Institution: University College London

Unit of Assessment: 1 - Clinical Medicine

Title of case study: UCL-Ventura CPAP breathing aids for COVID-19 patients: rapid innovation, manufacture and implementation during the 2020 pandemic

Period when the underpinning research was undertaken: 2004 - 2020

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting HEI:**
Mervyn Singer	Professor of Intensive Care Medicine	Apr 1989 – present
David Brealey	Hon Associate Professor of Intensive Care Medicine	Jun 2012 – present
Rebecca Shipley	Professor of Healthcare Engineering and Director of the UCL Institute of Healthcare Engineering	May 2012 - present
David Lomas	Vice Provost Health, Head of UCL Medical School	Jan 2013 - present

Period when the claimed impact occurred: 2020

Is this case study continued from a case study submitted in 2014? No

1. Summary of the impact

In March 2020 UCL critical care clinicians feared British intensive care units would be overwhelmed with COVID-19 admissions, with insufficient staff and resources to cope. UCL intensive care specialists teamed up with UCL engineers and Mercedes-AMG HPP to produce, test and modify a non-invasive ventilatory support device at speed and scale. In under a month, 10,000 “UCL-Ventura” continuous positive airway pressure (CPAP) devices were built and delivered to 125 UK hospitals. UCL’s clinical evidence led directly to new NHS guidelines and development and application of a clinical management pathway algorithm. Design, manufacturing instructions and clinical support were made freely available, enabling supply or manufacture in 20 countries.

2. Underpinning research

Mervyn Singer and David Brealey have a long-established background in device innovation and first-in-patient testing in critical care. For example, an oesophageal Doppler haemodynamic monitor developed by Singer is now in use in 30 countries worldwide and has been shown in multiple perioperative studies to improve clinical outcomes (**R1, R2**). A tissue perfusion monitor also developed by Singer is now in clinical trials run by Brealey and Singer at University College London Hospital (UCLH) in a Wellcome/Department of Health co-funded study (ClinicalTrials.gov ID: NCT03935477).

Singer also studied the care journey of 12,000 patients in 48 UK hospitals to determine the impact of critical care strain on decision-making and clinical outcomes (**R3**). Among other findings, this study determined that a substantial proportion of patients referred to critical care were not offered a bed, and this proportion increased when capacity was limited. Given that prompt critical care was likely to be more beneficial for some referrals than others,

optimising clinical outcomes required that the most at-risk patients were prioritised effectively for Intensive Care Unit (ICU) admission.

In mid-March 2020 admissions of COVID-19 patients to UK ICUs increased rapidly. At the start of UK national lockdown the NHS had only 3,500 ICU beds with access to 7,400 mechanical ventilators, many of which were unsuitable for very sick patients. Very few machines were available for purchase. Crucially, there was a lack of trained staff to manage the unprecedented numbers of patients, yet initial modelling suggested a need for up to 40,000 ventilators. The predicted patient numbers and limited resources available within the UK meant a real danger of care being rationed. To Singer and Brealey, the solution lay in avoiding the need for ICU mechanical ventilation.

Non-invasive respiratory support techniques such as continuous positive airway pressure (CPAP) are well-established as a “halfway house” between an oxygen mask and invasive mechanical ventilation and can be offered outside ICUs. However, fears surrounding risks to healthcare workers from aerosolization of viral particles led to initial NHS management guidelines that advised against use of CPAP.

In early March 2020, Singer sent a questionnaire to intensive care colleagues in Wuhan, China and across Italy to determine their COVID-19 management practices, with a particular focus on the risks and benefits of using CPAP as a less-invasive intervention. He found CPAP was being used widely (5-30% of all admissions), commonly outside ICUs, and the need for invasive mechanical ventilation was avoided in approximately half of patients. No respondent reported an increased risk of infection in their healthcare workers.

These data convinced clinicians at UCLH, supported by the hospital administration, that CPAP should be used with appropriate PPE precautions. A respiratory high dependency unit was established and a training programme instituted to educate inexperienced doctors and nurses in its use. Singer and colleagues developed a patient management pathway algorithm for CPAP use at UCLH.

