WORKSHEET for Evidence-Based Review of Science for Veterinary CPCR

1. Basic Demographics

Worksheet author(s)

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[redacted]

2. Clinical question:

In dogs and cats with cardiac or respiratory arrest (P), is the use of $EtCO_2$ monitoring (I) vs. observance of chest wall motion (c) a more accurate tool for verification of endotracheal intubation?

3. Conflict of interest specific to this question:

Do any of the authors listed above have conflict of interest disclosures relevant to this worksheet? None

4. Search strategy (including electronic databases searched):

4a. Databases

CAB direct

1) searching under "end-tidal carbon dioxide" + "cardiac arrest": 1 hit, 0 relevant
2) searching under "end-tidal carbon dioxide" + "intubation": 39 hits, 0 relevant
3) searching under "cardiac arrest" + "intubation": 11 hits, 0 relevant
4) searching under "end-tidal carbon dioxide" + "cardiac arrest" + "dog" + "cat": 0 hits
5) searching under "endotracheal intubation" + " verification": 0 hits
6) searching under "intubation" + "verification": 0 hits

PubMed

1) searching under "end-tidal carbon dioxide" + "cardiac arrest" + "dog" + "cat": 1 hit, 0 relevant
2) searching under "end-tidal carbon dioxide" + "cardiac arrest" + "intubation" + "dog" + "cat": 0 hits
3) searching under "cardiac arrest" + intubation" + "verification" + "dog" + "cat": 0 hits
4) searching under "intubation" + "verification" + "dog" + "cat": 0 hits
5) searching under "endotracheal intubation" + "verification" + "dog" + "cat": 0 hits
6) searching under "endotracheal intubation" + "verification" + "cardiac arrest": 10 hits, 3 relevant
7) searching under " endotracheal intubation:" + "verification" + "end-tidal carbon dioxide": 11 hits, 4 relevant
8) searching under "end-tidal carbon dioxide" + "intubation" + "cardiac arrest": 37 hits, 15 relevant

4b. Other sources

-hand search of relevant references from the European Resuscitation Council Guidelines for Resuscitation 2010; 18 relevant

4c. State inclusion and exclusion criteria for choosing studies and list number of studies excluded per criterion

Inclusion criteria

English language

Due to the lack to studies within the target population, studies of all species that examined EtCO2 monitoring for ETT verification were included.

Exclusion criteria

Review papers (8)
Case reports (3)
Non-english studies (3)
Failed to address clinical question (21)

4d. Number of articles/sources meeting criteria for further review:
18 studies meet the criteria for review. One LOE 3 and seventeen LOE 6.

5. Summary of evidence

Evidence Supporting Clinical Question

Good			Sayah 1990; E = endotracheal tube position			
Fair						*Grmec 2002; E = endotracheal tube position Sanders 1994; E = endotracheal tube position Vukmir 1991; E = endotracheal tube position*
Poor						
	1	**2**	**3**	**4**	**5**	**6**
Level of evidence (P)						

A = Return of spontaneous circulation
B = Survival of event
C = Survival to hospital discharge
D = Intact neurological survival
E = Other endpoint
Italics = Non-target species studies

Evidence Neutral to Clinical question

Good						*Knapp 1999; E = endotracheal tube position*
Fair						*Silvestri 2005; E = endotracheal tube position Takeda 2003; E = endotracheal tube position Bozeman 1996; E = endotracheal tube position Bhende 1995; E = endotracheal tube position and survival to ICU admission Hayden 1995; E = endotracheal tube position Bhende 1992; E = endotracheal tube position Ornato 1992; E = endotracheal tube position and survival to hospital admission Anton 1991; E = endotracheal tube position MacLeod 1991; E = endotracheal tube position Varon 1991; E = endotracheal tube position*
Poor						
	1	**2**	**3**	**4**	**5**	**6**
Level of evidence (P)						

A = Return of spontaneous circulation
B = Survival of event
C = Survival to hospital discharge
D = Intact neurological survival
E = Other endpoint
Italics = Non-target species studies

Evidence Opposing Clinical Question

Good						*Li 2002;* *E = endotracheal tube position*
Fair						*Tanigawa 2001;* *E = endotracheal tube position* *Tanigawa 2000;* *E = endotracheal tube position*
Poor						
	1	**2**	**3**	**4**	**5**	**6**
Level of evidence (P)						

A = Return of spontaneous circulation
B = Survival of event
C = Survival to hospital discharge
D = Intact neurological survival
E = Other endpoint
Italics = Non-target species studies

6. REVIEWER'S FINAL COMMENTS AND ASSESSMENT OF BENEFIT / RISK:

Due to the lack of studies within the target species, the comments below are primarily drawn from human trials. Based on similar CO_2 production and elimination physiology between humans and dogs/cats, it is presumed that these human studies are applicable to veterinary medicine and any conclusion will remain sound. Although many studies verified endotracheal tube (ETT) placement through primary clinical assessments including direct visualization of the ETT between the vocal cords, observation of chest rise, presence of breath sounds on auscultation of lung fields bilaterally, absence of breath sounds over the epigastrium, and presence of condensation in the ETT, there are no studies that directly compared $ETCO_2$ measurement to the presence of chest wall motion. For the purposes of this review, any clinical assessment (i.e. auscultation) will be used as a surrogate for the presence of chest wall motion.

To answer the clinical question proposed, the target population will need to be subdivided and considered as, 1) those in cardiac arrest with hemodynamic instability and, 2) those in respiratory arrest with a functioning cardiovascular system. The ability to measure $ETCO_2$ relies on CO_2 production at the cellular level, a competent circulatory system to transport CO_2 to the pulmonary system, and intact respiratory mechanics for CO_2 elimination.

In patients with respiratory arrest only, CO_2 transport to the pulmonary system remains intact and ventilation has failed. As such, once correctly intubated and artificial ventilation has been provided, a value for $ETCO_2$ can be obtained through capnometry or capnography. Esophageal intubation is not expected to produce a sustained high $ETCO_2$ value, and in this context, $ETCO_2$ monitoring may be used to verify ETT position. Few studies assessed support this conclusion (Takeda 2003, Knapp 1999). In one study (Varon 1991), the use of $ETCO_2$ for ETT verification was not directly compared to clinical assessments however, it examined subjects within the groups of respiratory arrest and cardiopulmonary arrest. The Varon study concluded that $ETCO_2$ monitoring can be reliable for confirming ETT placement in patients with respiratory distress/arrest.

