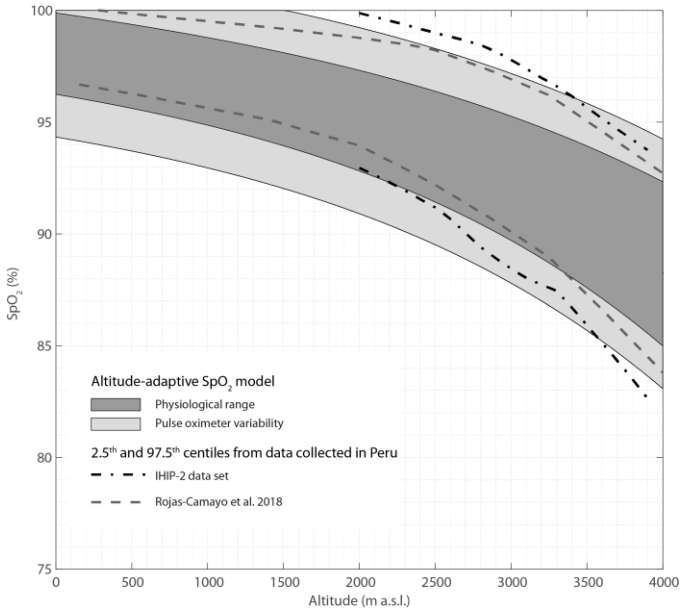

Figure 1: The proposed altitude-adaptive SpO_2 model is composed of a healthy SpO_2 range (dark area) and the measurement inaccuracy of the pulse oximeter (light areas). The 2.5th-97.5thcentile range of the SpO_2 data from Rojas-Camayo et al. (dashed lines) [13] *and the Integrated Home-environmental Intervention Package (IHIP-2) data set (dashed-doted lines) were both recorded in the Peruvian Andes. The reported number of measurements for the IHIP-2 data can be found in the supplementary material.*

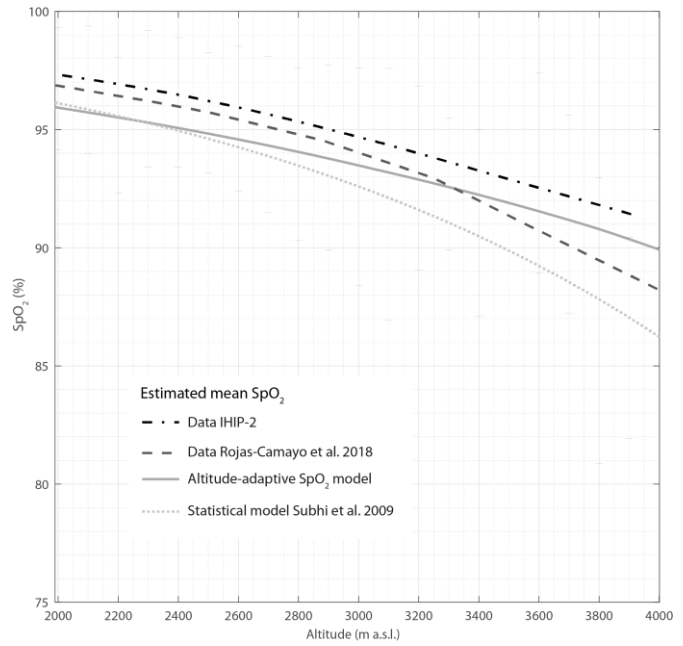

Figure 2: Comparison of mean SpO_2 between two models and two empirical data sets. The Integrated Home-environmental Intervention Package (IHIP-2) data set (dashed-dotted black) and the Rojas-Camayo et al.[13] *data (dashed gray) are smoothed with a lowess filter. The altitude-adaptive SpO_2 model estimates the mean SpO_2 based on physiological*

parameters and altitude (continuous line), the statistical model by Subhi et al.[14] *is based on descriptive statistics of data obtained through literature review (dotted line).*