However, CPAP devices were in short supply across the UK – UCLH only possessed 12 stand-alone devices outside ICU, and none were available for purchase at short notice. In response to the UK government’s ‘Ventilator Challenge’, launched on 16 March 2020, Singer met with UCL engineers (Professors Shipley and Baker) and suggested the focus should be on developing a simple CPAP device at speed and scale, rather than trying to build a more sophisticated ventilator.

The UCL team, comprising Singer, Brealey (UCL Medicine/UCLH), Lomas (Vice-Provost (Health) and Medicine), Shipley and Baker (UCL Engineering), formed a consortium with Mercedes AMG-High Performance Powertrains (HPP), who make engines for Formula-1 racing cars. Singer and Brealey sourced an existing out-of-patent CPAP device (Philips Respironics Whisperflow) that was purely mechanical. Within 100 hours a perfect replica prototype (named ”UCL-Ventura”) was reverse-engineered and successfully self-tested by Singer/Brealey. However, this device requires high oxygen flow rates. At the time, there were significant concerns about hospital oxygen availability, so the engineers set about improving efficiency. Within a week, a modified ‘Mark II’ device was designed, bench tested and then tested by Singer/Brealey on volunteers. With optimisation of the breathing circuits, reductions in oxygen use of up to 70% were achieved (**R4, R5**).

Following the Medicines and Healthcare products Regulatory Agency’s (MHRA) approval for use, testing was successfully performed in COVID-19 patients at UCLH by Singer and Brealey, and several other hospitals including the Royal Surrey, Guildford and Northwick Park Hospital and the Whittington in London, before being rolled out across the NHS.

3. References to the research

R1. McKendry M, McGloin H, Saberi D, Caudwell L, Brady AR, Singer M. Randomised controlled trial assessing the impact of a nurse delivered, flow monitored protocol for optimisation of circulatory status after cardiac surgery. *BMJ* 2004; 329(7460):258. doi: 10.1136/bmj.38156.767118.7C
R2. Parker T, Brealey D, Dyson A, Singer M. Optimising organ perfusion in the high-risk surgical and critical care patient: a narrative review. *British Journal of Anaesthesia*. 2019; 123:170-176. doi: 10.1016/j.bja.2019.03.027
R3. Harris S, Singer M, Sanderson C, Grieve R, Harrison D, Rowan K. Impact on mortality of prompt admission to critical care for deteriorating ward patients: an instrumental variable analysis using critical care bed strain. *Intensive Care Medicine* 2018; 44:606-15 doi: 10.1007/s00134-018-5148-2
R4. UCL Ventura Mark II Healthy Volunteer test data (PDF available on UCL Ventura website: https://www.ucl.ac.uk/healthcare-engineering/sites/healthcare-engineering/files/ucl_ventura_mark_ii_healthy_volunteer_tests_200420.pdf)
R5. Singer M, Shipley R, Baker T, Cowell, A Brealey D. Lomas D (2020) The UCL Ventura CPAP device for COVID-19. *Lancet Respiratory Medicine* 2020; 8:1076-8
doi: 10.1016/S2213-2600(20)30422-7

4. Details of the impact

Rapid delivery of UCL-Ventura CPAP machines and UCL developed oxygen analysers to hospitals in the UK and worldwide

In response to the UK Government Ventilator Challenge, launched on 16 March 2020, the UCL-led consortium of critical care specialists and engineers from UCL and Mercedes AMG-HPP reverse engineered, tested, modified and manufactured the UCL Ventura CPAP device that safely and effectively treated respiratory distress in COVID-19 patients. Authorisation for use in COVID-19 patients was secured from the MHRA within 36 hours of application. The modified, more oxygen-efficient Mark II device was MHRA-approved six days later (2 April). In tandem, the UCL team worked alongside two UK companies (Oxford Optronix and Life Racing) to design, build from scratch, benchmark and clinically test in-line oxygen analysers to monitor the oxygen concentration being delivered to the patient by the CPAP circuit. The Department of Health and Social Care (DHSC) ordered 10,000 devices plus oxygen analysers, which were delivered to the NHS by 15 April, less than a month from inception of the idea.