In patients with cardiac arrest, the cardiovascular system has failed and CO_2 is no longer being delivered to the pulmonary system effectively due to low cardiac output resulting in poor pulmonary perfusion. In this scenario, despite appropriate ETT placement and initiation of ventilation, a low $ETCO_2$ may be encountered, and may not distinguish from inadvertent esophageal intubation. This will result in poor test sensitivity (defined as the ability to detect correct tracheal intubation) with a higher degree of false negative results. This is supported by the majority of studies assessed (Takeda 2003, Li 2001, Tanigawa 2001, Tanigawa 2000, Bozeman 1996, Bhende 1995, Bhende 1992, Ornato 1992, Anton 1991, MacLeod 1991, Varon 1991). There are two human studies (Sanders 1994, Vukmir 1991) and one experimental canine study (Sayah 1990) that obtained a high test sensitivity supporting the use of $ETCO_2$ monitoring in the target population. It should be noted that both human studies contained a small number of subjects in cardiac arrest and the canine study used a mechanical chest compression device and no report of hemodynamic status was provided.

At this time, there is no convincing evidence to support that a single tool is superior to others for verification of ETT placement in dogs or cats in cardiopulmonary arrest. Besides the concern for a low sensitivity with $ETCO_2$ monitoring in cardiac arrest patients or any patient with poor pulmonary perfusion, $ETCO_2$ monitoring alone will not be able to distinguish endotracheal from endobronchial intubation. Chest wall motion is also not considered completely reliable in confirming ETT position as conditions including airway obstruction, chest wall trauma (or an otherwise non-compliant chest wall), and low tidal volumes may produce negative results. Due to a difference in anatomy between humans and dogs/cats, visualization of the endotracheal tube between the arytenoids cartilages in dogs/cats maybe less difficult and is considered to be positive confirmation of correct tube placement. In situations where this means of confirmation is not possible due to an obstructed

view of the glottis, then a combination of primary clinical assessments and the use of $ETCO_2$ monitoring or radiographic verification should be considered.

7. Conclusion

CONSENSUS ON SCIENCE: There were no studies available within the target species and population that adequately addressed the clinical question. Eleven studies in non-target species (all LOE 6) document concern for the use of $ETCO_2$ monitoring alone when verifying ETT position during cardiac arrest. One human study (Takeda 2003, LOE 6) documented that the clinical assessment of auscultation (not chest wall motion) for verification of ETT position was superior to $ETCO_2$ monitoring in cardiac arrest patients. Another human study (Gremec 2002, LOE 6) demonstrated no significant difference between the use of capnography and auscultation to verify ETT placement in cardiac arrest patients.

TREATMENT RECOMMENDATION: The recommendation for verification of ETT position in dogs and cats in cardiac or respiratory arrest is to use a combination of clinical assessment (i.e. direct visualization of the tube between the arytenoid cartilages, bilateral auscultation of the thorax, chest wall motion, ETT condensation) and secondary confirmatory tools like $ETCO_2$ monitoring. In patients where a high $ETCO_2$ value is obtained following intubation, endotracheal intubation is likely.

8. Acknowledgement

9. Citation list

Anton, W.R., R.W. Gordon, et al. (1991). “A disposable end-tidal CO_2 detector to verify endotracheal intubation.” Ann Emerg Med 20(3): 271-5.
Study objective: We compared the performance of the Fenem FEF™ end-tidal CO_2 detector with the TRIMED capnometer to verify endotracheal intubation. Design: The FEF™ indicates the presence of CO_2 by the color change of a chemically treated indicator; the TRIMED uses infrared technology. Both devices were used during 60 intubations. Setting: Intubations during in-hospital emergency situations outside of the operating room were studied. Type of participants: Adult patients undergoing intubation for respiratory failure, CPR, and other airway protection situations were enrolled in the study. Interventions: The TRIMED monitor and FEF™ detector were placed in series between the manual resuscitator and the patient's endotracheal tube adapter after endotracheal tube placement. Measurements and main results: We defined the acceptable criterion for detection of CO_2 as production of a positive signal within six manual resuscitator bag breaths. The TRIMED met this criterion in 58 of 60 patients (sensitivity, 0.97) and the FEF™ met this criterion in 59 of 60 patients (sensitivity, 0.98). A paired t test showed no statistically significant difference in performance between the two devices. In five of nine cases of intubation during CPR, the color change of the FEF™ was described as "subtle." In one CPR case, a positive signal was not obtained by either device. Conclusion: We conclude that the performance of the FEF™ CO_2 detector is equal to that of the TRIMED monitor for verification of endotracheal intubation in nonCPR situations. Interpretation of FEF™ color changes during CPR should be approached with caution until further studies using the FEF™ during CPR are completed.
Comment: Although the primary objective of this prospective study was to compare the performance of 2 different methods of detecting $ETCO_2$ to verify endotracheal intubation, 15% of intubations were in the target population. Both devices were found to have a sensitivity of 89% in CPR intubations. No

esophageal intubations were encountered thus there is no evaluation of the specificity of either device. Results support use of $ETCO_2$ in nonCPR situations however, is neutral for use during CRP.
FEF™ CO_2 detectors used in this study were provided by the manufacturers.
LOE 6 fair neutral

