The Respiratory Strategies in COVID-19; CPAP, High-flow, and Standard Care (RECOVERY-RS) trial has demonstrated that treating hospitalized COVID-19 patients who have acute respiratory failure with
continuous positive airway pressure (CPAP) reduces the need for invasive mechanical ventilation.

Preliminary data from the trial also suggests that the routine use of high flow nasal oxygenation (HFNO), which can consume large amounts of oxygen, should be reconsidered as it did not improve outcomes for COVID-19 patients compared with conventional oxygen therapy.

RECOVERY-RS, led by the University of Warwick and Queen's University Belfast, is the world's largest non-invasive respiratory support trial for COVID-19—with over 1200 participants taking part across 48 UK hospitals. The multi-center, adaptive, randomized controlled trial compared the use of CPAP (oxygen and positive pressure delivered via a tightly fitting mask), with HFNO (high pressure oxygen delivered up the nose), against standard care (standard oxygen therapy).

All three interventions are commonly used to treat COVID-19 patients before they are moved onto invasive ventilation in a critical care bed, but it was not known which, if any, resulted in better outcomes.

**Results**

Over 13 months, between April 2020 and May 2021, a total of 1,272 hospitalized COVID-19 patients with acute respiratory failure, aged over the age of 18, were recruited to the study and randomly allocated to receive one of three respiratory support interventions as part of their hospital care.

380 (29.9%) participants received CPAP; 417 (32.8%) participants received HFNO; and 475 (37.3%) received conventional oxygen therapy.

The primary outcomes assessed through the trial were whether the patient went on to require tracheal intubation (invasive mechanical
ventilation) or died within 30-days of beginning treatment through the trial.

In the comparison of CPAP and conventional oxygen therapy, the likelihood of patients going on to require invasive mechanical ventilation or die within 30-days of treatment was significantly lower in those who were treated with CPAP, than those who received standard care. In the CPAP group, 137 of 377 participants (36.3%) either needed mechanical ventilation or died within 30 days, compared with 158 of 356 participants (44.4%) in the conventional oxygen therapy group.

There was no difference in primary outcomes between patients in the HFNO and conventional oxygen therapy groups. In the HFNO group, 184 of 414 participants (44.4%) went on to require mechanical ventilation or die, compared with 166 of 368 participants (45.1%) in the conventional oxygen therapy group.

Based on these results, one person would avoid needing invasive ventilation within intensive care units (ICU) for every 12 people treated with CPAP instead of standard oxygen therapy.

Professor Gavin Perkins, Chief Investigator and Professor in Critical Care Medicine at Warwick Medical School at the University of Warwick said: "The RECOVERY-RS trial showed that CPAP was effective at reducing the need for invasive ventilation, thus reducing pressures on critical care beds. The routine use of high flow nasal oxygenation, which can consume large amounts of oxygen, should be reconsidered as it did not improve outcomes. By giving patients the most effective treatment to begin with, we can help prevent resource shortages in our NHS and make sure the right type of ventilation is available to patients when it is required.

"This is the first large trial of different types of ventilation in
COVID-19. While it is encouraging that these results can help reduce the number of people who require invasive ventilation, it is important to stress that, where it is needed, invasive ventilation can be lifesaving."

Professor Danny McAuley, Chief Investigator and Professor and Consultant in Intensive Care Medicine at the Royal Victoria Hospital and Queen's University Belfast said: "Over the COVID pandemic, we've seen a large number of patients requiring high levels of oxygen and admission to ICU for invasive ventilation, causing a huge strain on staff and beds.

"The results of this trial are really encouraging as they have shown that by using CPAP, invasive ventilation may not be needed for many patients with COVID-19 requiring high oxygen levels. Avoiding invasive ventilation is not only better for the patients, but it also has important resource implications as it frees up ICU capacity. This research should help healthcare professionals in the UK and beyond manage patients with COVID-19, to improve patient outcomes while helping to lessen the burden on resources."

Professor Jonathan Van-Tam, Deputy Chief Medical Officer said: "COVID-19 has placed huge pressure on our hospitals and intensive care units, and our doctors, nurses and all NHS staff have stepped up to meet that challenge. A key part of tackling COVID has been the improvements that staff have identified and then implemented in terms of how to best care for COVID patients.

"This study, funded by the NIHR, provides valuable evidence around how non-invasive respiratory support can be used to improve patient outcomes. Reducing invasive mechanical ventilation is better for patients and reduces pressures on mechanical ventilator capacity across the NHS.

"I want to thank the team of doctors, researchers and patient volunteers involved in today's excellent results—hospitals across the country can
now use these data to further improve care for patients and reduce the demand for mechanical ventilation as we get closer to what might still be a challenging winter period."

Professor Lucy Chappell, Chief Scientific Adviser (CSA) for the DHSC and the National Institute for Health Research (NIHR) Chief Executive Officer, said: "Research such as this has been a huge asset to the COVID-19 response, allowing us to fine-tune our approach and improve care for patients in hospital.

"I am hugely grateful to the teams at the University of Warwick and Queen's University Belfast for their contribution to our understanding of the virus through this NIHR-funded study, and particularly how to treat it.

"This data will help ensure hospitalized patients with COVID-19 get the best possible care, making a difference to patients and intensive care units across the country."

Professor Nick Lemoine, Medical Director at the National Institute for Health Research (NIHR) Clinical Research Network said: "Preliminary results from this NIHR-supported trial provide important evidence which will help shape clinical practice worldwide around respiratory support interventions for hospitalized COVID-19 patients. The study will undoubtedly help improve outcomes for patients—while potentially alleviating pressure on hospital beds and critical care services.

"We sincerely want to thank everybody involved—the patients who took part in their darkest hour, and the NHS doctors and nurses who helped deliver the study right across the UK."

Professor Simon Ball, Executive Medical Officer at University Hospitals Birmingham said: "This is an important study that will significantly
influence treatment decisions. It is an example of how well NHS hospitals can deliver studies to improve clinical practice. This includes the definition of treatments that are beneficial, in this case CPAP, but just as importantly those with no apparent benefit, in this case high flow nasal oxygen. The best possible care we deliver is that focused by evidence."

About RECOVERY-RS

Both CPAP and HFNO have been widely used worldwide in the management of COVID-19 throughout the pandemic for patients who need high levels of additional oxygen. If these treatments are not successful, patients need to be sedated and treated with a ventilator in intensive care. Although both CPAP and HFNO are commonly used in other lung conditions, prior to the RECOVERY-RS study, it was unknown how safe and effective they were for people with breathing difficulties arising from COVID-19.

The trial is led by Joint Chief Investigators Professor Gavin Perkins at the University of Warwick, and Professor Danny McAuley at Queen's University Belfast.

It was funded and supported by the National Institute for Health Research (NIHR) as a prioritized urgent public health COVID-19 study.

RECOVERY-RS was one of the first COVID-19 studies to be classed as urgent public health research by the UK's Chief Medical Officers in order to urgently identify strategies to reduce the need for invasive mechanical ventilation. Launched in April 2020 as COVID-19 hospitalization began to soar, the NIHR Clinical Research Network provided prioritized support to rapidly set the study up at hospital sites across the UK and enroll participants. The NIHR's research infrastructure, expertise and delivery support has been critical to the
trial's success.

Provided by University of Warwick

Citation: CPAP reduces need for invasive ventilation in hospitalized COVID-19 patients (2021, August 5) retrieved 21 December 2022 from https://medicalxpress.com/news/2021-08-cpap-invasive-ventilation-hospitalized-covid-.html

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