**International Guidance for UCL-Ventura**

**Table of Contents**

1. UCL-Ventura core team

2. Summary

3. Clinical rationale for employing CPAP in COVID-19 patients

4. UK response to the use of CPAP in the management of COVID-19

5. UCL-Ventura CPAP system

6. Regulatory approval

7. Infrastructure, safety and training requirements

8. Clinical experiences of using UCL-Ventura CPAPs in the UK

9. Accessing UCL-Ventura designs and manufacturing instructions

10. Appendices A-B

## 1. The UCL-Ventura core team

Mervyn Singer, Professor of Intensive Care Medicine and critical care consultant, University College London Hospitals (UCLH) and UCL

Dave Brealey, critical care consultant, UCLH

Andy Cowell, Managing Director, Mercedes AMG High Performance Powertrains (HPP)

Rebecca Shipley, Professor of Healthcare Engineering and Director of the Institute for Healthcare Engineering, University College London (UCL)

Tim Baker, Professor of Mechanical Engineering Design, UCL

David Lomas, Professor and Vice Provost (Health), UCL

This core team have received a wealth of support and input across UCL Institute of Healthcare Engineering, UCL Mechanical Engineering, UCL Business, Mercedes AMG HPP, and beyond.

## 2. Summary

UCL-Ventura is a breathing aid which has been developed specifically for the management of COVID-19 patients. It has received approval for the UK's Medicines and Healthcare Products Regulatory Agency (MHRA) and 10,000 of the devices have been delivered to the UK Department of Health for use in the NHS, including England, the devolved nations and crown dependencies. The designs and manufacturing instructions have been made available, at zero cost, to not-for-profits, manufacturers, academics and health experts globally.

Monday, 29 May 2020

## 3. Clinical rationale for employing CPAP in COVID-19 patients

The overwhelming reason for patients with COVID-19 requiring hospital admission is respiratory failure, specifically a failure to get sufficient oxygen from the lungs into bloodstream. The more severe cases need more oxygen than a standard facemask can deliver, in which case applying a positive pressure splints the lung bases open and significantly improves oxygenation. This high positive pressure can be applied through an invasive mechanical ventilator (IMV) or, much more easily, through a specialised mask system where the oxygen is delivered under constant pressure (CPAP, continuous positive airways pressure). The downside of IMV is that the patient needs to be heavily sedated to allow a tube to be inserted into their windpipe (trachea) to connect to the ventilator. This requires highly trained staff to look after them in an intensive care unit (ICU) environment with significantly more monitoring, and carries an increased risk of other types of life-threatening complication (e.g. compromise of the heart, kidneys and circulation leading to multi-organ failure, increased incidence of new infection, tube displacement or blockage, long-term lung damage). Because of these issues, in standard UK intensive care practice the nurse-to-ventilated patient ratio is 1:1

CPAP allows the patient to be awake, responsive and cooperative. They obviously still require healthcare worker supervision but considerably less than 1:1. They are far easier to manage, the level of training needed is far lower, and this can be delivered much more readily outside intensive care units. Indeed, CPAP is routinely used in patients with breathing problems in emergency departments, acute admissions units and in respiratory wards, and also at home by patients with sleep apnoea.

The UCL-Ventura team have engaged an extensive network of leading colleagues across China and Italy (including intensivists in the critical care response in Wuhan and the Lombardy Region) to learn from their early experience in treating COVID-19 patients. Their experience clearly indicated that their ICU capacity was quickly overwhelmed when they were intubating and mechanically ventilating patients needing more than facemask oxygen. They subsequently moved to using CPAP as a bridge to IMV and this has been successfully applied in many instances to keep patients off IMV. Direct contact with multiple colleagues in Italy suggest that ~50-60% of patients given CPAP have been kept off IMV, thus enabling this vital and scarce resource to be prioritized to those patients who need it the most.