Bhende, M.S., A.E. Thompson. (1995). "Evaluation of an end-tidal CO_2 detector during pediatric cardiopulmonary resuscitation." Pediatrics 95(3): 395-9.
OBJECTIVE: To determine the utility of a disposable colorimetric end-tidal CO_2 detector during pediatric cardiopulmonary resuscitation (CPR) for (1) confirming endotracheal tube (ETT) position, and (2) assessing the relationship between end-tidal CO_2 recorded by this method and outcome of pediatric CPR. DESIGN/SETTING: Prospective observations during CPR in a university children's hospital. PARTICIPANTS: Forty children (28 male, 12 female) aged 1 week to 10 years (25 children aged ≤ 1 year, mean age 27.2 months, median 7 months), weighing 2.5 to 40 kg (31 children weighing ≤ 15 kg, mean 10.94 kg, median 7 kg) who underwent a total of 48 endotracheal intubations during CPR. METHODS: After intubation, ETT position was verified by usual clinical methods including direct visualization. The device was attached between the ETT and ventilation bag, the patient was manually ventilated, and a first reading was obtained. Any color change from purple (Area A, end-tidal CO_2< 0.5%) to tan or yellow (Area B or C, end-tidal CO_2 ≥ 0.5%) was considered to be positive for airway intubation. CPR was conducted as per Pediatric Advanced Life Support guidelines. A second reading was obtained when the decision to discontinue CPR was made. RESULTS: All nine esophageal tube positions were correctly identified by the detector. Thirty-three of 39 tracheal tube positions were correctly identified (P < .001). For verifying ETT position, the device had a sensitivity of 84.6%, specificity of 100%, positive predictive value of 100%, and negative predictive value of 60%. Readings were obtained at the end of CPR in 25 patients. All 13 patients who regained spontaneous circulation and survived to ICU admission had a second reading in the C range, while none of the 12 patients with a second reading in the A or B range survived. Both the first and second end-tidal CO_2 readings in the C range correlated significantly with short-term survival (P = .01 and P < .001, respectively). Two patients were eventually discharged from the hospital. CONCLUSIONS: During CPR a positive test confirms placement of the ETT within the airway, whereas a negative test indicates either esophageal intubation or airway intubation with poor or absent pulmonary blood flow and requires an alternate means of confirmation of tube position. The detector may be of prognostic value for return of spontaneous circulation and short-term survival.
Comment: This prospective observational study demonstrates that a positive end-tidal CO_2 test can reliably confirm placement of the ETT (specificity of 100%), however additional means of tube confirmation is required with negative test results (sensitivity of 85%).
No comment on industry funding.
LOE 6 fair neutral

Bhende, M.S., A.E. Thompson, el al. (1992)."Validity of a disposable end-tidal CO_2 detector in verifying endotracheal tube placement in infants and children." Ann Emerg Med 21(2): 142-5.
Study objective: To examine the validity of a disposable, colorimetric end-tidal CO_2 detector in verifying endotracheal tube (ETT) placement in infants and children. Design: The detector was studied prospectively in 151 intubations. Setting: Operating room, ICU, and emergency department of a children's hospital. Participants: One hundred thirty-seven children undergoing endotracheal intubation for anesthesia (52), respiratory support (76), or CPR (23). Interventions: After endotracheal intubation, tube position was verified, the detector was attached, and readings were obtained. Measurements and results: The detector correctly identified tube position (trachea, 124; esophagus, four) in all 120 patients who were not in cardiac arrest (P< .01). In the cardiac arrest setting, all six esophageal intubations were correctly identified, but two of the 17 tracheal intubations were incorrectly interpreted as esophageal intubations (P< .01). Conclusion: The detector accurately identifies ETT position in children with spontaneous circulation who weigh more than 2 kg. During

CPR, a positive test correctly indicates that the ETT is in the airway, but a negative result (suggesting esophageal placement) requires an alternate means of confirming ETT position.
Comment: This prospective study in hospitalized infants and children included 12% of patients within the target population. The accuracy of an $ETCO_2$ detector in verifying endotracheal tube placement in this population subset was found to be 88% sensitive and 100% specific with a 75% negative predictive value and 100% positive predictive value. Other means to confirm ETT position are required with negative $ETCO_2$ results.
FEF™ CO_2 detectors used in this study were provided by the manufacturers.
LOE 6 fair neutral

Bozeman, W.P., D. Hexter, et al. (1996). "Esophageal detector device versus detection of end-tidal carbon dioxide level in emergency intubation." Ann Emerg Med 27(5): 595-9.
Study objectives: To confirm the ability of the esophageal detector device (EDD) to indicate positioning of endotracheal tubes (ETTs) in patients intubated under emergency conditions and to compare the performance of the EDD with that of end-tidal carbon dioxide ($ETco_2$). Methods: This single-subject study comprising a prospective case series was conducted in the emergency department of an urban university hospital. All adult patients were intubated either in the ED or by paramedics in the field. ETT position was initially evaluated by means of auscultation, then EDD, and, finally, spectrographic qualitative $ETco_2$ monitoring in each patient. Discrepancies between the EDD and $ETco_2$ results were resolved by means of direct laryngoscopy. Results: In 100 intubated patients, both the EDD and $ETco_2$ monitoring detected the single esophageal intubation that occurred. Of the remaining 99 tracheal intubations, the EDD correctly indicated tracheal placement in 98 (sensitivity, 99%)and was indeterminate in 1 case because of blockage of the ETT by secretions resulting from pulmonary edema. By comparison, $ETco_2$ monitoring correctly indicated tracheal placement in 86 cases (sensitivity, 87%) and was incorrect in 13 cases ($P<.01$). $ETco_2$ monitoring failed in 2 patients with pulmonary edema and in 11 patients with cardiac arrest. Among the 37 patients in the cardiac arrest group, the EDD correctly indicated ETT placement in 37 patients (sensitivity, 100%). In contrast, $ETco_2$ monitoring correctly indicated ETT placement in 26 patients (sensitivity, 70%; $P<.01$). Conclusion: The EDD reliably confirms tracheal intubation in the emergency patient population. The EDD is more accurate than $ETco_2$ monitoring in the overall emergency patient population because of its greater accuracy in cardiac arrest patients.
Comment: Although the primary objective of this prospective case series was to evaluate the ability of an EDD in identifying the position of ETTs in patients under emergency conditions, $ETco_2$ was also examined. The study subjects included 37% of patients within the target population (cardiac arrest). The accuracy of the $ETco_2$ in identifying ETT position in the target population was reported to be 70% sensitive and 100% specific. However, only 1 of 100 intubations in the study was esophageal. The authors suggest that a negative $ETco_2$ result in patients with cardiac arrest require confirmation of the ETT position through alternate means.
Chesapeake Medical Corporation provided one end-tidal CO_2 detector.
LOE 6 fair neutral

