Background and Study Objective(s):
Oxygen is a fundamental treatment in any form of acute or chronic respiratory failure. Different tools have been developed to deliver oxygen to patients. High-Flow Nasal Cannula is a newer oxygen delivery system that provides heated/humidified oxygen using large bore nasal cannula that provide FiO2 up to 100% with airflow rates up to 60L/min. Previous studies have shown greater patient comfort compared to CPAP/BiPAP masks.

Research Question: In patients with acute hypoxemic respiratory failure without hypercapnia, does high-flow oxygen therapy decrease intubation rates compared to non-invasive ventilation (BiPAP) or non-rebreather oxygen masks?

Study Design:
23 ICUs in France and Belgium in 2011-2013

Inclusion:
- Adult patients
- RR >25
- PaO2:FiO2 ≤300 mmHg
- PaCO2 ≤ 45 mmHg
- No history of chronic respiratory disease

Exclusion:
- Asthma/COPD exacerbation
- Cardiogenic Pulmonary edema
- Hemodynamic Instability
- Contraindications to Non-invasive PPV (GCS<12)
- Urgent need for intubation
- Patients who are DNR or declined participation

Multi-centre, un-blinded, randomized control trial

3 Treatment arms (N=310)
– High-Flow Oxygen (N=106)
– Standard Oxygen (N=94)
– Noninvasive Ventilation (N=110)

Complete follow-up at 90 days

Intention to treat analysis (Allows cross over)

Randomization at 3 hours after enrolment

Primary Outcome:
• Proportion of patients who required intubation within 28 days after randomization

Secondary Outcomes:
• Mortality at 90 days
• Ventilator-free days (days alive and without invasive mechanical ventilation)
• Comfort
• Complications

Results:
• No difference of baseline characteristics/demographics between the 3 treatment arms
• Majority of enrolled patients had pneumonia (82%)
• 21% of the patients did not have bilateral pulmonary infiltrates (thus not meeting criteria for ARDS)
• No significant difference in severity of hypoxemic respiratory failure (using PaO2:FiO2 ratio) between groups
• Non-significant trend towards decreased intubation rates in HFNC group compared to NRB
• Post-hoc analysis shows significantly decreased intubation rates in patients with PaO2:FiO2 <200 mmHg (P=0.009)
• Significant increase in ventilator-free days in HFNC compared to NRB and Non-invasive ventilation
• Significant decrease in ICU-mortality and 90-day mortality in HFNC group compared to NRB and Non-invasive ventilation (Hazard ratio for death at 90 days for NRB vs HFNC was 2.01, p=0.046, with NNT of 10)
• Higher probability of survival in HFNC group (p=0.02)
• Worse mortality in Non-invasive ventilation group

Validity of Results:
• Poor study design given that 3 treatment arms to the study
• The study investigators pre-selected a population that were mostly severe pneumonia and thus, the validity of using BiPAP as a treatment arm is questionably ethical given previous data that shows that patients with pneumonia have higher mortality/morbidity rates when treated with BiPAP
• Patients were from the HFNC and NRB group were allowed to cross over to BiPAP treatment if they did not respond well -- this could have blurred the differences of effects between groups

Generalizability of Results:
The results of this study should only be applied to patients with hypoxemic respiratory failure due to pneumonia because that is what the large majority of the patients in this study had.

This was an ICU study in France and Belgium -- patients were already admitted to the ICU with hypoxemic respiratory failure and they were excluded if they required urgent intubation (therefore they selected patients who were stable for a long period of time without immediate airway protection). These results may have marginal applicability to the assessment and management of a septic pneumonia or ARDS patient who presents to the ER, because there is a much wider range of stability/instability in the patients at initial evaluation.

The Bottom Line:
HFNC (compared to BiPAP and NRB) leads to decreased mortality rates in a select group of patients with hypoxemia secondary to severe pneumonia