Critical Review Form
Therapy

Bobrow BJ, Ewy GA, Clark L, Chikani V, Berg RA, Sanders AB, et al. Passive oxygen insufflation is superior to bag-valve-mask ventilation for witnessed ventricular fibrillation out-of-hospital cardiac arrest. Ann Emerg Med. 2009 Nov;54(5):656-662.

Objectives: To compare "outcomes of out-of-hospital cardiac arrest patients receiving minimally interrupted cardiac resuscitation with initial passive ventilation with those receiving minimally interrupted cardiac resuscitation with initial bag-valve-mask ventilation."

Methods: This was a retrospective cohort study conducted in Arizona using information obtained through the Save Hearts in Arizona Registry and Education (SHARE) program from January 1, 2005 to September 28, 2008. The SHARE program collects information from EMS incident reports for 60 EMS agencies comprising approximately 80% of the state's population. Included patients were adults aged > 18 years with cardiac arrest, defined as "the absence of a pulse and the lack of normal breathing." Exclusion criteria were:

1) **Obvious signs of death (rigor mortis, lividity)**
2) **Do not resuscitate (DNR) documentation**
3) **Cardiac arrest witnessed by EMS personnel**
4) **Cardiac arrest as a result of trauma, drowning, or other noncardiac causes.**

Twenty-five of the 60 EMS agencies in the SHARE program elected to use the minimally interrupted cardiac resuscitation (MICR) protocol, which consisted of:

1) **200 uninterrupted pre-shock chest compressions**
2) **200 uninterrupted post-shock chest compressions before pulse-check and rhythm analysis**
3) **Delayed endotracheal intubation for 3 cycles of 200 compressions**
4) **Attempted intravenous or intraosseous epinephrine prior to or during the 2nd cycle of compressions.**

The decision to perform passive ventilation versus bag-valve-mask (BVM) ventilation during the initial 3 cycles of compression was at the discretion of the EMS personnel.

Data was manually extracted from the SHARE database by the SHARE program research and quality improvement director. Only cases that met all 4 of the criteria for the minimally interrupted cardiac resuscitation protocol were included. Final outcomes were obtained through local hospitals and the Office of Vital Statistics at the Arizona Department of Health Services.

The primary outcome measure was neurologically intact survival to hospital discharge. Secondary outcomes were return of spontaneous circulation, survival to hospital admission, and survival to discharge with a favorable neurologic outcome as measured by the Cerebral Performance Category (CPC) scale. Neurologic outcome was assessed by mail or telephone survey versions of the CPC; scores of 1 or 2 were defined as favorable, and scores of 3 or 4 were defined as unfavorable. Adjusted odds ratios were calculated using multivariate logistic regression models adjusted for age, bystander CPR, initial rhythm, arrest location, sex, bystander-witnessed arrest, and EMS response time. An *a priori* decision was made to perform a subgroup analysis of patients with witnessed ventricular fibrillation or ventricular tachycardia arrest.

There were 5097 EMS-attended out of hospital cardiac arrests documented during the study period. After exclusion criteria, there were 1019 cases involving MICR, of whom 459 received initial passive ventilation and 560 received initial BVM ventilation.

Guide		Comments
I.	**Are the results valid?**	
A.	**Did experimental and control groups begin the study with a similar prognosis (answer the questions posed below)?**	
1.	Were patients randomized?	No. The decision to utilize BVM versus passive ventilation was entirely at the discretion of the EMS personnel, introducing selection bias. While similarities in demographics, arrest rhythm, and dispatch time would argue that such bias was not introduced, there may be unknown confounders not accounted for.
2.	Was randomization concealed (blinded)?	No. Patients were not randomized and treatment was not concealed.
3.	Were patients analyzed in the groups to which they were randomized?	Yes. Patients were not randomized. Patients were ventilated by either BVM or passive techniques at EMS discretion, and were analyzed according to these groups.
4.	Were patients in the treatment and control groups similar with respect to known prognostic factors?	Uncertain. According to Table 1, patients were similar with respect to age, gender, initial rhythm, and dispatch time. Medical comorbidities (such as pre-existing cardiac disease) were not included. Transport times and time to defibrillation were also not included. **Table 1.** Demographics of study participants and event characteristics by ventilation method. **Characteristics (N=1,019)** / **PV (n=459)** / **BVM (n=560)** Age, y, mean (SD) — 66.6 (14.5) — 64.8 (16.0) Male — 313/459 (68.2) — 377/560 (67.3) **Location** Home — 323/459 (70.4) — 393/560 (70.2) Public place — 73/459 (15.9) — 76/560 (13.6) Medical facility — 63/459 (13.7) — 91/560 (16.3) Witnessed % (No.) — 200/459 (43.6) — 252/560 (45.0) Bystander CPR performed — 177/459 (38.6) — 242/560 (43.2) **Initial rhythm*** Shockable (ventricular fibrillation/ ventricular tachycardia) — 143/459 (31.2) — 178/560 (31.8) Nonshockable — 316/459 (68.9) — 381/560 (68.2) EMS dispatch to arrival time, min, median (IQR) — 5.0 (2.0) — 5.0 (2.0)
B.	**Did experimental and control groups retain a similar prognosis after the study started (answer the questions posed below)?**	
1.	Were patients aware of group allocation?	Yes and no. While blinding of participants is generally recommended when feasible, these were patients suffering cardiac arrest and hence were unresponsive. They were unlikely to be subject to performance bias.
2.	Were clinicians aware of group allocation?	Yes. Blinding of EMS personnel to the use of BVM or passive ventilation would not be feasible. Additionally, in this study the