While data is lacking on outcomes of CPAP versus early intubation and mechanical ventilation, intensivists and respiratory clinicians working closely together in many hospitals in the London area have successfully employed this strategy to decrease the requirement for mechanical ventilation, especially when ventilators and trained staff are in very short supply. While we would not claim CPAP to be a panacea, we are finding that approximately 50% of patients treated with CPAP do not progress to mechanical ventilation, and this is consistent with data from Italy. Clearly, if the patient is moribund, or does not respond to a trial of CPAP in terms of oxygenation, comfort or work of breathing, or is non-compliant with the mask/hood then intubation and mechanical ventilation should be considered, if appropriate.

## 4. UK Response to the use of CPAP in the management of COVID-19

NHS England Guidance was issued on 26 March 2020 based on a consensus document drawn up by 22 UK experts in critical care and respiratory medicine, and with backing from the National Emergency Committee for Critical Care (NECCC) (comprising the Royal College of Anaesthetists,

Faculty of Intensive Care Medicine, Intensive Care Society, Association of Anaesthetists). This guidance states:

- "CPAP is the preferred form of non-invasive ventilatory support in the management of the hypoxaemic COVID-19 patient. Its use does not replace invasive mechanical ventilation (IMV), but early application may provide a bridge to IMV)"
- "Assess the response to CPAP in a monitored environment within 30 to 60 minutes, with regular review as clinically indicated thereafter. Where there is no adequate response, where clinical decline continues, or where the patient tolerance limits its use, early intubation and mechanical ventilation should be sought where appropriate"

National Health Service (NHS) guidance for the role and use of non-invasive respiratory support (including CPAP) in adult patients with COVID-19 is available on the NHS website here.

The UK Department of Health and Social Care ordered 10,000 UCL-Ventura CPAPs for use across the UK National Health Service (including England, devolved nations, crown dependencies and overseas territories). To date, devices have been delivered to over 60 NHS hospitals.

## 5. UCL-Ventura CPAP system

The UCL-Ventura device is a CPAP flow generator. A high-flow jet of oxygen from a piped oxygen supply draws room air in around it to generate a high output flow of oxygen-enriched air. An adjustable mechanical valve is used to set the desired continuous positive pressure to keep the airways open and another valve controls the delivered oxygen mix. It contains no moving parts and no embedded electronics and requires no power supply.

The system has been reverse engineered from the off-patent Respironics WhisperFlow CPAP flow generator which has been used in the NHS (and globally) for decades.

Both the CPAP device and the patient breathing circuit have been configured to minimise oxygen consumption and increase patient comfort, and this design optimization reduced oxygen utilization by up to 70% compared to the original WhisperFlow model. The complete UCL-Ventura package (Figures 1, 2) comprises:

1. UCL-Ventura CPAP
2. Oxygen analyser (to measure the concentration of oxygen in the inhaled air)
3. Nasal mask or helmet
4. Positive End Expiratory Pressure (PEEP) valves
5. Tubing
6. Viral/ bacterial filters

Of these, 1-2 are manufactured through the UCL-Ventura consortium (e.g. 1. is manufactured by Mercedes AMG HPP), whereas 3-6 are currently acquired from medical manufacturers. The specification for the flow generator is provided in Appendix A.

