Institution: University College London

Unit of Assessment: 12- Engineering

Title of case study: UCL-Ventura CPAP breathing aids for COVID19 patients: using engineering practice to solve healthcare challenges

Period when the underpinning research was undertaken: 2000-2020

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:**
Rebecca Shipley	Professor of Healthcare Engineering and Director of the UCL Institute of Healthcare Engineering	May 2012-date
Tim Baker	Professor (Teaching) of Mechanical Engineering Design	November 2013-date

Period when the claimed impact occurred: 2020

Is this case study continued from a case study submitted in 2014? N

1. Summary of the impact

In March 2020 the UCL-Ventura team designed a simple, cost-effective and reusable breathing aid for COVID-19 patients which received MHRA (regulatory) approvals in just 10 days. The UK Government ordered 10,000 devices, manufactured within one month, with 125 NHS hospitals supplied to-date across England, the devolved nations and crown dependencies. The UCL-Ventura blueprints were released at no cost and downloaded by over 1,900 teams from 105 countries by December 2020. As a result, more than 20 countries (including India, Mexico, Pakistan, Peru, Paraguay and South Africa) have successfully manufactured large numbers of the devices locally and deployed the UCL device to hospitals. By December 2020, the Ventura team had been featured in over 2,000 global news articles including BBC World, Sky News and Aljazeera. As engineering co-lead, Professor Tim Baker's effort during the pandemic has been recognised in 2020's new Honours list, and he has been awarded an MBE for services to healthcare in the UK and abroad.

2. Underpinning research

Professor Shipley has worked extensively in combining computational modelling with bench and lab-based experimental studies to inform device design in medicine and healthcare. This has included developing mathematical and computational models to define design parameters and operating criteria for medical devices. For example, she has developed computational simulations of fluid and oxygen transport in tissue engineering bioreactors, alongside benchtop testing of flows, pressures to calibrate the models. Professor Shipley has also developed optimization methods that use these data to calibrate the models, and thus accurately define design requirements and operating parameters that optimise bioreactor outputs (**R1, R2**). These integrated frameworks of computational modelling and experimentation have been extended to a range of healthcare devices, for example the optimisation of spraying parameters to deliver therapeutic cells to the retina in ophthalmology (**R3**). This includes collaboration with Professor Tim Baker (UCL-Ventura Engineering co-lead), bringing together his extensive track record in engineering design from the motorsports industry, with Professor Shipley's expertise in healthcare and simulation, to work together on medical device design (**R3**). These established capabilities in simulation, bench characterisation and engineering design were pivotal to the success and rapid delivery of the UCL-Ventura device.

The first SARS-CoV-2 (COVID-19) cases were detected in the UK on the 31 January 2020, and by March admissions to intensive care units (ICU) across the country began to increase

rapidly. The UCL-Ventura team (spanning UCL engineers and University College London Hospital (UCLH) intensive care specialists) first met to discuss their response to the COVID-19 pandemic on 17 March 2020 and, having formed a consortium with industry partners (Mercedes High Performance Powertrains, Oxford Optronix), delivered 10,000 non-invasive breathing aids for treating COVID-19 patients by 15 April 2020 (**R4**). The UCL-Ventura is a continuous positive airways pressure (CPAP) device, providing non-invasive respiratory support for treating COVID-19 patients with advanced respiratory failure. It is purely mechanical, making it simple to rapidly manufacture and train healthcare workers to use – these were both essential criteria for both delivery and NHS update within the tight timescale of the first wave of COVID-19 in March 2020.

The UCL-Ventura team were highly cognisant of the rapid timescales pressures of the first COVID-19 wave - they needed to design a medical device, submit and receive medical approvals from the Medicines and Healthcare products Regulatory Agency (MHRA), mass manufacture and deploy to the NHS in weeks. The team started by reverse-engineering an off-patent, previously CE-marked device (the Phillips WhisperFlow), given its established clinical safety and efficacy base, and the potential for quick regulatory approvals. The NHS were anticipating unprecedented demand on hospital oxygen systems to provide oxygen therapy to a large volume of patients. In response and building on Professors Shipley and Baker's expertise in engineering design and computational modelling, the UCL-Ventura team redesigned specific features of the flow generator, such as the air-entrainment port, to minimise oxygen utilisation, forming the Mark II device. Concurrently, they optimised the breathing circuit configuration for single use (tubing, valves, filters, masks), which connect the CPAP to the patient, to minimise circuit resistance, improve patient comfort and minimise oxygen wastage.