Gremec, S. (2002). "Comparison of three different methods to confirm tracheal tube placement in emergency intubation." Intensive Care Med 28(6): 701-4.
Objectives: Verification of endotracheal tube placement is of vital importance, since unrecognized esophageal intubation can be rapidly fatal (death, brain damage). The aim of our study was to compare three different methods for immediate confirmation of tube placement: auscultation, capnometry and capnography in emergency conditions in the prehospital setting. Design and setting: Prospective study in the prehospital setting. Patients and interventions: All adult patients (>18 years) were intubated by an emergency physician in the field. Tube position was initially evaluated by auscultation. Then, capnometry was performed with infrared capnometry and capnography with infrared capnography. The examiners looked for the characteristic CO_2

waveform and value of end-tidal carbon dioxide ($EtCO_2$) in millimeters of mercury. Determination of final tube placement was performed by a second direct visualization with laryngoscope. Data are mean ± SD and percentages. Measurements and results: Over a 4 year period, 345 patients requiring emergency intubation were included. Indications for intubation included cardiac arrest (n=246; 71%) and non-arrest conditions (n=99; 29%). In nine (2.7%) patients, esophageal tube placement occurred. The esophageal intubations were followed by successful endotracheal intubations without complications. The capnometry (sensitivity and specificity 100%) and capnography (sensitivity and specificity 100%) were better than auscultation (sensitivity 94% and specificity 83%) in confirming endotracheal tube placement in non-arrest patients ($p<0.05$). Capnometry was highly specific (100%) but not sensitive (88%) for correct endotracheal intubation in patients with cardiopulmonary arrest (capnometry versus auscultation and capnometry versus capnography, $p<0.05$). Conclusion: Capnography is the most reliable method to confirm endotracheal tube placement in emergency conditions in the prehospital setting.
Comment: Capnography was determined to be 100% sensitive and 100% specific in both cardiac arrest and non-cardiac arrest patients. In cardiac arrest patients, capnometry was found to be significantly less sensitive at 88% when compared with either auscultation or capnography. Limitations may include a low incident of esophageal intubation (3%).
No comment on industry funding.
LOE 6 fair supportive

Hayden, S.R., J. Sciammarella, et al. (1995). "Colorimetric end-tidal CO_2 detector for verification of endotracheal tube placement in out-of-hospital cardiac arrest." Acad Emerg Med 2(6): 499-502.
Objective: To evaluate the ability of a disposable, colorimetric end-tidal CO_2, detector to verify proper endotracheal (ET) tube placement in out-of-hospital cardiac arrest, and to correlate semiquantitative CO_2, measurements with the rate of return of spontaneous circulation (ROSC). Methods: Prospective, observational study using a convenience sample of intubated out-of-hospital cardiac arrest patients. A disposable, colorimetric end-tidal CO_2 detector was attached to the ET tube after intubation. In the absence of a colorimetric change, the paramedics reassessed the tube placement and could reintubate the patient. Tube placement was verified at the hospital. Paramedics were instructed to contact the base station and report the colorimetric change upon hospital arrival. ROSC was defined as restoration of a self-sustaining pulse until hospital arrival. Results: Between December 1990 and May 1993, ET tubes were placed in 566 victims of out-of-hospital cardiac arrest. 541 of the 566 intubations (95.6%) were associated with a color change. In one case with a color change and out-of-hospital clinical evidence of proper tube placement, the tube was determined to be in the esophagus at the hospital. Correct placement of the remaining 565 of 566 (99.8%) tubes was verified. Of the 566 patients who had a colorimetric change, 91 (16%) had ROSC vs one of 25 (4%) patients who did not have a color change. In one subgroup ($n = 179$), the degree of color change was highly associated with ROSC ($p = 0.004$). Conclusions: A disposable, colorimetric end-tidal CO_2, detector appears reliable in verifying proper ET tube placement in victims of out-of-hospital cardiac arrest. The degree of color change correlates with the probability of ROSC.
Comment: This prospective observational study on adult out-of-hospital cardiac arrest patients reported an accuracy of the end-tidal CO_2 detector in verifying endotracheal tube placement as 96% sensitive. A specificity could not be calculated as there were no true negative results. In 68% of the patients, the degree of end-tidal CO_2 colour change was not quantified and simply reported as "positive". Authors recommend combination of clinical assessment of correct endotracheal tube placement with end-tidal CO_2 detector use.
No industry funding.
LOE 6 neutral

Knapp, S., J. Kofler, et al. (1999). "The assessment of four different methods to verify tracheal tube placement in the critical care setting." Anesth Analg 88(4): 766-70.
One of the most serious complications of conventional endotracheal intubation is unidentified placement of the tube in the esophagus. The aim of our study was to evaluate four different methods for immediate detection of the tube position: auscultation, capnographic determination of $ETco_2$, esophageal detection method (EDM) using a self-inflating bulb, and the transillumination method using a lighted stylet (Trachlight™; Laerdal, Armonk, NY). Thirty-eight endotracheally intubated patients admitted to our medical intensive care unit were enrolled in the study. A second identical tube was inserted into the esophagus under laryngoscopic control. The endotracheal tube was then disconnected from the ventilator. Two blinded examiners, one experienced, the other inexperienced, determined the tube position within 30 s using one of the four methods. The order of the tubes tested and the methods used were randomized. In 130 of 152 examinations, both examiners correctly diagnosed the position of the tube. The wrong result was obtained by both examiners 4 times; only the experienced examiner was wrong 4 times, and only the inexperienced examiner was wrong 14 times. Using $ETco_2$, both examiners were correct in all cases. Auscultation showed an obvious relation to the examiner's experience: the experienced examiner was correct in all cases, the inexperienced examiner was correct in only 68% of cases. Using the self-inflating bulb, there were two wrong results of the experienced examiner and one wrong result of the inexperienced examiner. The transillumination technique was associated with a high error rate by both examiners (16%and 13%, respectively). Comparing all four methods showed that capnography is superior to auscultation (P= 0.0005) and to the Trachlight™ detection method (P = 0.0078). EDM was not statistically superior to auscultation and transillumination. Capnography was the most reliable method for rapid evaluation of tube position, followed by EDM, whereas auscultation and Trachlight™ did not seem to be of comparable value. Experience was a determining factor for auscultation. Implications: To prevent unidentified esophageal intubation, a serious complication in the critical care setting, four methods for detecting tube position were tested by two examiners (one experienced, the other inexperienced) in endotracheally intubated patients after insertion of a second tube into the esophagus.
Comment: This prospective randomized blinded study enrolled 38 consecutive intubated adult patients requiring prolonged controlled mechanical ventilation. Although 42% (n = 16) of the patients underwent cardiopulmonary resuscitation, hemodynamic and respiratory stability were prerequisites for study entry. $ETco_2$ was found to have 100% sensitivity and 100% specificity in both examiners. Clinical assessment of tube placement (auscultation) appears to be influenced by examiner experience, with proper tube position correctly identified in all cases by an experienced examiner. The majority of cardiac arrest patients in veterinary medicine are not hemodynamically stable and therefore the evidence from this is balanced.
No comment on industry funding.
LOE 6 good neutral