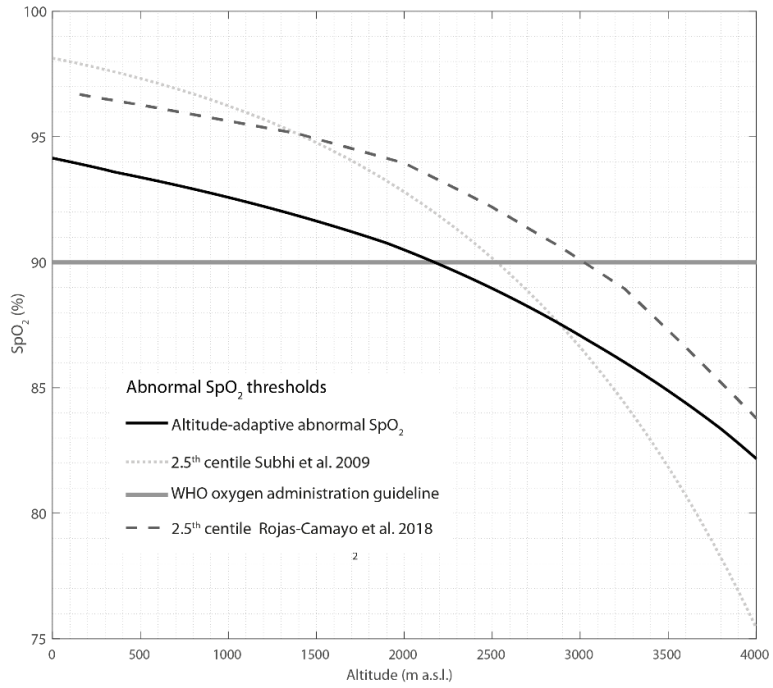

Figure 3: Comparison o proposedf hypoxemia thresholds that would lead to oxygen administration in ill patients. The altitude-adaptive abnormal SpO_2 threshold is based on the physiological model derived in this work with a virtual shunt of 10% (continuous black line), the threshold from Subhi et al.[14] *is derived from the 2.5th centile of observations obtained from literature review (dotted grey line), the 90% threshold from the WHO guideline is a result of a working group consensus (thick continuous grey line) and the 2.5th centile from Rojas-Camayo et al.*[13] *originates from a prospectively collected paediatric sample in the Preruvian Andes (dashed line).*

DISCUSSION

We proposed an altitude-adaptive model describing the normal SpO_2 range for acclimatised children living permanently at altitude. From this model, we derived an altitude-adaptive threshold for abnormal SpO_2 values. This is the first work to suggest a parametrised, altitude-adaptive SpO_2 model, and a corresponding abnormal SpO_2 threshold to interpret pulse oximeter readings from children with respiratory tract infections living permanently at altitude. The diagnosis of pneumonia and other respiratory diseases is challenging at altitude, as the most common diagnostic criteria such as the respiratory rate are dependent on altitude. Our work contributes towards making the management of childhood pneumonia, one of the major causes of child mortality in low resource settings, more objective. Equipping health workers with mobile pulse oximeters has become an affordable solution, is being evaluated at a large scale [30] and has tremendous potential for improving pneumonia treatment at resonable cost [31]. However, the measurement and interpretation of SpO_2 can be complicated. Computerised assistance and interpretation of the measurements could ensure reliability of these measurements and provide a meaningful decision support tool to health workers at the central and peripheral level. The proposed adaptive, physiology-based model could provide a basis for the necessary computations.

We developed an altitude-adaptive SpO_2 model that is based on physiological parameters. This model is unique as the adaptation of the parameters can be performed individually, based either on measurements or on known parameter ranges. The current model was developed considering literature-based physiological parameter values of Peruvian Andes residents that are acclimatised to this environment. These parameters can now easily be adapted to other populations with known differences in genetic or physiological acclimatization mechanisms [32] (e.g. Himalayan residents) or subjects that are not yet acclimatised. In clinical settings where blood gas

measurements are available, the cHb, $pACO_2$, and RQ measurements can be used to personalise the model output for higher accuracy.

In contrast to our parameterised model, Subhi and colleagues fitted empirical data collected from across the world into a statistical model describing the SpO_2 distribution using centiles [14]. This statistical model is therefore highly dependent on the data included in the modelling process. This is illustrated by the observed mismatch between this model and the empirical data sets obtained by Rojas-Camayo et al. [13] as well as our own data collection in the IHIP-2 trial. On the one hand, the statistical model was built using aggregated data collected from mixed populations while using pulse oximeters with partially unknown specifications. On the other hand, the two empirical data sets presented in this work originate solely from the Peruvian Andes and a single type of pulse oximeter. Therefore, our model fits a specific studied population and applied technologies and provides, thus, a limited basis for generalization.

For the evaluation of our model, we limited the comparison to altitudes from 2000 to 4000 m a.s.l. where empirical data was available. The data contained a high number of repeated measurements per child, which increased the robustness. Among the children recruited from the Cajamarca region during the IHIP-2 trial, only 21 lived above 3000 m a.s.l., introducing uncertainty in the data at these higher altitudes. Nevertheless, we observe very similar SpO_2 ranges in the data from Rojas-Camayo et al. [13]. Despite the high numbers of repeated measurements, both datasets show a high variability in the measured SpO_2. Inter- and intra-individual variability could originate from a number of sources. Circadian variation in pediatric SpO_2 has been reported [33] und we could not control for stable daytime measurements. Furthermore, there are known gender differences in adults [34], which could also apply to the pediatric population. Although we used most recent pulse oximeter technology and performed continuous measurements for at least a minute with a rigorous approach to PPG post-processing for high quality, not all the limitations of pulse oximetry, such as poor perfusion, probe positioning, or ambient light interference [35], could be fully excluded. To further validate the model, it will be crucial to apply data from other regions and ethnicities and establish if a customised model is required when used in different parts of the world. Such data collection should be accompanied by a gold standard, such as blood gas measurements with information on cHb, SaO_2, paO_2 and $paCO_2$, in order to pinpoint the exact sources in observed variability.

