Capillary blood gas as a substitute for arterial blood gas: a meta-analysis

Arterial blood gas sampling forms a vital part of bedside investigation but is invasive and physician dependent. This study aimed to determine whether capillary blood gas sampling could provide an accurate and less invasive substitute for the measurement of blood gases and pH.

The measurement of blood gases and pH forms a vital part of bedside investigation in patients with respiratory and metabolic disorders. This is most commonly performed using arterial blood gas sampling from the radial artery. This technique is invasive, painful and almost always needs to be undertaken by a physician.

The most recent European Respiratory Society and American Thoracic Society chronic obstructive pulmonary disease guidelines and the Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease by Global Initiative for Chronic Obstructive Lung Disease (2014) rely heavily on arterial blood gas for assessment and management of both acute and chronic exacerbations of chronic obstructive pulmonary disease. The British Thoracic Society, however, has recognized the shortcomings of the arterial blood gas and recommends a capillary blood gas as an alternative, except in shocked patients:

> **'Arterialised earlobe specimens should be used more widely than at present as a safer and less painful alternative to arterial blood gas sampling.' (O'Driscoll et al, 2008).**

In this technique, perfusion of the earlobe is enhanced ('arterialised') by applying heat or vasoactive creams. The earlobe is then pinpricked to collect 35–95 µl of blood in a similar way to fingertip sampling for blood glucose monitoring, and the sample is analysed by the same machine as is used for arterial blood gases. Capillary blood gases give the same range of data values (gases, glucose, lactate and electrolytes) as arterial blood gases.

Capillary blood gases are currently routinely used to estimate arterial blood gases in paediatric patients and are the first-line technique in adult patients in Germany (Vogelmeier, 2007). The only two circumstances where capillary blood gases are not used are if the patient is in shock or if an arterial catheter needs to be placed for continuous monitoring. Indeed, adult patients have been shown to generally favour capillary blood gases over arterial blood gases (Godfrey et al, 1971; Eaton et al, 2001; Russomano et al, 2006). Capillary blood gases can be performed by any trained member of staff as there is no need to locate an artery or to have a qualified prescriber available to administer local anaesthetic.

Despite the simplicity of capillary blood gas technique and clear patient preference, Thompson et al (2005) discovered that British physicians are reluctant to use them. The most common reason, other than local unavailability of equipment and training, is the concern that capillary values may not accurately reflect arterial values. To date, only one meta-analysis has examined whether this concern is justified: Zavorsky et al (2007) found that earlobe capillary samples can substitute arterial samples for all blood gas parameters, except for partial pressure of oxygen (pO_2) in patients breathing a high oxygen fraction. They attempted to predict the arterial blood gas–capillary blood gas difference using a regression model, but the model did not consider covariates (i.e. the effect of method of arterialisation or clinical setting) or within-patient correlation. Furthermore, the data used had not been normalized, the model not been validated and new data have since been published. Therefore a new and more comprehensive meta-analysis was necessary.

Given that capillary blood gas is physician independent and more patient-friendly than arterial blood gas, this meta-analysis aimed to determine whether capillary blood gas values can accurately predict arterial blood gas values using multi-level regression models.

Material and methods

This systematic review and meta-analysis was performed and written in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Moher et al, 2009).

Eligibility criteria

Full criteria can be found in *Appendix 1* (available at www.bjhm.co.uk). In brief, studies were eligible if they

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compared capillary and arterial blood gas samples in human adults with respect to pH, partial pressure of carbon dioxide (pCO_2), partial pressure of oxygen (pO_2) and/or oxygen saturation (sO_2). Arterial samples from any site were acceptable but capillary blood gases had to be taken from the earlobe as this is more accurate than fingerprick sampling (Zavorsky et al, 2007). Studies had to be reported in English.

Search strategy

The Embase, PubMED and Web of Knowledge databases (all sub-databases) were searched for all published articles from the earliest available date up to 13 March 2012. Key words relating to blood gas, arterial, capillary and arterialised/arterialized were searched, using limits according to the eligibility criteria if the database allowed. The full search protocol can be found in *Appendix 2*. This electronic search was followed by manually searching references of relevant articles. Titles and abstracts were screened for relevance and then assessed for eligibility by two independent reviewers (SR and CK). In cases of disagreement a third reviewer's opinion (NH) was sought. *Figure 1* summarizes the search.

Data collection and quality assessment

Data were extracted by two independent reviewers (NH and CK) using piloted forms (*Appendix 3*). The method of arterialisation of earlobe blood flow was classified as 'not arterialised' (if no attempt was made to improve earlobe blood flow before sampling), 'heated' (by massaging or warming) or 'chemical' (using a vasodilator cream). The absolute arterial blood gas and capillary blood gas values were collected for pH, pO_2, pCO_2 and sO_2 for each patient in each study. If studies did not provide raw data, the corresponding author was contacted. If raw data were still not available, the mean arterial blood gas–capillary blood gas difference and its standard deviation were recorded and used for preliminary analysis only.

The included studies were assessed for quality and risk of bias using the QUADAS tool developd by Whiting et al (2003) for the assessment of diagnostic accuracy studies (*Appendix 4*). Two reviewers (NH and CK) undertook the assessment independently and agreed on all items. Furthermore, the risk of selection bias arising from certain clinical settings being overrespresented was evaluated during preliminary analysis.

Statistical meta-analysis

Stage 1: Preliminary analysis

Preliminary analysis was performed to determine which covariates should be included in the prediction model. Details are available in *Appendix 5*.

Stage 2: Developing a model to calculate arterial blood gas from capillary blood gas

Fourteen studies provided raw data. A two-level multilevel regression model was created using these raw data to calculate arterial blood gas from capillary blood gas. Statistical analysis of the data was carried out using R (Ihaka and Gentleman, 1996). This model accounted for normality, independence and covariates.