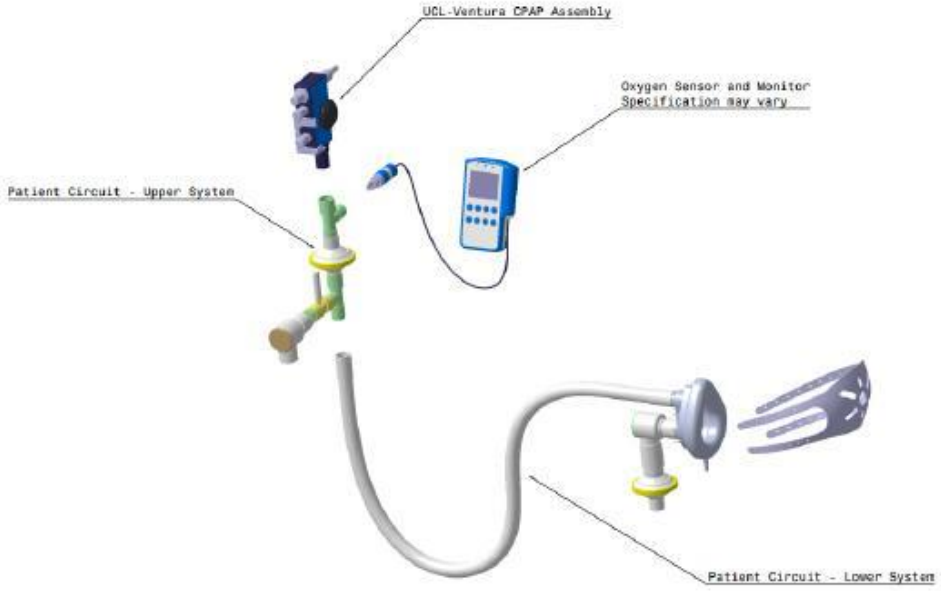


***Figure 1:*** Schematic of complete UCL-Ventura CPAP assembly

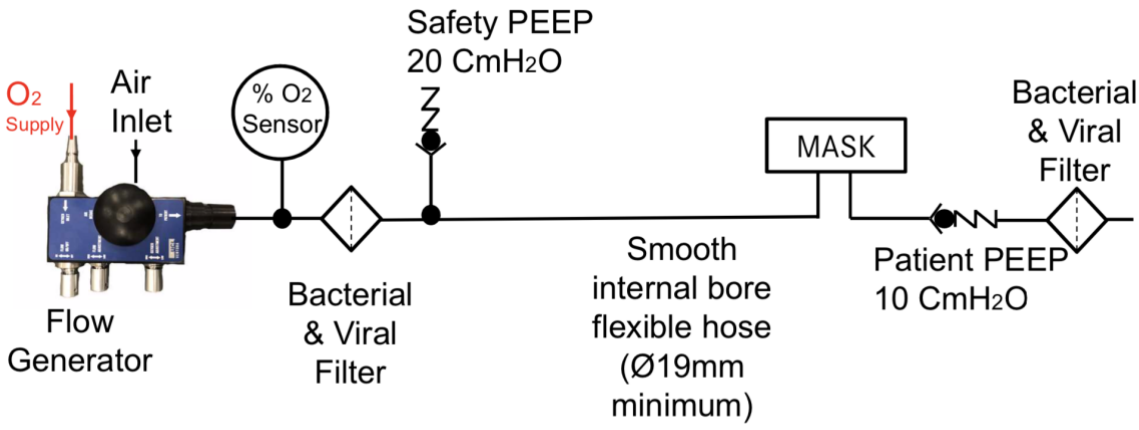


***Figure 2:*** Breakdown of the patient circuit configuration. PEEP values are indicative and a range of options are available.

## 6. Regulatory approval

The UCL-Ventura CPAP system has been approved for manufacture by UCL by UK regulators, the Medicines and Healthcare products Regulatory Agency (MHRA) under special conditions. These conditions state that this is a non-CE marked CPAP, given approval for use in the NHS for the interest of public health protection under the Covid-19 pandemic emergency.

The MHRA covers regulatory approval in the UK only. For use in other countries, local regulator approval will be required.

## 7. Infrastructure, safety and training requirements

National Health Service (NHS) guidance for the role and use of non-invasive respiratory support (including CPAP) in adult patients with COVID-19 is available on the NHS website here.

World Health Organisation (WHO) has issued guidance on the technical specifications for invasive and non-invasive ventilators for COVID-19, available here, as well as a list of priority medical devices for COVID-19 case management, and oxygen sources and distribution for COVID-19 treatment centres.

### 7.1 Oxygen Supply

UCL-Ventura CPAPs require a piped oxygen supply to provide a continuous oxygen supply to the patient. All hospitals must work with their oxygen engineering teams and ascertain their VIE outflow and downstream flows and pressures to specific ward areas before deploying these devices.

In healthy volunteer testing, at normal breathing at 40% oxygen concentration, CPAP 10cm $H_20$ required 13.6 litres of $O_2$/ min, while 60% oxygen used 17.4 litres/ min. Flow rates need to be increased in patients with a higher work of breathing. In volunteers who were maximally hyperventilating for 30-60 seconds, 40% oxygen requirement required 25.4 litres/ min of oxygen flow, and 60% required 46.7 litres/ min. This is significant decrease in oxygen utilization compared to existing stand-alone high-flow CPAP devices.