<table>
<tr><td></td><td></td><td>method of ventilation was at the discretion of EMS personnel. This could result in the introduction of performance bias.</td></tr>
<tr><td>3.</td><td>Were outcome assessors aware of group allocation?</td><td>Yes. The data was manually extracted by a single data collector to include all treatment information as well as outcomes.</td></tr>
<tr><td>4.</td><td>Was follow-up complete?</td><td>Yes and no. Survival outcomes were available for all 1019 patients included in the study, however of the 99 survivors, only 60 had CPC scores available to assess neurologic outcomes.</td></tr>
<tr><td>II.</td><td>What are the results (answer the questions posed below)?</td><td></td></tr>
<tr><td>1.</td><td>How large was the treatment effect?</td><td>
<table>
<tr><th>Outcomes</th><th>PV</th><th>BVM</th><th>aOR</th></tr>
<tr><td>ROSC</td><td>27% (123/459)</td><td>30% (169/560)</td><td>0.8 (0.7-1.0)</td></tr>
<tr><td>Neuro Intact @ hospital discharge</td><td>10%</td><td>9.5%</td><td>1.2 (0.8-1.9)</td></tr>
<tr><td>Neuro intact Witnessed VF/VT</td><td>38.2% (39/102)</td><td>25.8% (31/120)</td><td>2.5 (1.3-4.6)*</td></tr>
<tr><td>Neuro intact Non-witnessed VF/VT</td><td>7.3%</td><td>13.8%</td><td>0.5 (0.2-1.6)</td></tr>
<tr><td>Neuro intact Non-shockable rhythm</td><td>1.3%</td><td>3.7%</td><td>0.3 (0.1-1.0)</td></tr>
</table>
*We can convert OR to NNT: NNT = 5 to provide one neurologically intact cardiac arrest victim with initial VF/VT rhythm. Alternatively, we can convert the unadjusted ARR to NNT: NNT = 8 (95% CI 4-infinity).
</td></tr>
<tr><td>2.</td><td>How precise was the estimate of the treatment effect?</td><td>See above.</td></tr>
<tr><td>III.</td><td>How can I apply the results to patient care (answer the questions posed below)?</td><td></td></tr>
<tr><td>1.</td><td>Were the study patients similar to my patient?</td><td>Yes. Patients were typically older (mean age 66.6 and 64.8) and male (68.2% and 67.3%) with predominantly non-shockable rhythms (68.9% and 68.2%). This seems similar to cardiac arrest patients seen in our practice. No data was given with respect to past medical history, specifically history of prior cardiac disease, though I would expect this to be similar.</td></tr>
</table>

2.	Were all clinically important outcomes considered?	Yes. The primary outcome was neurologically intact survival, though overall survival and neurologic outcomes were assessed as well. Healthcare cost and hospital length of stay could also be considered, as could quality of life.
3.	Are the likely treatment benefits worth the potential harm and costs?	Uncertain. Overall neurologically intact survival rates appear to be similar between the two approaches, which would suggest no benefit. Subgroup analysis suggests a benefit for passive ventilation in patients with witnessed VF/VT cardiac arrest with an OR of 2.5 (95% CI 1.3-4.6), suggesting the need for further research in this population.

Limitations:

1) **In this non-randomized trial the decision to perform BVM vs. passive ventilation was at paramedic discretion and may have been dictated by factors that would affect the outcome. A randomized trial would limit such selection bias. As noted by the authors, there may have been patient characteristics "that led EMS personnel to select a particular ventilation method."**
2) **Paramedics were allowed to attempt ETI after 3 cycles of compression, but we are not given data regarding ETI attempts or alternate airway use.**
3) **Proper BVM ventilation (8 breaths/minute) was not assessed. Higher rates of ventilation would lead to decreased coronary perfusion and poorer outcomes.**
4) **While the authors used multivariable logistic regression to control for known confounding factors, unknown confounders may still bias the results (such as time to defibrillation, comorbid illnesses, and transport times).**
5) **The study does not address other airway management techniques, such as endotracheal intubation and supraglottic airway insertion, which are utilized by many EMS agencies.**
6) **Neurologic outcome data was not available in 39 of 99 (39%) of patients who survived, limiting the validity of these results.**

Bottom Line:

For the primary outcome, overall adjusted neurologically intact survival was similar between passive ventilation and BVM (OR 1.2; 95% CI 0.8-1.9). Passive ventilation and BVM ventilation also showed similar rates of survival to discharge in patients with unwitnessed VF/VT and non-shockable rhythms. Passive ventilation was superior to BVM ventilation for witnessed VF/VT; while statistically significant, this finding was for a secondary outcome and applicability will be controversial.