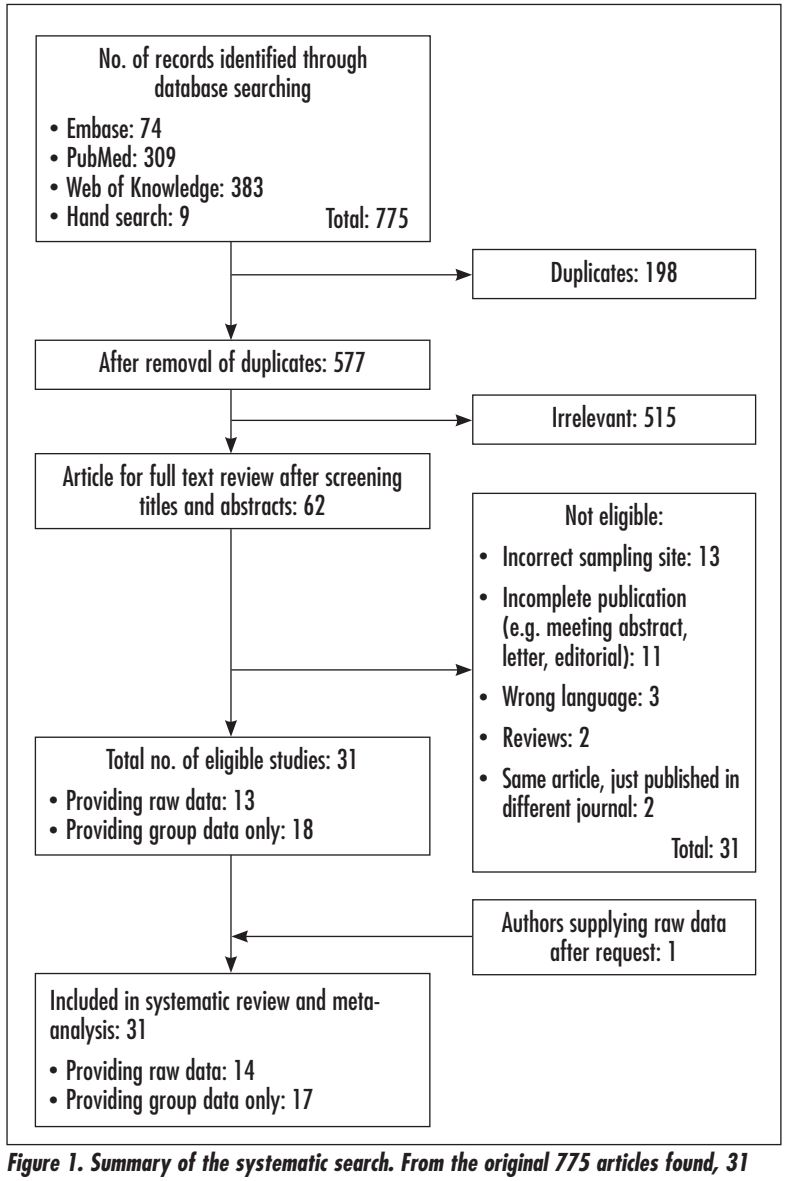


Figure 1. Summary of the systematic search. From the original 775 articles found, 31 qualified for inclusion in the meta-analysis.

Normality

The data need to be normally distributed before incorporation into the model. However, raw data for pO_2 and pH (as can be expected from its logarithmic scale) were not normally distributed and had to be transformed. Box-Cox plots were used to identify transformations which were optimal in terms of obtaining normality and stability of variance in the residuals. Regression diagnostics were carried out on the residuals and confirmed that the models were satisfactory. Back-transforming the expected response introduces a small bias which is negligible for practical purposes.

Independence

Several studies measured some patients multiple times. Samples from the same patient will not be independent. Hence a two-level multilevel model was used, which included 'Patient-ID' as the second level in order to make suitable allowance for within-patient correlation. An exchangeable/compound symmetry correlation matrix was used for parameterisation. The alternative of using 'Patient-ID' as a covariate would have resulted in a drastic degree of over-parameterisation and was therefore not an option. Heterogeneity by study was also considered. When the model was fitted using 'Study-ID' as a third level to 'Patient-ID', the same log likelihood ratio (to 7 significant figures) was produced.

Table 1. Summary of the 31 studies included for meta-analysis, including QUADAS scores

Reference	Number of patients	Clinical setting*	Parameters studied				Raw data available	QUADAS score
			pH	pO_2	PCO_2	sO_2		
Lilienthal and Riley (1944)	11	Unspecified	-	-	-	√	√	9
Lilienthal and Riley (1946)	12	Unspecified	-	-	√	-	√	8
Maas and Vanheijs (1961a)	22	Unspecified	√	-	-	-	√	8
Maas and Vanheijs (1961b)	20	Unspecified	-	-	√	-	√	9
Cooper and Smith (1961)	10	surg	-	-	√	-	-	10
Knudsen and Hansen (1962)	30	surg	√	-	√	-	√	10
Laughlin et al (1964)	33	c-p	-	√	-	-	-	9
Howland et al (1964)	15	surg	√	-	√	-	-	11
Maas et al (1964)	20	Unspecified	-	-	-	√	√	9
Langland and Wallace (1965)	16	c-p + h	√	√	√	-	√	9
Torjussen (1965)	21	Unspecified	-	-	-	√	-	9
Torjussen and Nitter-Hauge (1967)	21	c-p	√	√	-	-	-	9
Wallman et al (1968)	23	c-p	√	√	√	-	√	9
Yordanov (1968)	12	surg	-	√	-	-	√	9
MacIntyre et al (1968)	14	shock	-	√	-	-	√	9
Koch (1968)	42	Unspecified	-	√	√	-	-	9
Christoforides and Miller (1968)	30	Unspecified	-	√	-	-	√	8
Godfrey et al (1971)	16	Unspecified	√	√	√	-	√	11
Olivia et al (1973)	85	Unspecified	-	√	-	-	-	7
Hofford et al (1973)	20	c-p	√	√	√	-	-	10
Sadove et al (1973)	84	surg	√	√	√	-	-	10
McEvoy and Jones (1975)	13	c-p	√	√	√	-	√	11
Spiro and Dowdeswell (1976)	17	Unspecified	√	√	√	-	-	9
Pitkin et al (1994)	40	c-p	√	√	√	-	-	10
Dal'Ava-Santucci et al (1996)	81	Unspecified	-	√	-	-	-	8
Sauty et al (1996)	115	Unspecified	-	√	√	-	-	10
Fajac et al (1998)	70	Unspecified	-	√	√	-	-	10
Eaton et al (2001)	100	c-p	√	√	√	√	-	10
Russomano et al (2006)	6	h	√	√	√	-	-	9
Honarmand and Safavi (2008)	67	c-p	-	√	√	-	-	11
Mollard et al (2010)	10	h	√	√	√	√	√	11
Total no. of studies (no. for which raw data available)	1076	n/a	15 (7)	22 (8)	20 (8)	5 (3)	31 (14)	n/a
Total no. of measurements (no. for which paired sample data available)	n/a	n/a	439 (178)	1061 (233)	762 (186)	142 (61)	2404 (658)	n/a

pCO_2= partial pressure of carbon dioxide; pO_2 = partial pressure of oxygen; sO_2 = oxygen saturation. For clinical setting, c-p = cardiopulmonary disease (most patients had lung disease only, but some had cardiac disease and some had both); shock =shocked patients with peripheral vasoconstriction; surg = surgical (pre-, intra- and postoperative); h=healthy volunteers.

Therefore the model with the lowest parametrisation (i.e. 'Patient-ID' only) was used.

Covariates

Based on results from the preliminary analysis (*Appendix 5*), method of arterialisation (none, heated or chemical) and use of high flow supplemental oxygen (fraction of inspired oxygen (FiO_2) >80%) were included as covariates in the model.