Li, J. (2001). "Capnography alone is imperfect for endotracheal tube placement confirmation during emergency intubation." J Emerg Med 20(3): 223-9.
This analysis primarily sought to determine the effectiveness of end-tidal capnography for tube placement confirmation during emergency airway management. Secondary objectives were validation of the rate of unanticipated esophageal placement during emergency intubation and quantification of the portion of intubations performed in patients with cardiac arrest where capnography is not recommended. The study was performed in two phases. For the primary objective, a meta-analysis was performed on all experimental capnography trials enrolling emergency populations. For the secondary objectives, inadvertent esophageal intubation and cardiac arrest rates were calculated from a large prospective multicenter observational study of emergency intubation cases. Data analysis included calculation of descriptive statistics, sensitivity, specificity, and confidence intervals (CI). Based on 2,192 intubations, a meta-analysis of previous capnography trials resulted in an aggregate sensitivity of 93% (95% CI 92–94%) and an aggregate specificity of 97% (CI 93–

99%) for emergency tube placement confirmation. Thus, for emergency capnography use, the false-negative failure rate (tube in trachea but capnography reports esophagus) was 7% and the false-positive rate (tube in esophagus but capnography reports trachea) was 3%. This translates to potential harm for one patient in every 10 treated with capnographic confirmation alone (number needed to harm: 14 for false negative, 33 for false-positive, and 10 for both). A further literature review demonstrated no sole method of tube placement confirmation is completely foolproof. Of 4,602 consecutive intubations reported to the National Emergency Airway Registry, 4% of emergency intubation attempts resulted in accidental esophageal intubation, and 10% occurred in nontraumatic cardiac arrest patients. During tracheal intubation of critically ill patients, it is concluded that the rate of accidental esophageal tube placement warrants continued improvement in emergency airway techniques. Misidentification of esophageal placement in the emergency setting may occur with capnography. Multiple methods of tube placement confirmation are superior to any single method because no single method has perfect accuracy.

Comment: This meta-analysis of trials assessing end-tidal CO_2 devices for confirming endotracheal tube placement in an emergency population included 49% of patients within the target population. The accuracy of end-tidal CO_2 devices in cardiac arrest intubations alone could not be reported due to lack of data. Overall accuracy of end-tidal CO_2 devices in confirming emergency tube placement was reported to be 93% sensitive and 97% specific with a false negative failure rate of 7% and a false positive rate of 3%. This study emphasizes the use of multiple techniques to confirm tube placement in emergency situations and that end-tidal CO_2 alone should not be considered the gold standard for emergency tube placement confirmation.

No comment on industry funding.

LOE 6 fair/good opposing

MacLeod, B.A., M.B. Heller, et al. (1991). "Verification of endotracheal tube placement with colorimetric end-tidal CO_2 detection." Ann Emerg Med 20(3): 267-70.

Study objective: To determine the ability of a disposable colorimetric CO_2 detector to accurately confirm or refute endotracheal tube placement. Design: Two hundred fifty prospective emergency intubations. Setting: Emergency intubations performed in the emergency department, helicopter, and prehospital ground environment. Type of participants: Intubations were performed by emergency medicine residents, paramedics, and flight nurses. Interventions: The FEF^{TM} CO_2 detector was applied after 250 emergency intubations. Notation of color change indicating intratracheal placement was recorded in each case. Confirmation or refutation of the detector's results was determined subsequently through traditional methods. Results: The sensitivity for confirmation of endotracheal intubation in the 137 patients with a palpable pulse was 100%. However, only 76 of 103 patients (sensitivity, 72%) in cardiac arrest had endotracheal intubation confirmed by color change. The device was uniformly specific for tracheal intubation in 73 arrested patients in whom a color change was noted (100%). There was one instance (of a total of seven misintubations) in which a positive color change was noted, but the tube was not intratracheal (specificity, 86%). Overall sensitivity for tracheal intubation was 88% (95% confidence limits; range, 0.83 to 0.92), and specificity for tracheal intubation was 92% (95% confidence limits; range, 0.62 to 0.99). Conclusion: The FEF^{TM} colorimetric detector reliably detects intratracheal placement in the nonarrested patient. Its use in prolonged cardiac arrest merits further study.

Comment: This prospective study used a convenience sample involving adult patients requiring emergency intubation. Forty-two percent of the patients were in cardiopulmonary arrest. The end-tidal CO_2 detector has a sensitivity of 72% and specificity of 100% in the target population. Limitations of the study include a low number of esophageal intubations. Authors suggest further studies prior to recommending use in patients with prolonged cardiac arrest.

Funded in part by the Pittsburgh Emergency Medicine Foundation.