A summary of UCL-Ventura CPAP healthy volunteer evaluation data is supplied in Appendix B.

The NHS has issued the following patient safety notice regarding the use of high flow oxygen therapy devices (including CPAP).

Link to NHSE/I – 2020/001 Use of high flow Oxygen therapy devices (including wall CPAP and high flow face mask or nasal oxygen) during the Coronavirus epidemic – urgent patient safety notice


NHSEI - 31 March.pdf

### 7.2 Personal Protective Equipment (PPE)

UK guidance on the use of **personal protection equipment** (PPE) is available on the Government website here.

WHO guidance on the use of PPE is available of their website here.

Environmental testing at UCLH returned no evidence of COVID-19 in air samples as close as 1 metre from CPAP patients (unpublished). There has been widespread use of CPAP in many countries (e.g. China, Italy, Spain, France and UK) and severe infection of healthcare workers looking after such patients has not been reported.

COVID-19 Infection. Implications for Perioperative and Critical Care Physicians. Greenland et al, Anesthesiology March 2020. doi.org/10.1097/ALN.0000000000003303

Use of non-invasive ventilation for patients with COVID-19: a cause for concern? Arulkumaran et al. Lancet Respiratory Medicine 2020. doi.org/10.1016/S2213-2600(20)30181-8

### 7.3 Training

The following documents and training materials for the UCL-Ventura CPAPs are available:

(1) Clinical guidance document:

https://www.ucl.ac.uk/healthcare-engineering/sites/healthcare-engineering/files/clinical_guidance_v1.0.pdf

(2) User manual for the CPAP flow generator:

https://www.ucl.ac.uk/healthcare-engineering/sites/healthcare-engineering/files/cpap_manual_v8-4_spread.pdf

(3) Training video:

https://www.ucl.ac.uk/healthcare-engineering/covid-19/ucl-ventura-breathing-aids-covid19-patients/accessing-ucl-ventura-cpap-nhs

We note that these materials require translation, and amendments to factor in local healthcare systems.

### 7.4 Re-supply of breathing circuits

Whereas the flow generator and oxygen sensor are supplied through the UCL-Ventura consortium, the breathing circuits are currently acquired through medical manufacturers. These breathing circuits should be replaced for each patient.

## 8. Clinical experiences of using UCL-Ventura system in the UK

The UCL-Ventura is very similar to the Philips Respironics WhisperFlow, a device with decades of use across the globe. The UCL-Ventura CPAP was evaluated on 21 COVID-19 patients with severe respiratory failure in 2 hospitals and patients closely monitored for up to 60 hours. Results were consistent with other CPAP devices, and improved or maintained oxygen levels compared to conventional oxygen devices. No safety concerns were raised. Local and international data suggests CPAP reduces the need for mechanical ventilation by 50-60%.

Data on the use of CPAPs (including UCL-Venturas) in the UK is currently being compiled for publication.

## 9. Accessing UCL-Ventura Designs and Manufacturing Instructions

Our humanitarian intention is to share the UCL-Ventura designs and manufacturing instructions to help public health efforts during the Covid-19 pandemic emergency.

We will only authorise requests from people representing the following organisations:

- Manufacturers
- Research Institutions
- Healthcare providers
- Non-profit sector

Requests from people applying in a personal capacity will be rejected due to licensing restrictions.

Requests must be made using an organisational email address.

The full release provides:

- Manufacturing drawings
- System schematics and characteristics
- Bill of materials and type of manufacturing machines used for CPAP production
- Development tests information
- Assembly procedures, including build tooling requirements
- Test procedure and pass-off protocol

Any manufacture and use of this CPAP by third parties must require the third party to have local regulatory approval in place, as required in the third party's own country and must fully comply with any stipulated conditions, laws and regulations that ensure full patient safety.

The technical specifications for this CPAP are being shared for humanitarian purposes, to help support the international community addressing pressing demands to care for Covid-19 patients. This is not a business venture. There is an expectation that those using these specifications to manufacture these devices follow the same guiding principles.