Stage 3: cross validation of the model

The models were validated by repeated random subsampling cross validation, with a subsample n=6. The process was repeated to obtain 10 000 predictive errors which were used to assess the accuracy of the model.

Results

Results of literature search

Thirty one (31) eligible studies were found (*Table 1*), involving a total of 2404 sample pairs taken from 1076 patients and dating from 1944 to 2010. The QUADAS assessment showed all studies to be of moderate to high quality, with a minimum score of 7 out of 11 items (*Appendix 4*).

Results of the preliminary analysis, involving all 31 studies, can be found in *Appendix 5*. This analysis suggested that selection bias as a result of overrepresentation of certain clinical settings is unlikely. The presence of hyperoxic conditions (caused by the use of supplemental oxygen) does seem to affect the arterial blood gas–capillary blood gas difference and thus must be integrated into the model.

A total of 14 studies provided raw data for individual sample pairs. These were used in generating the model to predict arterial blood gas from capillary blood gas. A total of 178, 233, 186 and 61 paired samples were found for pH, pCO_2, pO_2, and sO_2 respectively. The complete collected data can be found in *Appendix 6*.

Using capillary blood gas to predict arterial blood gas: multilevel modelling

As described above, a two level multilevel regression model for each of the four parameters was created (*Table 2*).

Using these models, capillary blood gas values can be predicted from arterial blood gas values. For example, if a chemically arterialised capillary blood gas from a patient results in a pH of 7.40, we can now predict the arterial pH: arterial blood gas pH = ln (0.984e(7.40) + 28.432 - 15.154) = 7.39

Validating the model

Results from the cross validation are shown in *Table 3*.

These predictive errors for pCO_2, pH and sO_2 are illustrated in *Figure 2* where predicted values (y-axis) are plotted against actual arterial blood gas values (x-axis). In all cases, the line is a reference y=x line, indicating perfect predictability of the model.

The scatter is greater with pO_2 measurements at high levels of pO_2, leading to an increasing mean difference and decreasing precision of the mixed effects model (*Figure 3a*). Subgroup analysis was therefore carried out on just the pO_2 values <20 kPa as shown in *Figure 3b*. This excluded all patients breathing high flow supplemental oxygen (FiO_2 >80%). For this range, the predictability clearly improved and was confirmed in cross validation (predictive error <1.90%).

Discussion

Arterial blood gases are commonly used in the acute care setting, yet they are unpopular with patients and the technique usually needs to be performed by a physician. This is the first meta-analysis predicting arterial blood gas levels from capillary blood gas levels, taking into account within-patient correlation, method of arterialisation and oxygen supplementation.

This meta-analysis concluded that capillary blood gas levels can accurately predict arterial blood gas levels

Table 2. Two level multilevel regression models used to predict the arterial blood gas values from the capillary blood gas values of pH, pCO_2, pO_2 and sO_2

Parameter	No. of studies contributing raw data	Model
pH	7	Arterial blood gas = ln (0.984e (capillary blood gas) +28.342 – 2.783 (if heated) – 15.154 (if chemical))
pCO_2 (kPa)	8	Arterial blood gas = 0.9795 (capillary blood gas) + 0.1839 – 0.1613 (if heated) – 0.0568 (if not arterialised)
pO_2 (kPa)	8	For all pO_2 values, arterial blood gas =e(0.9841 ln(capillary blood gas) +0.0318 + 0.0331 (if heated) + 0.1376 (if FiO_2 > 80%))
		For pO_2 values <20 kPa, arterial blood gas = e (0.9792 ln(capillary blood gas) +0.0542 + 0.0047 (if heated))
sO_2 (%)	3	Arterial blood gas = 1.048 (capillary blood gas) – 4.694 + 1.024 (if heated)

FiO_2 = fraction of inspired oxygen; pCO_2= partial pressure of carbon dioxide; pO_2 = partial pressure of oxygen; sO_2 = oxygen saturation.

Table 3. Predictive errors for each parameter, using the models in *Table 2*

Parameter	Predictive error
pH	Better than 0.43%, maximum error in 10 000 cross-validations 1.02%
pCO_2	Better than 3.00%
pO_2	For all pO_2 values: better than 14.8%
	For pO_2 <20 kPa: better than 1.90%
sO_2	Better than 2.80%

pCO_2= partial pressure of carbon dioxide; pO_2 = partial pressure of oxygen; sO_2 = oxygen saturation