LOE 6 fair neutral

Ornato, J.P., J.B. Shipley, et al. (1992). "Multicenter study of a portable, hand-size, colorimetric end-tidal carbon dioxide detection device." Ann Emerg Med 21(5): 518-23.
Study objectives: To evaluate continuous, semiquantitative end-tidal carbon dioxide ($ETCO_2$) monitoring in the prehospital and emergency department setting for confirming proper endotracheal tube placement and assessing prognosis and blood flow during CPR. Type of participants: Adult patients were included if an endotracheal tube was inserted by prehospital care providers or emergency physicians for cardiac arrest, respiratory arrest, respiratory insufficiency, or airway protection. Design and interventions: A small, portable, colorimetric $ETCO_2$detector was attached to the endotracheal tube immediately after each attempted endotracheal tube insertion. The color of the detector membrane was noted at the seventh breath following intubation. The color also was noted and recorded if there was return of spontaneous circulation (defined as a palpable pulse) immediately prior to and following conversion from manual to mechanical CPR. Survival to hospital admission was used as an end point to assess the prognostic value of the initial $ETCO_2$ reading. Main results: A total of 227 patients (144 with cardiopulmonary arrest) were studied. In the 83 patients intubated but not in cardiopulmonary arrest, a reading on the $ETCO_2$ detector signifying more than 0.5% $ETCO_2$ was 100% sensitive and 93% specific in detecting proper endotracheal tube placement (100% specific with the endotracheal tube cuff inflated). In cardiac arrest patients, a longer period of estimated arrest appeared to be associated with a lower $ETCO_2$ detector reading. A reading signifying more than 0.5% $ETCO_2$ was 69% sensitive and 100% specific in detecting proper endotracheal tube placement. After proper endotracheal tube placement, all cardiac arrest patients who survived to hospital admission had an initial $ETCO_2$ measurement signifying more than 0.5% $ETCO_2$. Return of spontaneous circulation was usually accompanied by an improved $ETCO_2$ value. Mechanical CPR always produced an $ETCO_2$ value that was as high or higher than that produced by manual CPR. Conclusion: The colorimetric $ETCO_2$ device is highly accurate for confirming endotracheal tube position in nonarrest patients. In cardiac arrest patients, a reading signifying more than 0.5% $ETCO_2$ confirms correct endotracheal tube placement, while a value signifying less than 0.5% $ETCO_2$ during resuscitation suggests that something is wrong (eg, esophageal intubation, inadequate circulatory flow, prolonged downtime interval, hypothermia, or significant ventilation/perfusion mismatch).
Comment: This prospective multicenter study included 63% of patients within the target population (cardiopulmonary arrest). Supports other studies with concern that despite a 100% specificity, the $ETCO_2$ device has a low sensitivity (69%) in detecting correct endotracheal tube placement in the target population.
No comment on industry funding.
LOE 6 fair neutral

Sanders, K.C., W.B Clum, III, et al. (1994). "End-tidal carbon dioxide detection in emergency intubation in four groups of patients." J Emerg Med 12(6): 771-7.
A prospective clinical trial was conducted at a level I trauma center to assess the efficacy of end-tidal carbon dioxide (CO_2) detection in four groups of patients requiring emergency intubation because of cardiac arrest, major trauma, respiratory failure, or the need for airway protection. A semiquantitative, colorimetric FEF^{TM} end-tidal CO_2 detector (Fenem, Inc, New York, NY) was used to evaluate endotracheal versus esophageal intubation. This disposable, bedside detector registers three ranges of CO_2 concentration: "A" (purple) indicates low levels and probable esophageal intubation; "B" (beige) indicates moderate levels and probable tracheal intubation with hypocarbia; "C" (yellow) indicates high levels and tracheal intubation. Clinical observation, patient response, chest x-ray films, and arterial blood gas results were used to corroborate placement of the endotracheal tube. The FEF^{TM} detector was found to be 100% reliable for confirming tracheal placement when registering levels in the B and C ranges and 100% reliable for detecting esophageal intubation when registering levels in the A range. In conclusion, the FEF^{TM} CO_2 detector is a reliable and useful adjunct for airway management of diverse groups of patients in the emergency setting.

Comment: This prospective trial evaluated 43 hospitalized adult patients requiring emergency intubation with 23% (n = 10) within the target population (cardiac arrest). The CO_2 detector was found to have 100% sensitivity and 100% specificity in verifying endotracheal intubation for all patients. The authors recommend that larger studies are needed to confirm these results.
No comment on industry funding.
LOE 6 fair supportive

Sayah, A.J., W.F. Peacock, et al. (1990). "End-tidal CO_2 measurement in the detection of esophageal intubation during cardiac arrest." Ann Emerg Med 19(8): 857-60.
Measurement of end-tidal carbon dioxide ($ETco_2$) has been used to detect accidental esophageal tube placement in noncardiac arrest situations. The purpose of our study was to determine whether $ETco_2$ measurement could distinguish tracheal from esophageal tube placement during closed-chest massage (CCM). Twelve large dogs were anesthetized, and endotracheal tubes were placed in both the trachea and the esophagus. Placement was verified by fiberoptic endoscopy. Ventricular fibrillation was induced by a 60-Hz discharge through a right ventricular pacemaker. After four minutes of cardiac arrest, CCM was initiated and continued for 20 minutes. The dogs were divided into two groups: Group A was ventilated through the tracheal tube, and group B was ventilated through the esophageal tube. Unused tubes were removed. $ETco_2$ was recorded continuously beginning two minutes before arrest until the end of the experiment. There were no significant between-group differences in mean arterial pressure, weight, blood loss, IV fluid volume administered, or prearrest arterial blood gases. $ETco_2$ differed significantly between the two groups throughout CCM (P = .001). In group A, $ETco_2$ ranged from 13 to 34 mm Hg (median, 20 mm Hg). In group B, $ETco_2$ ranged from 2 to 11 mm Hg (median, 3 mm Hg). In this experimental model, measurement of $ETco_2$ reliably distinguished esophageal from tracheal intubation during cardiac arrest and CCM. If confirmed in human beings, this may prove to be a quick, reliable method of detecting esophageal intubation during cardiac arrest.
Comment: This is the only study available in the target species and target population. This randomized controlled experimental study demonstrated that capnography can verify tracheal intubation during cardiac arrest. Although direct continuous blood pressure was measured in the study, no results on this variable were reported and the hemodynamic conditions of the subjects are unknown. Largest limitation includes the small study size with 6 dogs in each group.
Supported by a grant from the William Beaumont Hospital Research Institute.
LOE 3 good supportive