The altitude-adaptive model describes the SpO_2 ranges observed from the empirical data sets. At higher altitudes above 3500 m a.s.l., we notice higher deviations due to a slower decline of SpO_2 compared to what is seen in the empirical data. We suspect that this is directly linked to the assumptions we made during the modelling of healthy ranges. We assumed that cHb and RQ change linearly with altitude. However, the adaptation process is likely more active at higher altitudes [36] and other processes might equally contribute to varying parameters not captured in the modelling. As mentioned above, further work with access to blood gas measurements is needed to establish models that describe the dependence of these parameters on altitude.

Also, the assumptions used to define the abnormal physiological parameters could be a limiting factor. The oxygen cascade was originally developed based on adult compartments which did not consider children. For example, neonatal blood is known to benefit from the high affinity of fetal haemoglobin and would have changed considerably the oxygen dissociation curve [37]. As also oxygen administration is much more delicate in neonates [38], this will require a more detailed, separate discussion. The physics of the studied cardio-respiratory compartments are expected to be very similar in infants, children and adults. The differences are rather expressed in a change of individual parameters and not the model itself. Nevertheless, also pathological states could lead to altered physiological responses. For example, anaemic children display altered ranges for blood gas parameters and their actual health status is not entirely captured through our cardio-respiratory model based on SpO_2 measurements. SpO_2 and derived hypoxemia estimations reflect only the proportion of O_2 that is bound to Hb and not the total O_2 carrying capacity and concentration. Consequently, pulse oximeter assessments are blind to the effective O_2 available in the tissues. Furthermore, cardiac output, an alternative path to modulate O_2 delivery [39], is not easily obtainable with pulse oximetry alone. Thus, clinicians need to take the overall clinical situation of the child into consideration and evaluate treatment options accordingly when interpreting

hypoxemia thresholds [40]. Therefore, to improve clinical diagnosis, non-invasive point-of-care blood gas sensing technologies with multi-parameter readout capabilities would be desirable. Unfortunately, such multi-parameter technologies are currently rather exploratory in nature, with high cost, inadequate performance and durability properties for the target settings, and therefore not yet appropriate for clinical use.

We established an altitude-adaptive abnormal SpO_2 threshold based on physiologically plausible values. Our results show that using such a threshold is most relevant at altitudes above 2000 m a.s.l. At this altitude, the threshold clearly passes the 90 % mark recommended by the WHO for oxygen administration in patients. Compared to the previously published altitude-dependent threshold by Subhi et al. [14], our threshold is more conservative. While they also promoted to apply an altitude-dependent threshold at higher altitudes (2500 m a.s.l.) and not use the WHO oxygen administration guideline, their threshold presents a very steep curve at these higher altitudes which might exclude a number of patients in need of supplemental oxygen. Upon availability of data from sick children suffering from ALRI, a receiver operating curve (ROC) analysis could determine an optimal altitude-dependent threshold that is inclusive for all patients in need, while not burdening the health system with too many false referrals. This analysis would then also provide further indications to the generalizability of the model to other populations. Until such analysis is available, we recommend that the highly conservative WHO guideline of 90 % should only be applied below 2000 m a.s.l. and in altitudes above, additional considerations, such as danger signs other than low SpO_2, altitude, and oxygen availability should be taken into account.

Thus far, experts have not agreed on a definition for abnormal SpO_2 thresholds at altitudes higher than sea level. In the present work, we suggest the use of a physiological model to derive abnormal SpO_2 levels. However, to date, no reliable SpO_2 data from children suffering from hypoxemia and ALRI at altitude are available. The advancement of research for developing better tools to diagnose pneumonia and ALRI at altitude would greatly benefit from access to publicly available, comprehensive data sets obtained from sick children.

CONCLUSION

Improvement of SpO_2-altitude models and the development of valid altitude-dependent diagnostic thresholds for childhood pneumonia and ALRI present a first step towards an integration of pulse oximetry in low resource settings. We developed an altitude-adaptive threshold for abnormal SpO_2 values using an existing physiological model adjusted for published ranges of values for $paCO_2$, cHb, and RQ. Based on this model, healthy ranges and a new altitude-dependent abnormal SpO_2 thresholds are suggested that are based on physiological variations of vital parameters. With the increased availability of sensors and digitalised systems in low resource settings, parametrised models could provide additional valuable support to health workers in central, but also peripheral levels in understanding the patient's condition at the point of care, and choosing treatment options based on objectively obtained physiological measurements.

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COMPETING INTERESTS

The authors declare no competing interests.

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