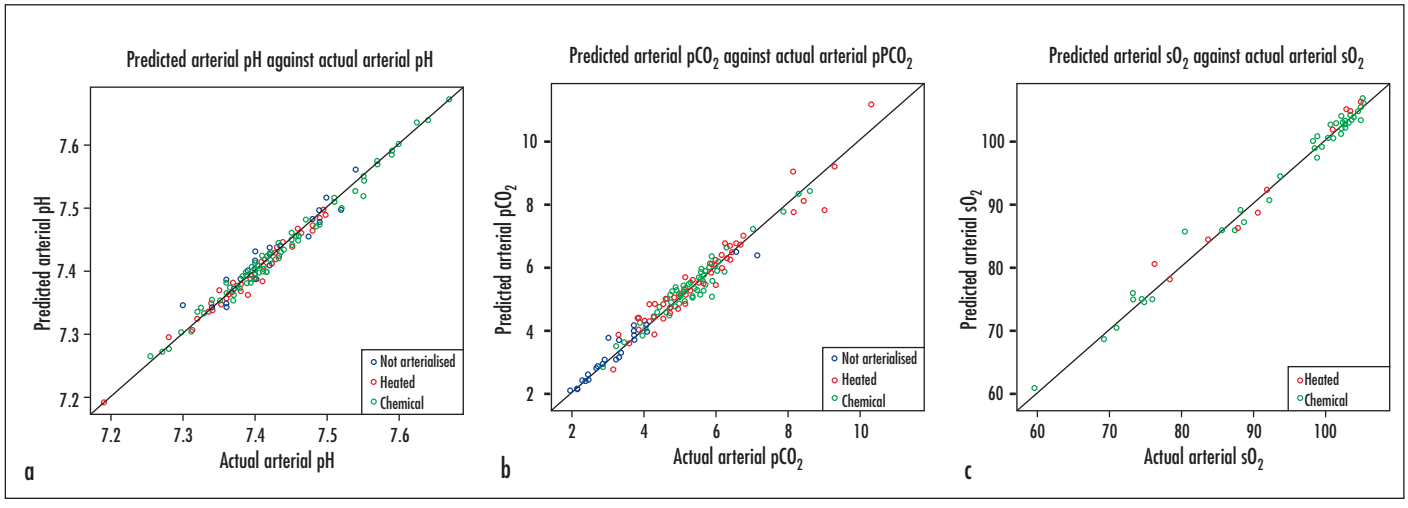
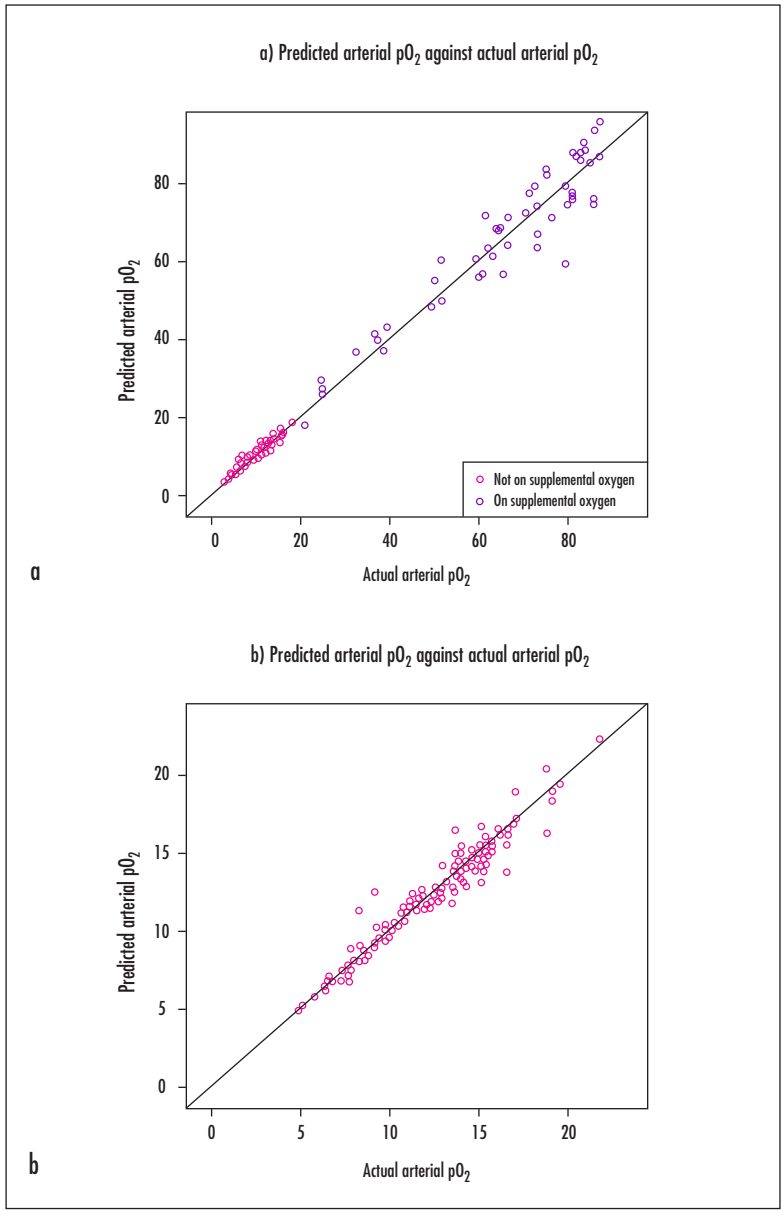


Figure 2. Predictive abilities of the linear mixed effects models for (a) pH, (b) pCO_2 (partial pressure of carbon dioxide) and (c) sO_2 (oxygen saturation). The data are colour coded to show different arterialisation methods.



and could be used as a viable alternative to arterial blood gas levels.

For pH, pCO_2 and sO_2, the prediction models proved to be highly accurate for all capillary blood gas values (predictive error < 0.43%, <3.00% and <2.80% for pH, pCO_2 and sO_2 respectively). Zavorsky et al (2007) observed a lack of accuracy for higher values of pH and pCO_2. They also found that the publication date (in this case 'study-ID') had an effect on the arterial blood gas–capillary blood gas difference. These findings were not replicated in the current analysis, perhaps because covariates introduced into the model eliminated any sources of inaccuracy. In addition, cross-validation had not been performed in the previous meta-analysis.

The pO_2 model was found to accurately predict the arterial blood gas value from capillary blood gas with the exception of the highest oxygen levels. This is consistent with the findings of Zavorsky et al (2007). While it is important to detect hyperoxia, the exact level would not change patient management. Thus, a subgroup of oxygen levels below 20 kPa was examined separately, a clinically useful range encompassing hypoxia, normoxia and mild hyperoxia (normal range = 12–16 kPa, *Figure 3b*). For this range of pO_2, the model was very accurate and precise (predictive error <1.90%). Importantly, this means capillary blood gases can not only be reliably interpreted at values <10 kPa, as recommended by the British Thoracic Society, but can be trusted up to values of 20kPa, covering all clinically relevant values.

This contradicts the recommendation of the 2013 guidelines of the American Association for Respiratory

Figure 3. a. Predictive ability of the linear mixed effects model for partial pressure of oxygen (pO_2) (kPa) colour coded to show whether or not supplemental oxygen was given. b. In the subgroup of patients not breathing supplemental oxygen there is much less scatter about the line y=x, indicating better predictability at this lower range of pO_2 values.

Care (Davis et al, 2013) not to use capillary blood gases to assess oxygenation status. However, the guidelines looked at absolute capillary blood gas pO_2 values rather than at the arterial values that can be predicted from them. Predictive models similar to this one have previously been developed to predict arterial blood gas from venous blood gases (Toftegaard et al, 2009; Raoufy et al, 2011). The advantages of predicting arterial blood gas from capillary blood gas rather than venous blood gas include greater accuracy and a simpler, less invasive technique.

How this work can change clinical practice

Since highly accurate and precise two level multilevel models are now available for all four parameters, these models can be used to create new normal reference intervals for pH, pCO_2, pO_2 and sO_2. Local laboratory arterial blood gas reference values for these parameters can simply be inserted into the corresponding model (see results) to create new capillary blood gas reference intervals for the locally preferred method of arterialisation. *Table 4* gives an example of capillary blood gas reference intervals for chemically arterialised samples using the arterial blood gas reference intervals at the authors' institution. These reference ranges are almost identical to the arterial blood gas reference ranges, simplifying the transition to capillary blood gas for the interpreting physician.

Using capillary blood gases as a physician-independent substitute for arterial blood gases could have widespread positive implications for patient care and health-care costs. Hospital admissions of patients with chronic conditions such as chronic obstructive pulmonary disease, neuromuscular conditions or obesity hypoventilatory syndrome could be prevented if their community nurses could use capillary blood gases to diagnose and manage worsening type 2 respiratory failure early. Triage of patients with acute type 1 respiratory failure such as asthma attacks, pulmonary oedema or pneumonia could be accelerated if paramedics and emergency triage nurses could carry out immediate capillary blood gases to assess the level of oxygenation.

Capillary blood gases would allow more frequent sampling and hence closer monitoring of inpatients for multiple reasons. Being less painful and less prone to complications it is more acceptable to patients, smaller volumes of blood are drawn per sample and the ease of sampling means monitoring can continue in the absence of a physician. For example specialist nurses or chest physiotherapists could perform blood gas analysis themselves to assess response to treatment.