Silvestri, S., G.A. Ralls, et al. (2005). "The effectiveness of out-of-hospital use of continuous end-tidal carbon dioxide monitoring on the rate of unrecognized misplaced intubation within a regional emergency medical services system." Ann Emerg Med 45(5): 497-503.
Study objective: We evaluate the association between out-of-hospital use of continuous end-tidal carbon dioxide ($ETCO_2$) monitoring and unrecognized misplaced intubations within a regional emergency medical services (EMS) system. Methods: This was a prospective, observational study, conducted during a 10-month period, on all patients arriving at a regional Level I trauma center emergency department who underwent out-of hospital endotracheal intubation. The regional EMS system that serves the trauma service area is composed of multiple countywide systems containing numerous EMS agencies. Some of the EMS agencies had independently implemented continuous $ETCO_2$ monitoring before the start of the study. The main outcome measure was the unrecognized misplaced intubation rate with and without use of continuous $ETCO_2$ monitoring. Results: Two hundred forty-eight patients received out-of-hospital airway management, of whom 153 received intubation. Of the 153 patients, 93 (61%) had continuous $ETCO_2$ monitoring, and 60 (39%) did not. Forty-nine (32%) were medical patients, 104 (68%) were trauma patients, and 51 (33%) were in cardiac arrest. The overall incidence of unrecognized misplaced intubations was 9%. The rate of unrecognized misplaced intubations in the group for whom continuous $ETCO_2$ monitoring was used was zero, and the rate in

the group for whom continuous $ETCO_2$ monitoring was not used was 23.3% (95% confidence interval 13.4% to 36.0%). Conclusion: No unrecognized misplaced intubations were found in patients for whom paramedics used continuous $ETCO_2$ monitoring. Failure to use continuous $ETCO_2$ monitoring was associated with a 23% unrecognized misplaced intubation rate.

Comment: None of the 14 unrecognized misplaced intubations were within the target population (cardiac arrest) however, the study otherwise presents compelling evidence that use of continuous $ETCO_2$ monitoring could reduce the rate of unrecognized esophageal intubations. The evidence from this study is considered neutral until the inclusion of misplaced esophageal intubation is assessed within the target population.

The 3rd author is a consultant for a capnography manufacturer with funding and support received.

LOE 6 fair neutral

Tanigawa, K., T. Takeda, et al. (2000) "Accuracy and reliability of the self-inflating bulb to verify tracheal intubation in out-of-hospital cardiac arrest patients." Anesthesiology 93(6): 1432-6.

Background: To determine the sensitivity and specificity of the self-inflating bulb (SIB) to verify tracheal intubation in out-of-hospital cardiac arrest patients. Methods: Sixty-five consecutive adult patients with out-of-hospital cardiac arrest were enrolled. Patients were provided chest compression and ventilation by either bag–valve–mask or the esophageal tracheal double-lumen airway by ambulance crews when they arrived at the authors' department. Immediately after intubation in the emergency department, the endotracheal tube position was tested by the SIB and end-tidal carbon dioxide ($ETCO_2$) monitor using an infrared carbon dioxide analyzer. We observed the SIB reinflating for 10 s, and full reinflation within 4 s was defined as a positive result (tracheal intubation). Results: Five esophageal intubations occurred, and the SIB correctly identified all esophageal intubations. Of the 65 tracheal intubations, the SIB correctly identified 47 tubes placed in the trachea (72.3%). Delayed but full reinflation occurred in one tracheal intubation during the 10-s observation period. Fifteen tracheal intubations had incomplete reinflation during the observation period, and two tracheal intubations did not achieve any reinflation. Thirty-nine tracheal intubations were identified by $ETCO_2$ (60%). When the SIB test is combined with the $ETCO_2$ detection, 59 tracheal intubations were identified with a 90.8% sensitivity. Conclusions: The authors found a high incidence of false negative results of the SIB in out-of-hospital cardiac arrest patients. Because no single test for verifying endotracheal tube position is reliable, all available modalities should be tested and used in conjunction with proper clinical judgment to verify tracheal intubation in cases of out-of-hospital cardiac arrest.

Comment: This prospective observational study examined 65 consecutive adult out-of-hospital cardiac arrest patients. Although the primary objective was to evaluate the sensitivity and specificity of the SIB in detecting esophageal intubation, $ETCO_2$ was also monitored and determined to have a sensitivity of 60%, specificity of 100%, negative predictive value of 16%, and positive predictive value of 100%. This does not support the use of a single test to verify endotracheal tube position.

No comment on industry funding.

LOE 6 fair opposing

Tanigawa, K., T. Takeda, et al. (2001) "The efficacy of esophageal detector devices in verifying tracheal tube placement: a randomized cross-over study of out-of-hospital cardiac arrest patients." Anesth Analg 92(2): 375-8.

We performed this prospective study to evaluate the efficacy of esophageal detector devices (EDDs), both the bulb and the syringe-type, to indicate positioning of endotracheal tubes (ETTs) in out-of-hospital cardiac arrest patients. Forty-eight adult patients with out-of-hospital cardiac arrest were enrolled. Immediately after tracheal intubation and ETT cuff inflation in the emergency department, the patients were allocated randomly to two cross-over groups. In Group 1 (n = 24), patients underwent a bulb test and a syringe test in sequence. In Group 2 (n = 24), patients underwent a syringe test and a bulb test in sequence. End-tidal carbon dioxide ($ETCO_2$)

was also monitored. In 56 attempts at tracheal intubation, the bulb, the syringe, and $ETCO_2$indicated all eight esophageal intubations. In 48 tracheal intubations, the bulb test correctly indicated 34 tracheal intubations (sensitivity, 70.8%). The syringe test identified 35 tracheal intubations (sensitivity, 72.9%). The results of both tests agreed in 33 tracheal intubations. $ETCO_2$ was detected in 31 tracheal intubations (sensitivity, 64.6%). No statistical difference was found among the tests. EDDs were less sensitive in detecting tracheal intubation for out-of-hospital cardiac arrest patients. Therefore, proper clinical judgment in conjunction with these devices should be used to confirm ETT placement in these difficult situations.
Comment: This prospective randomized cross-over study evaluated 48 adult out-of-hospital cardiac arrest patients. Although the primary objective was to evaluate the efficacy of two types of EDDs to indicate endotracheal tube positioning, $ETCO_2$ was also examined and determined to have a sensitivity of 64.6%, specificity of 100%, negative predictive value of 32%, and positive predictive value of 100%. This does not support the use of a single test to verify the endotracheal tube position.
No comment on industry funding.
LOE 6 fair opposing