The instructions for manufacture should be followed precisely to ensure quality and safety, with no deviations or substitutions.

Requests for a license can be made directly at: https://covid19research.uclb.com/product/ucl-cpap

**9.1 Requests for supply of manufactured devices**

If you do not have access to the manufacturing capabilities to produce devices using the designs and manufacturing instructions, and you have a specific request for devices to be supplied internationally please contact CPAPcovid19@ucl.ac.uk.

**9.2 Technical Support**

If you have a technical query please read these Frequently Accessed Questions (FAQs) first:

https://www.ucl.ac.uk/healthcare-engineering/sites/healthcare-engineering/files/faq_iss03.pdf

Following that please contact ihecovid19response@ucl.ac.uk

**9.3 Local Manufacturing Support**

We have established a facebook group to connect manufacturers in different countries globally:

https://www.facebook.com/groups/177228076956018/requests/

**APPENDIX A UCL-Ventura CPAP Flow Generator Specification**

| | |
|---|---|
| **Device Reference** | GIN7055_02 |
| **Dimensions** | 158x140x48 mm |
| **Mass** | 495 g |
| **Operating Range** | 0 - 40°C (Temperature)<br>0 - 95% RH (Humidity) |
| **Inlet Connection (4 bar oxygen)** | Schrader male probe<br>(BS 5682:2015) |
| **Outlet Connection** | 22mm male taper<br>(BS 5356:2015) |
| **Patient Flowrate (operating range)** | 5 - 60 LPM |
| **Patient Flowrate (peak)** | 120 LPM |
| **Oxygen Fraction, $FiO_2$% (operating range)** | 30 - 80% |
| **Oxygen Fraction, $FiO_2$% (peak)** | 95% |
| **CPAP** | 2.5 - 20 $cmH_2O$ (2.5 - 20 hPa) |
| **Typical Oxygen Consumption** | |
| Calm Breathing, 40% $FiO_2$ | 14 LPM |
| Calm Breathing, 60% $FiO_2$ | 17 LPM |
| Heavy Breathing, 40% $FiO_2$ | 25 LPM |
| Heavy Breathing, 60% $FiO_2$ | 46 LPM |

| **Materials** | |
|---|---|
| **Main Body** | Tecaform AH MT Black<br>(Acetal Polyoxymethylene) |
| **Control Valves and Oxygen Probe** | 316S11 Stainless Steel |
| **O Rings** | FKM (fluorocarbon) rubber |
| **Lubricant** | Fomblin-0T20 |

**APPENDIX B Oxygen utilization based on healthy volunteer assessments**

The following data shows the results of a study conducted on healthy volunteers to assess the oxygen requirements of the UCL-Ventura CPAP system.

(a) Normal breathing at 10 cm H2O CPAP

| Inhaled air $O_2$ (%) | Oxygen flow rate (l/min) |
|---|---|
| 30 | 10.8 |
| 40 | 13.6 |
| 50 | 12.9 |
| 60 | 17.4 |
| 70 | 17.3 |
| 80 | 17.8 |

(b) Normal breathing at 10 cm H2O CPAP versus breathing to mimic a COVID-19 patient breathing deeply at 30 breaths/min

| | Oxygen flow rate (l/min) | |
|---|---|---|
| $O_2$ (%) | Normal breathing | COVID-19 mimicked |
| 60 | 16.6 | 21.4 |
| 90 | 32.2 | 47.0 |

Note that mimicking the respiratory pattern of a COVID patient increased flow rates. Typical oxygen requirements range from 40-60% requiring oxygen flow rates of 10-12 $l.min^{-1}$ which are similar to those required by mechanical ventilation.

(c) Forced maximal hyperventilations over 30-60 seconds at 10 cm H2O CPAP

| $O_2$ (%) | Oxygen flow rate (l/min) |
|---|---|
| 30 | 14.3 |
| 40 | 25.4 |
| 50 | 40.4 |
| 60 | 46.7 |
| 70 | 55.7 |
| 80 | 76.7 |

Note that this corresponds to maximally stressing the system (no patient or healthy volunteer could maintain this level of hyperventilation for longer than 1-2 minutes)