Limitations and recommendations for future research

Most of the modern literature on the validity of capillary blood gases is written in English but restricting the search to one language may have omitted other relevant studies. A total of 31 eligible papers was found but only 13 of these included raw data for full analysis. Attempts were made to contact the authors for the remaining 18 papers but only Mollard et al (2010) were able to provide raw data. A publication bias may be present since studies that challenge common practice (in this case arterial blood gas) are more likely to be published.

The model does not account for the method of capillary blood gas sampling (i.e. whether a scalpel or lancet was used to draw blood) and this could introduce error. On analysis of the raw data, the method of arterialisation and the setting in which the study was carried out were adjusted for. However, since data were not available for non-arterialised samples for pO_2 and sO_2, the models for these parameters cannot predict arterial blood gas values from non-arterialised capillary blood gas values. More data are therefore needed to extend the model. Furthermore, this meta-analysis did not seek to identify the most reliable method of arterialisation. This needs to be further investigated in order to allow standardization of capillary blood gas sampling technique.

It is difficult to draw conclusions on the effect of the clinical setting (healthy volunteers *vs* cardiopulmonary disease *vs* surgical *vs* shocked patients) because of the lack of raw data available for each parameter. The impact of clinical setting is of particular interest as it has been argued that peripheral shutdown in shocked patients may increase the arterial blood gas–capillary blood gas difference, impairing the validity of capillary blood gases (O'Driscoll et al, 2008). Further trials are therefore needed to fully evaluate the validity of capillary blood gas in shocked patients.

Conclusions

Capillary blood gas sampling provides a patient-friendly, physician-independent substitute for arterial blood gas sampling without compromising diagnostic accuracy. This meta-analysis proves the diagnostic capability of capillary blood gas to accurately predict arterial blood gas values to within 0.43%, 3.00%, 2.80% and 1.90% respectively for pH, pCO_2, sO_2 and pO_2 values less than 20 kPa. Given these advantages and the latest recommendations of the British Thoracic Society, capillary blood gas should replace arterial blood gas at the bedside for the investigation and monitoring of respiratory and metabolic disorders in non-shocked patients. BJHM

Table 4. Capillary blood gas reference intervals calculated using calibration models and local institution arterial blood gas reference intervals

	Reference interval	
Parameter	Arterial blood gas	Capillary blood gas
pH	7.36–7.44	7.37–7.45
pCO_2 (kPa)	4.5–6.0	4.4–5.9
pO_2 (kPa)	12.0–16.0	12.0–16.1
sO_2 (%)	94.0–100.0	94.2–99.9

pCO_2= partial pressure of carbon dioxide; pO_2 = partial pressure of oxygen; sO_2 = oxygen saturation

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Contributorship: Dr S Richter conceived and designed the study and is the guarantor. Dr A Chari helped design the study and is the corresponding author. The literature search was undertaken by Dr S Richter, Dr C Kerry and Dr N Hassan. Data collection and assessment was done by Dr N Hassan and Dr C Kerry. Statistical analysis was performed by Dr D Lunn, Dr S Richter and Dr A Chari. All authors were involved in the writing and editing of the manuscript and approved the final version before submission. Conflict of interest: none.

KEY POINTS

- Arterial blood gas sampling forms a valuable component of bedside investigation in medicine but is invasive and physician-dependent.
- Capillary blood gas sampling from the earlobe provides a less painful alternative which is preferred by patients, uses the same blood gas analysers as arterial blood gas and can be performed by any trained health-care professional.
- Capillary blood gas is routinely used in the paediatric population and is recommended by the British Thoracic Society. However, its use by British physicians has been limited by continued doubts over its accuracy.
- Using these models, earlobe capillary blood gases accurately predict arterial blood gases to within 0.43%, 3.00%, 2.80% and 1.90% for pH, pCO_2, sO_2 and clinically relevant pO_2 values respectively.
- This meta-analysis demonstrates that capillary blood gas provides a highly accurate substitute for arterial blood gas which is less painful, less invasive and physician-independent.

These are the key references. A complete bibliography can be found at www.bjhm.co.uk in *Appendix 7*.

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Davis MD, Walsh BK, Sitting SE, Restrepo RD (2013) AARC clinical practice guideline: blood gas analysis and hemoximetry: 2013. *Respir Care* **58**(10): 1694–703

Eaton T, Rudkin S, Garrett JE (2001) The clinical utility of arterialized earlobe capillary blood in the assessment of patients for long-term oxygen therapy. *Respir Med* **95**(8): 655–60

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Vogelmeier C (2007) Leitlinie der Deutschen Atemwegsliga und der Gesellschaft für Pneumologie und Batmungstherapie zur Diagnostik und Therapie mit chronisch obstruktiver Bronchitis und Lungenemphysem (COPD). *Pneumologie* **61**: 1–40

Zavorsky GS, Cao J, Mayo NE, Gabbay R, Murias JM (2007) Arterial versus capillary blood gases: a meta-analysis. *Respir Physiol Neurobiol* **155**(3): 268–79

Appendix 1. Eligibility criteria

	Criteria	Rationale
Population	Adults in any setting. Animal studies and paediatric studies were excluded	Capillary blood gases are already used in the paediatric population of UK hospitals. Blood gas parameters and sampling sites can differ in animals compared to humans
Intervention and comparison	The arterial sample can have been taken from any artery but the capillary sample must have been taken from the earlobe. If a study used both fingertip and earlobe sampling, but reported the two sites independently, the study was eligible	Earlobe sampling is the method used in Germany and proved to be more accurate than fingertip sampling in a meta-analysis by Zavorsky et al (2007). Arterial blood is assumed to be the same throughout the body
	The arterial and capillary samples must have been taken simultaneously (i.e. within 5 minutes of each other) from the same patient	This should minimize imprecision secondary to intra- and inter-individual variation in blood gas parameters
Outcome	Analytic studies comparing arterial blood gases and capillary blood gases with respect to any or all of the following: pH, pO_2, pCO_2, sO_2, i.e. studies looking only at glucose, haemoglobin or ammonia were not eligible	These are the parameters for which arterial blood gases are commonly used. Electrolytes, glucose and haemoglobin can already be reliably measured from venous samples, so the validity of capillary samples can be assumed
Reporting	Full text articles	The methods of the study must be available to assess eligibility
	Studies must be reported in English	Reviewers were only fluent in English
	If raw data are not available, a mean arterial blood gas–capillary blood gas difference and the number of samples was required	Sample number is needed to weight studies in the preliminary group analysis

pCO_2= partial pressure of carbon dioxide; pO_2 = partial pressure of oxygen; sO_2 = oxygen saturation