Takeda, T., K. Tanigawa, et al. (2003). "The assessment of three methods to verify tracheal tube placement in the emergency setting." Resuscitation 56(2): 153-7.
We studied prospectively the reliability of clinical methods, end-tidal carbon dioxide ($ETCO_2$) detection, and the esophageal detector device (EDD) for verifying tracheal intubation in 137 adult patients in the emergency department. Immediately after intubation, the tracheal tube position was tested by the EDD and $ETCO_2$ monitor, followed by auscultation of the chest. The views obtained at laryngoscopy were classified according to the Cormack grade. Of the 13 esophageal intubations that occurred, one false-positive result occurred in the EDD test and auscultation. In the non-cardiac arrest patients (n=56), auscultation, the $ETCO_2$, and EDD test correctly identified 89.3, 98.2*, and 94.6%* of tracheal intubations, respectively (*, $P<0.05$ vs. the cardiac arrest patients). In the cardiac arrest patients (n=81), auscultation, the $ETCO_2$, and the EDD tests correctly identified 92.6**, 67.9, and 75.3% of tracheal intubations, respectively (**, $P<0.05$ vs. EDD and $ETCO_2$). The frequencies of Cormack grade 1 or 2 were 83.9% in the non-cardiac arrest, and 95.1% in the cardiac arrest patients. In conclusion, the $ETCO_2$ monitor is the most reliable method for verifying tracheal intubation in non-cardiac arrest patients. During cardiac arrest and cardiopulmonary resuscitation, however, negative results by the $ETCO_2$ or the EDD are not uncommon, and clinical methods are superior to the use of these devices.
Comment: This prospective study examined 137 consecutive patients requiring emergency tracheal intubation with 59% (n = 81) within the target population (cardiac arrest patients). Within the target population, $ETCO_2$ had a sensitivity if 67.9%, specificity of 100%, negative predictive value of 25.7%, and positive predictive value of 100%. Although $ETCO_2$ monitoring appears to be superior for verifying tracheal intubation in non-cardiac arrest patients, there is a significant degree of false negative results in the target population thus clinical methods of endotracheal tube verification are recommended. No comment on industry funding.
LOE 6 neutral (may be supportive for respiratory arrest however, opposing for cardiac arrest)

Varon, A. J., J. Morrina, et al. (1991). "Clinical utility of a colorimetric end-tidal CO_2 detector in cardiopulmonary resuscitation and emergency intubation." J Clin Monit 7(4): 289-93.
The purposes of this study were to evaluate the clinical utility of a colorimetric end-tidal CO_2 ($ETCO_2$) detector in confirming proper endotracheal intubation in patients requiring emergency intubation, to determine if this new device can be used as an adjunct to judge the effectiveness of cardiopulmonary resuscitation (CPR), and to determine whether the device can predict successful resuscitation from cardiopulmonary arrest. We studied prospectively 110 patients requiring emergency intubation for either respiratory distress (53 patients) or cardiopulmonary arrest (57 patients) by recording the color range of the indicator after the initial intubation. In patients who suffered a cardiopulmonary arrest, the color range was also recorded during CPR after the

endotracheal tube was confirmed to be in the tracheal position and perfusion optimized, and at the moment CPR was stopped. The $ETCO_2$ detector was 100% specific for correct endotracheal intubation in all patients. It was also highly sensitive (0.98) for correct endotracheal intubation in patients with respiratory distress. However, it was not sensitive (0.62) in patients with cardiopulmonary arrest and low perfusion. The sensitivity improved (0.88) when we used the $ETCO_2$ range obtained after attempts to increase perfusion. A low $ETCO_2$color range in 19 patients undergoing CPR was interpreted as low cardiac output and prompted the physicians to attempt to increase perfusion. Of the patients who underwent CPR, no patient whose $ETCO_2$level remained less than 2% was successfully resuscitated. Those patients who had an $ETCO_2$level ≥ 2% had a significantly higher incidence of successful resuscitation. We conclude that the colorimetric $ETCO_2$ detector is reliable and provides reassurance of correct endotracheal tube placement in patients requiring emergency intubation for respiratory distress. This device helps identify patients with low perfusion during CPR and is a useful prognostic indicator of successful short-term resuscitation.

Comment: This prospective study supports the use of $ETCO_2$ monitoring in patients with respiratory distress with a sensitivity of 98%, specificity of 100%, negative predictive value of 83%, and positive predictive value of 100%. This subset of patients contains an unknown percentage of the target population as those in respiratory arrest were included within this category. The usefulness of $ETCO_2$ monitoring to confirm endotracheal intubation in cardiopulmonary arrest patients remains unknown due to a low sensitivity of 62% (specificity 100%, negative predictive value 20%, and positive predictive value 100%). It should be noted that this study required the $ETCO_2$ level to be ≥ 2% to be positive for endotracheal intubation. The majority of other studies using the same $ETCO_2$ device (FEF™) define an $ETCO_2$ level ≥ 0.5% to be positive for correct tube placement.

No comment on industry funding.

LOE 6 fair neutral

Vukmir, R.B., M.B. Heller, et al. (1991). "Confirmation of endotracheal tube placement: a miniaturized infrared qualitative CO_2 detector." Ann Emerg Med 20(7): 726-9.

Study objectives: A miniaturized, infrared, solid-state, end-tidal CO_2 detector was used to confirm emergency endotracheal tube (ETT) placement. Design: This prospective, clinical study used a miniature, infrared, solid-state end-tidal CO_2 detector to confirm ETT placement in an acute setting. Setting: The ICU, emergency department, and hospital floor. Type of participants: There were 88 consecutive adult patients requiring 100 emergency intubations. Measurements and main results: The indication for airway intervention was considered urgent in 79% and under arrest conditions in 21%. The mean number of intubation attempts was 1.83 (range, one to five) with difficulty of intubation of 6.48 and confirmation of 7.75, on a linear scale from 0 (lowest) to 10 (highest). Determination of ETT position revealed intratracheal intubation in 96% and esophageal intubation in 4%. Placement was confirmed by direct visualization or radiography in all cases. Sensitivity and specificity for ETT localization was 100% ($P < .0001$). Conclusion: This hand-held infrared capnometer reliably confirms ETT placement under emergency conditions.

Comment: This prospective observational study examined 88 consecutive adult patients requiring emergency intubations with 21% within the target population (cardiac or traumatic arrest). This study reported a 100% sensitivity and 100% specificity for end-tidal CO_2 confirmation of ETT placement. Limitations include the small number of esophageal intubations encountered (4%). This study supports the use of capnometry to confirm endotracheal tube placement.

No comment on industry funding.

LOE 6 fair supporting