CPAP (using available devices augmented by the UCL Ventura device) has enabled UK hospitals to “offer life-saving treatments to patients in a timely fashion”, “accommodate patients from local trusts” and “prevented many patients from being exposed to the risks of sedation and mechanical ventilation” (**S1**)**.** The MHRA interim Director of Devices, said in a press release on 31 March 2020: “This achievement is a brilliant example of cross-disciplinary and collaborative teamwork ahead of the anticipated London surge in coronavirus patients” (**S2**).

To support the worldwide healthcare crisis that was unfolding, the UCL team released the design blueprints and manufacturing instructions of the UCL Ventura device at zero-cost to support in-country manufacture. The designs have been downloaded over 1884 times by 105 countries (**S3**). The UCL-Ventura team are working with in-country teams to support local manufacture through technical and manufacturing support, local supply chains, regulatory support, and have provided clinical guidance through the dedicated UCL website, including educational videos, instructions for use and by email and webinars with local clinicians. Approximately 30 groups are now manufacturing devices in countries including Peru, Pakistan, the Philippines, Ukraine and South Africa (**S4**). Charities, companies and governments have also purchased devices at cost for use in Uganda, Palestine, Tajikistan and South Africa.

In August 2020, the UCL-Ventura team (including Brealey, Lomas, Shipley and Singer) won a Royal Academy of Engineering award for exceptional services during a pandemic, and in recognition of the team's impact. Lord Agnew, Minister of State said: "The UCL-Ventura team has been a remarkable collaboration of medicine, science and industry brought together through engineering innovation at pace with few examples in modern British Life. The availability of these devices has helped frame the debate for less invasive oxygen treatment, a result from which everyone benefits - the patient who is in hospital for a shorter period of time, and the hospital as it puts less strain on their infrastructure" (**S5**).

Changing the patient care pathway for patients with severe COVID-19 symptoms
Initial NHS guidelines in early March 2020 did not recommend use of CPAP for COVID-19 patients due to a theoretical increased risk of virus transmission to healthcare staff. However, Singer's data from China and Italy showing healthcare worker safety and clinical effectiveness, convinced UCLH clinicians and UCL administration that a CPAP care pathway commencing in the Emergency Department, should be instituted from the beginning of the pandemic. A respiratory unit outside the ICU was quickly established to provide CPAP support in a supervised environment. A care pathway algorithm was developed in collaboration with UCL Health Creatives and made freely available as the mobile App *UCLH COVID 19 Clinical Guidance for use in clinical settings* (downloaded 3,700 times) (**S6**), This assessed the clinical response to CPAP in patients not improving with standard oxygen therapy and, depending on the response, the patient could be assigned to an Amber pathway and maintained on CPAP, or to a Red pathway where they would undergo mechanical ventilation. Patients were monitored closely thereafter for consideration of invasive ventilation, if failing.

Singer also presented his data from China and Italy to the Department of Health, NHS England and NHS Scotland. In combination with initial clinical experience of CPAP gained at UCLH and other London hospitals, and with input from Singer and other intensive care and respiratory clinicians, NHS England changed guidance on 25 March 2020 stating: "CPAP is the preferred form of non-invasive ventilatory support in the management of the hypoxaemic COVID-19 patient" (**S7**).

The model of care, pioneered at UCLH, with establishment of respiratory units offering non-invasive respiratory support, has been copied by many hospitals around the UK (**S8**). Clinicians who adopted the pathway early in the pandemic said: "We adopted the use of the UCL-Ventura into our routine clinical treatment alongside our established cohort of CPAP machines. They were embraced by staff as they were simple and effective to use... Moreover, the UCL-Ventura was well tolerated by patients. All the patients treated with the Ventura survived to leave hospital. Without this equipment we could have not delivered this life saving therapy to many of our patients" (**S1**).

Another specialist said: "I have looked through our clinical data and can confidently say that for patients with Covid19 they (Ventura CPAP) helped reduce rates of invasive mechanical ventilation by over 50%. This had a huge positive impact upon our staffing and resource utilisation in critical care, and I believe led to improved patient survival too (by reduction in secondary harm caused by mechanical ventilation and associated organ dysfunction)" (**S1**).

Published reports from individual UK hospitals show an average 50% avoidance of mechanical ventilation in patients for full escalation of therapy. In such patients, hospital survival rates of more than 90% are reported in those managing on CPAP alone, with overall survival rates of ~75% when patients who failed CPAP and progressed to ventilation are included (**S9).** CPAP has also been used to support patients not deemed suitable for escalation to mechanical ventilation because of their underlying comorbidities and/or frailty; published reports from UK hospitals show survival rates of 25-30% in these very frail patients (**S10**).