Appendix 2. Search protocol

Search engine	Date	Limits	Run	Terms	Found	After exclusion of duplicates	After screening†	After eligibility check
MEDLINE using PubMed	11.03.2012	Humans, English, All adult: 19+ years, Field: title/abstract	1	arterial blood gas* AND capillary blood gas*	2			
			2	arterial blood AND arterialised blood	12			
			3	ABG* AND CBG*	4			
			4	arterial blood gas* AND site	29			
			5	arterial blood AND arterialized blood	99			
			6	arterial AND ear lobe	21			
			7	artery AND ear lobe	18			
			8	artery AND earlobe	20			
			9	arterial AND earlobe	37			
			10	artery capillary sample	18			
			11	capillary blood gas*	40			
			12	arterialised AND capillary	9			
				Subtotal	309	268		
ISI Web of Knowledge	11.03.2012	Title	1	arterial blood AND capillary blood	159			
			2	ABG AND CBG	0			
			3	ABGs AND CBGs	0			
			4	arterial blood AND arterialised blood	40			
			5	arterial blood gas* AND site	5			
			6	arterial blood AND arterialized blood	40			
			7	arterial AND ear lobe	15			
			8	artery AND ear lobe	25			
			9	artery AND earlobe	18			
			10	arterial AND earlobe	9			
			11	artery capillary sample	1			
			12	arterialised AND capillary	71			
				Subtotal	383			
EMBASE 1974–2012	13.03.2012	Full text, humans, English language, age 18–65 and 65+, article, abstract	1	arterial blood AND capillary blood	12	8	0	
			2	ABG AND CBG	0	0	0	
			3	ABGs AND CBGs	0	0	0	
			4	arterial blood AND arterialised blood	0	0	0	
			5	arterial blood gas* AND site	11	0	0	
			6	arterial blood AND arterialized blood	3	0	0	
			7	arterial AND ear lobe NOT crease	9	1	0	
			8	artery AND ear lobe NOT crease	1	1	0	
			9	artery AND earlobe NOT crease	2	0	0	
			10	arterial AND earlobe NOT crease	12	1	0	
			11	artery AND capillary AND sample	5	0	0	
			12	capillary AND arterialized OR arterialised	19	13	0	
				Subtotal	74	24	0	
Hand search	13.03.2012	none	-	-	9	9	9	7
Summary					775	577	62	31†

ABG = arterial blood gas, CBG = capillary blood gas. *screening of titles and abstracts to exclude: of titles/abstracts to exclude: children, not humans, fingertip only, glucose only and irrelevant or arterial *vs* venous instead of capillary, if not in English, abstract only, ammonia only, a review, ketones only, hb only. † Three more articles had to be excluded when neither primary data nor the setting in which the group data were collected could be obtained from authors

All 31 studies that fulfilled the initial eligibility criteria were reviewed by two reviewers independently. The piloted form in *Appendix 3* was used to extract data from each study.

Appendix 3. Piloted forms

Author, year, journal	
Type of study	
Department	
Time frame	
Aim of the study	
Patient population	Population
	Number of patients
	Inclusion criteria
	Exclusion criteria
	Drop outs?
Samples	Number of samples
	Arterial blood gas and capillary blood gas taken from same patient? at same time?
Arterial blood gas details	Site
	Volume
	Local anaesthetic?
	Taken by? (doctor/specialist nurse)
Capillary blood gas details	Site
	Volume
	Chemical/heat/not arterialised
	Needle/blade?
	Taken by? (doctor/specialist nurse)
	Other sampling comments
	Analysed when?
Analysis	Statistical test for accuracy
	Statistical test for comfort
	Bias recognised by authors
	Bias recognised by us
	Used CONSORT?
Results	Number of usable samples
	Procedural problems
	Patient preference
	pCO_2 (units!)
	pO_2 (units!)
	pH
	SO_2 (units!)
Comments	

pCO_2= partial pressure of carbon dioxide; pO_2 = partial pressure of oxygen; sO_2 = oxygen saturation

Appendix 4. QUADAS tool

QUADAS number		1	2	3	4	5	6	7	8	9	10	11	12	13	14	Total
Lilienthal and Riley (1944)		U	U	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
Lilienthal and Riley (1946)		U	N	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	U	8
Maas and Vanheis (1961a)		U	N	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	U	Y	8
Maas and Vanheis (1961b)		U	N	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	Y	9
Cooper and Smith (1961)		Y	N	Y	Y	Y	Y	Y	Y	Y	U	U	Y	Y	U	9
Knudsen and Hansen (1962)		Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	U	10
Laughlin et al (1964)		Y	U	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	U	10
Howland et al (1964)		Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	U	11
Maas et al (1964)		U	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	11
Langland and Wallace (1965)		Y	U	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	U	9
Torjussen (1965)		U	N	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	U	9
Torjussen and Nitter-Hauge (1967)		Y	N	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	U	9
Wallman et al (1968)		Y	U	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	U	9
Yordanov (1968)		Y	N	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	U	9
Koch (1968)		Y	U	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	U	9
MacIntyre et al (1968)		Y	U	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	U	9
Christoforides and Miller (1968)		U	U	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	U	8
Godfrey et al (1971)		Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	U	11
Sadove et al (1973)		Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	U	10
Olivia et al (1973)		U	U	Y	Y	Y	Y	Y	Y	Y	U	U	Y	U	U	7
Hofford et al (1973)		Y	U	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	U	10
McEvoy and Jones (1975)		Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	U	11
Spiro and Dowdeswell (1976)		Y	N	Y	Y	Y	Y	Y	Y	Y	U	U	Y	Y	U	9
Pitkin et al (1994)		Y	Y	Y	Y	Y	Y	Y	Y	Y	U	U	Y	Y	U	10
Sauty et al (1996)		Y	Y	Y	Y	Y	Y	Y	Y	Y	U	U	Y	Y	U	10
Dal'Ava-Santucci et al (1996)		U	U	Y	Y	Y	Y	Y	Y	Y	U	U	Y	Y	U	8
Fajac et al (1998)		Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	U	10
Eaton et al (2001)		Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	U	10
Russomano et al (2006)		N	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	Y	9
Honarmand and Safavi (2008)		Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	11
Mollard et al (2010)		Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	11

Items 10-12 were omitted as interpretation of the blood gases was fully automated and hence not subject to bias

Appendix 5. Preliminary analysis

Methods of preliminary analysis

All 31 studies included in this meta-analysis were relatively small and therefore should have normalised their data before calculating a mean. While the pCO2 and sO2 samples were already normally distributed, pO2 and pH were not and this therefore infers an error. Furthermore, pH is measured on a logarithmic scale so taking an arithmetic difference (arterial blood gas–capillary blood gas) is misleading and instead a ratio of arterial blood gas:capillary blood gas should be used. Forest plots could therefore not be used as they assume normality. Box plots were used instead to present the combination of raw and mean group data using SPSS. Where available, raw data were used instead of the means provided by studies. The mean values were weighted according to the number of patients in the study. Bland–Altman plots were used for preliminary analysis of the 14 studies providing raw data.

Results: method of arterialisation

The method of arterialisation was taken into account when fitting the model if a) data were available for that method and b) if the method produced results which were significantly different from chemical arterialisation (*Table A1*). Chemical arterialisation was used as a reference point since this is currently the most commonly used method for capillary blood gas analysis.

Results: clinical setting

Box plot frequencies for different clinical settings for each parameter are shown in *Tables A2–A5*. The median arterial blood gas–capillary blood gas difference for each parameter appears to be similar for all clinical settings on preliminary

Table A1. *P* values comparing chemical arterialisation with heated and non-arterialised for each parameter

	Heated	Non-arterialised
pH	0.015*	0.070
pCO_2	<0.001*	0.325
pO_2	0.103	No data
sO_2	0.011*	No data

pCO_2= partial pressure of carbon dioxide; pO_2 = partial pressure of oxygen; sO_2 = oxygen saturation. *denotes statistically significant difference $P<0.05$

Table A2. Box plot frequencies for pO_2 (partial pressure of oxygen) for each clinical setting

	Subsetting				
Clinical setting	Exercise	Rest + room air	Rest + suppl. O_2	Unspecified	Total
Healthy	24	8	0	8	40
Surgical	0	96	0	0	96
Cardiopulmonary disease	15	287	42	0	344
Shocked	19	28	14	0	61
Unspecified	81	255	18	166	520
Total	139	674	74	174	1061

suppl. O_2 = supplementary oxygen

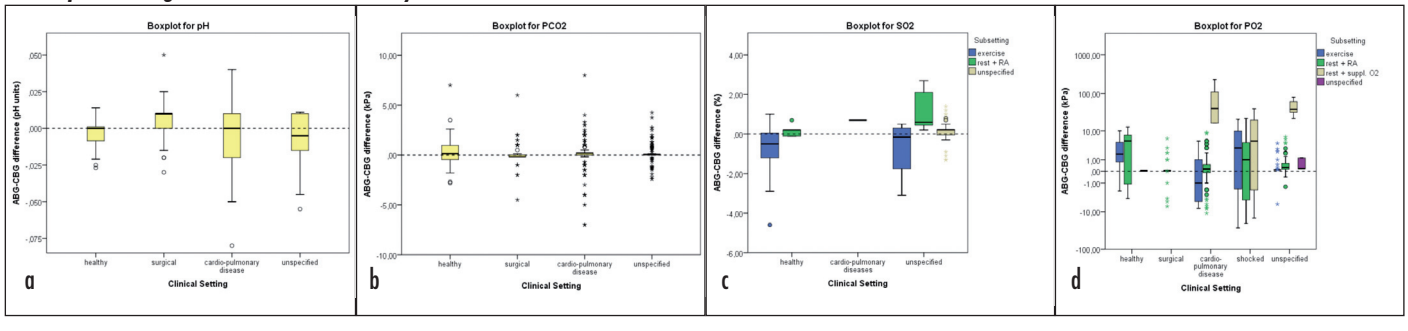
Table A3. Box plot frequencies for pH for each clinical setting

Clinical setting	Frequency
Healthy	40
Surgical	124
Cardiopulmonary disease	226
Unspecified	49
Total	439

Table A4. Box plot frequencies for pCO_2 (partial pressure of carbon dioxide) for each clinical setting

Clinical setting	Frequency
Healthy	40
Surgical	124
Cardiopulmonary disease	264
Unspecified	334
Total	762

Figure A1. Effect of clinical setting on the arterial blood gas (ABG)–capillary blood gas (CBG) difference for (a) pH, (b) pCO_2 (partial pressure of carbon dioxide), (c) pO_2 (partial pressure of oxygen) and (d) sO_2 (oxygen saturation). Outliers (>1.5 x interquartile range from box) are denoted by 'o' and extreme values (>3 x interquartile range from box) are denoted by '*'. RA = room air.

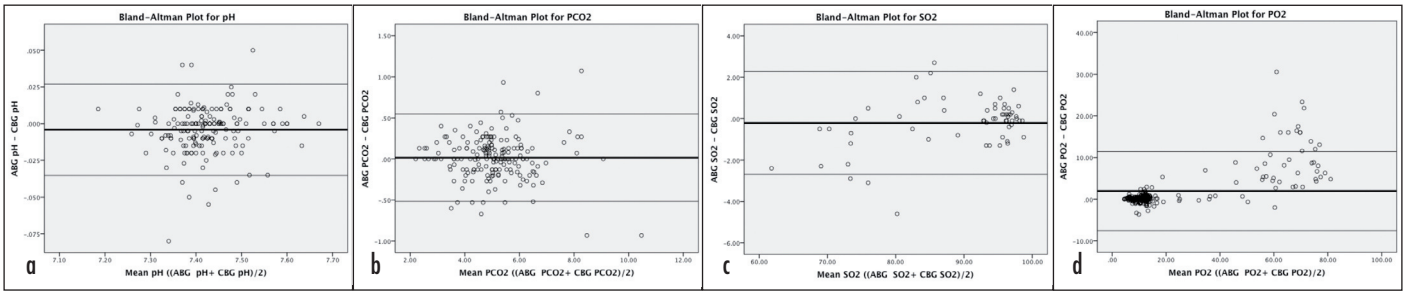


analysis (*Figure A1*). Therefore the over/underrepresentation of certain clinical settings is unlikely to introduce bias into the authors' prediction model. The exception is samples taken from patients on supplemental high flow oxygen (FiO_2 >80%) which clearly increases the arterial blood gas–capillary blood gas difference, suggesting this may need to be accounted for in the model. The effect of supplemental oxygen was also observed on Bland–Altman analysis (*Figure A2*). However, since not every study provided information on clinical setting, these box plots are limited to preliminary analysis and clinical setting could not be incorporated into the prediction model.

Table A5. Box plot frequencies for sO_2 (oxygen saturation) for each clinical setting

	Subsetting			
Clinical setting	Exercise	Rest + room air	Unspecified	Total
Healthy	24	6	0	30
Cardiopulmonary diseases	0	61	0	61
Unspecified	4	7	40	51
Total	28	74	40	142

Figure A2. Bland–Altman plots from the paired sample data for (a) pH, (b) pCO_2 (partial pressure of carbon dioxide), (c) pO_2 (partial pressure of oxygen) and (d) sO_2 (oxygen saturation). The bold central line is the mean difference and the other lines indicate two standard deviations away from the mean. ABG = arterial blood gas; CBG = capillary blood gas.