National increase in the use of CPAP as an alternative treatment pathway

The Intensive Care National Audit and Research Centre (ICNARC) provides weekly reports on all COVID-19 patients admitted to critical care across England, Wales and Northern Ireland. The 12 Feb 2021 report (**S11**) compares demographics, organ support and outcomes in patients admitted in the first wave (10,927 admissions between 1 Feb – 31 Aug 2020) and second wave (21,859 admissions from 1 Sept onwards) of the pandemic. The data show that for patients in the second wave, "despite a higher degree of illness severity", only 49.9% received advanced respiratory support. Duration of stay for survivors reduced from 12 days to a median of 6 days, reflecting the faster turnover of patients who avoid invasive ventilation. As 17% of patients were still receiving critical care at the time of this report, survival rates cannot be compared at present.

The ICNARC group also reported changes in management during the first wave (**S12**), identifying a fall in use of invasive ventilation from 85% in the pre-peak phase to 61.1% in the post-peak phase. Over the same period 28-day hospital mortality improved from 43.6% to 33.6% whereas ICU stay for survivors fell from a median 16.5 to 14.1 days.

5. Sources to corroborate the impact

S1 Letters of support from clinicians using Ventura CPAP
S2 https://www.gov.uk/government/news/mhra-approves-new-life-saving-breathing-aid-to-help-keep-coronavirus-covid-19-patients-out-of-intensive-care
S3 https://my.visme.co/view/z4jmqez1-cpap-approval-orders-4-june
S4 Evertiq (Philippines) https://evertiq.com/news/48634 ; emails showing CPAP uptake internationally
S5 Lord Agnew Kt, DL, House of Lords, quoted in UCL press release on RSE award: https://www.ucl.ac.uk/healthcare-engineering/news/2020/aug/ucl-ventura-team-wins-prestigious-engineering-award
S6 Mobile App - *UCLH COVID 19 Clinical Guidance for use in clinical settings* Freely available from Apple, Google Store etc (downloaded 3700 times)
S7 London NIV respiratory support guidelines 25 March updates;
NHS guldelines Guidance for the role and use of non-invasive respiratory support in adult patients with coronavirus (confirmed or suspected) Nov 2020
https://www.nice.org.uk/Media/Default/About/COVID-19/Specialty-guides/specialty-guide-NIV-respiratory-support-and-coronavirus.pdf Earlier version published 6 April 2020 (PDF)
S8 Dushianthan A, Cumpstey A, Ferrari M, et al. Intensive care physicians' perceptions of the diagnosis & management of patients with acute hypoxic respiratory failure associated with COVID-19: A UK based survey. Journal of the Intensive Care Society. March 2021. doi: 10.1177/17511437211002352
S9 Ashish A, Unsworth A, Martindale J, et al. CPAP management of COVID-19 respiratory failure: a first quantitative analysis from an inpatient service evaluation. *BMJ Open Respiratory Research*. 2020; 7(1):e000692. doi: 10.1136/bmjresp-2020-000692
S10 Burns GP, Lane ND, Tedd HM, Deutsch E, Douglas F, West SD, Macfarlane JG, Wiscombe S, Funston W. Improved survival following ward-based non-invasive pressure support for severe hypoxia in a cohort of frail patients with COVID-19: retrospective analysis from a UK teaching hospital. *BMJ Open Respiratory Research* 2020; 7:e000621. doi:10.1136/ bmjresp-2020-000621
S11 ICNARC report on COVID-19 in critical care: England Wales and Northern Ireland 12 Feb 2021. https://www.icnarc.org/Our-Audit/Audits/Cmp/Reports
S12 Doidge JC, Gould DW, Ferrando-Vivas P, Mouncey PR, Thomas K, Shankar-Hari M, Harrison DA, Rowan KM. Trends in Intensive Care for Patients with COVID-19 in England, Wales and Northern Ireland. *American Journal of Respiratory Critical Care Medicine* 2021; 203:565-574. doi: 10.1164/rccm.202008-3212OC