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Continued on p A7

Appendix 6. Collected data – group data

Reference	No of patients	Clinical setting	Oxygen status	Arterialisation method	Capillary method	pH n=	pH mean diff.	pH mean diff. SD	pO_2 n=	pO_2 mean diff.	pO_2 mean diff. SD	pCO_2 n=	pCO_2 mean diff.	pCO_2 mean diff. SD	sO_2 n=	sO_2 mean diff.	sO_2 mean diff. SD
Lilienthal and Riley (1944)	11	Unspecified		Heating	Scalpel										11	0.52	1.55
Lilienthal and Riley (1946)	12	Unspecified		Heating	Scalpel							12	-0.19	0.15			
Maas and Vanheis (1961a)	22	Unspecified		Chemical	Lancet	22	0.00	0.01									
Maas and Vanheis (1961b)	20	Unspecified		Chemical	Lancet							20	0.02	0.16			
Cooper and Smith (1961)	10	Surgical	Normoxia	Chemical	Lancet							21		0.17			
Knudsen and Hansen (1962)	30	Surgical	Normoxia	None		30	0.00	0.01				30	0.05	0.23			
Maas et al (1964)	20	Unspecified		Chemical	Lancet										20	0.10	0.80
Howland et al (1964)	15	Surgical	Normoxia	Chemical	Lancet	10	-0.01	0.09				10	0.13	0.43			
Laughlin et al (1964)	33	Lung disease	Normoxia	Heating					33	0.40	0.67						
Langland and Wallace (1965)	16	Lung disease + healthy	Normoxia	Heating	Scalpel	12	-0.01	0.01	16	0.08	0.55	11	0.14	0.21			
Torjussen (1965)	21	Unspecified		Heating	Lancet										20	0.21	1.74
Torjussen and Nitter-Hauge (1967)	21	Cardiopulmonary	Normoxia	Heating	Lancet	21	0.00	0.01	21	0.04	0.38						
Wallman et al (1968)	23	Lung disease	Normoxia	Heating	Scalpel	19	0.00	0.01	19	0.19	0.39	19	-0.10	0.41			
		Lung disease	Normoxia	Heating	Scalpel	22	0.00	0.01	22	13.98	6.44	22	-0.18	0.29			
Yordanov (1968)	12	Surgical	Normoxia	Chemical					12	-0.01	0.49						
Macintyre et al (1968)	14	Shocked	Normoxia	Chemical					14	0.05	0.70						
		Shocked	Normoxia	Heating					14	-0.16	1.42						
		Shocked	Suppl. 02	Chemical					14	1.17	2.17						
		Shocked	Exercise	Chemical					11	0.16	0.66						
		Shocked	Exercise	Heating					8	0.51	2.58						
Koch (1968)	42	Unspecified	Normoxia	Chemical					42	-0.02	0.44	20	0.04	0.20			
Christoforides and Miller (1968)	12	Unspecified	Normoxia	Heating					12	0.16	0.25						
		Unspecified	Suppl. 02	Heating					18	6.04	2.41						
Godfrey et al (1971)	16	Unspecified	Normoxia	Chemical	Scalpel	16	-0.02	0.02	16	0.20	0.38	16	0.19	0.20			
Olivia et al (1973)	85	Unspecified		Heating	Lancet				85	0.17							
Sadove et al (1973)	84	Surgical	Normoxia	Heating	Lancet	84	0.01	0.34	84	0.03	0.94	84	-0.19	0.64			
Hofford et al (1973)	20	Cardiopulmonary	Normoxia	Heating	Lancet	20	0.01	0.02	20	-0.08	0.50	20	-0.19	0.49			
		Cardiopulmonary	Normoxia	Heating	Lancet				20	16.53	10.08						
McEvoy and Jones (1975)	13	Cardiopulmonary	Normoxia	Chemical	Scalpel	12	-0.01	0.03	12	-0.44	0.69	12	0.08	0.19			
		Cardiopulmonary	Exercise	Chemical	Scalpel	15	0.00	0.02	15	-0.23	0.56	15	0.13	0.19			

pCO_2= partial pressure of carbon dioxide; pO_2 = partial pressure of oxygen; sO_2 = oxygen saturation; SD = standard deviation. n = number of arterial blood gas–capillary blood gas sample pairs; pCO_2 and pO_2 in mmHg; sO_2 in %

Appendix 6. Collected data – group data (cont'd)

Reference	No of patients	Clinical setting	Oxygen status	Arterialisation method	Capillary method	pH n=	pH mean diff.	pH mean diff. SD	pO_2 n=	pO_2 mean diff.	pO_2 mean diff. SD	pCO_2 n=	pCO_2 mean diff.	pCO_2 mean diff. SD	sO_2 n=	sO_2 mean diff.	sO_2 mean diff. SD
Spiro and Dowdeswell (1976)	17	Unspecified	Normoxia	Chemical	Scalpel	11	0.01	0.02	11	0.10	0.22	11	0.13	0.25			
		Unspecified	Exercise	Chemical	Scalpel	6	0.02	0.01	6	0.13	0.41	6	0.07	0.21			
Pitkin et al (1994)	40	Lung disease	Normoxia	Chemical	Scalpel	40	0.01	0.05	40	-0.17	2.97	40	0.21	1.45			
Sauty et al (1996)	115	Unspecified	Normoxia	Chemical	Scalpel				115	0.59	0.59	115	0.07	0.20			
Dall'Ava-Santucci et al (1996)	81	Unspecified		Chemical					81	1.20	0.85						
Fojac et al (1998)	70	Unspecified	Normoxia	Chemical	Lancet				67	0.12	0.11	67	0.03	0.20			
		Unspecified	Exercise	Chemical	Lancet				67	0.08	0.10	67	0.05	0.20			
Eaton et al (2001)	100	Lung disease	Normoxia	Chemical	Lancet	61	-0.02	0.05	61	0.50	1.70	61	0.20	1.35	61	0.70	6.11
Russomano et al (2006)	6	Healthy		Chemical	Scalpel	8	0.00	0.00	8	0.03	0.17	8	0.13	0.10			
Honarmand and Safavi (2008)	67	Lung disease	Normoxia	None	Scalpel				67	0.14	0.29	67	0.19	0.78			
Mollard et al (2010)	10	Healthy	Normoxia	Chemical		10	-0.01	0.04	10	0.80	1.27	10	0.07	0.69	10	0.10	1.42
		Healthy	Exercise	Chemical		10	-0.01	0.04	10	0.60	1.01	10	0.09	0.64	10	-0.30	1.98
		Healthy	Exercise	Chemical		10	0.00	0.05	10	0.77	1.42	10	0.17	0.75	10	0.00	1.98
		Healthy	Exercise	Chemical		10	0.00	0.04	10	0.32	1.40	10	0.09	0.63	10	-0.10	5.09
		Healthy	Exercise	Chemical		10	-0.01	0.04	10	0.11	0.88	10	0.09	0.48	10	-1.90	8.17
		Healthy	Exercise	Chemical		10	-0.01	0.04	10	0.01	0.96	10	0.12	0.67	10	-1.50	8.70

pCO_2= partial pressure of carbon dioxide; pO_2 = partial pressure of oxygen; sO_2 = oxygen saturation; SD = standard deviation. n = number of arterial blood gas–capillary blood gas sample pairs; pCO_2 and pO_2 in mmHg; sO_2 in %

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