The redesign of the Ventura flow generator and breathing circuit configuration was underpinned by a platform of computational fluid dynamics (CFD) modelling and bench testing, adapted from Professor Shipley's publications (**R1-R3**) and building on the existing research portfolio that Professors Shipley and Baker have developed over the last decade. For example, CFD simulations were used to map the flow and profile pressure profiles throughout the UCL-Ventura and connected breathing circuits, and computational experiments were performed to explore the impact on oxygen utilisation of varying features of the air-entrainment port and breathing circuit configuration. Concurrently, a bench-top simulator was setup to mimic patient breathing, and to measure the pressures and flows at different locations in the circuits. Design changes implemented in the Mark II device were defined by a combination of these approaches and went forward to mass manufacture.

Ultimately, the team designed and received UK-regulatory approval for the reusable UCL-Ventura CPAP in 10 days, manufactured 10,000 devices within one month, supplied 125 NHS hospitals, and released the designs for international uptake with at least 25,000 devices manufactured by other global teams to-date (**R4**).

3. References to the research

R1. **Shipley RJ**, Jones GW, Dyson RJ, Sengers BG, Bailey CL, Catt CJ, Please CP, Malda J. (2009) Criteria for a Printed Tissue Engineering Construct: A Mathematical Homogenization Approach. *J Theoretical Biol*. Aug; 259(3):489-502. doi:10.1016/j.jtbi.2009.03.037.

R2. **Shipley RJ**, Davidson AJ, Chan K, Chaudhuri JB, Waters SL, Ellis MJ. A (2011) Strategy to Determine Operating Parameters in Tissue Engineering Hollow Fiber Bioreactors. *Biotechnology and Bioengineering.* 108(6):1450-1461. doi.org/10.1002/bit.23062.

R3. Nweze M, **Baker T**, Limb GA, **Shipley RJ**. (2020) Insights into the Design of Spray Systems for Cell Therapies for Retinal Disease using Computational Modelling. *Mat Biosci Eng* 17(3):2741-2759. doi:10.3934/mbe.2020150.

R4. Singer M, **Shipley R**, **Baker T**, Cowell A, Brealey D, Lomas D. (2020) The UCL Ventura CPAP Device for COVID-19. *Lancet Respiratory Medicine* 8(11) P1076-1078, doi: 10.1016/S2213-2600(20)30422-7.

4. Details of the impact

In a "*remarkable collaboration of medicine*" (Lord Agnew (**S1**)), the UCL-Ventura team brought together engineers at UCL and Mercedes AMG High Performance Powertrains (HPP) with critical care consultants at UCLH – one of the largest UK teaching hospitals. Against the national backdrop of the UK Ventilator Challenge and predicted need for up to 30,000 mechanical ventilators, the UCL engineers and UCLH critical care specialists, recognised that CPAP devices that are well-established as a "halfway house" between an oxygen mask and invasive mechanical ventilation and can be offered outside ICUs could help, but there was an acute national shortage of CPAP devices available.

Based on the experiences of China and Italy, CPAP had the potential to alleviate around 50% of patients from progressing to mechanical ventilation, improving patient outcomes as well as enabling vital critical care resource to be reserved for those patients who needed it the most. Computational modelling and engineering design were pivotal components to the innovation pipeline, in turn enabling national and international collaborations with engineering companies, international governments and not-for-profit organisations, to address global healthcare needs.

The UCL-Ventura team first met on 17 March 2020. Within 100 hours, they had designed and manufactured the first reusable UCL-Ventura prototypes and began testing them on the wards at UCLH. Within 10 days (27 March), the Mark I UCL-Ventura received regulatory approvals for use as part of the emergency COVID-19 response from the MHRA, with the Mark II device following days later. By 15 April 2020, Mercedes HPP had manufactured 10,000 devices, with 125 NHS hospitals supplied by December 2020. On 5 April, the blueprints of the UCL-Ventura were released at zero cost, downloaded over 1900 times across 105 countries, with extensive manufacture and hospital deployment by around 20 teams internationally by December 2020.

From computational modelling to regulatory approvals and mass-manufacture

Professors Shipley and Baker's expertise in computational modelling, bench testing, engineering design and medical devices (**R1-R3**) was pivotal in the rapid design and deployment of the UCL-Ventura. This expertise enabled the reverse-engineering of the Philips WhisperFlow, with prototypes ready for testing at UCLH within 100 hours. Simulation work on the flow profiles generated in the flow generator and accompanying breathing circuits were essential for their redesign to form the Mark II UCL-Ventura device, approved by the MHRA within 13 days of the first meeting. This simulation and design work enabled a 70% reduction in oxygen utilisation, essential for deployment in the NHS at a time of unprecedented demand on hospital oxygen supplies (**S2**). Ultimately, five MHRA approvals were obtained (Mark I and Mark II CPAP, 2 oxygen analysers, 1 CPAP hood), all progressing to mass manufacture and distribution to NHS hospitals. The manufacturing excellence provided through Mercedes AMG HPP was pivotal; machines that would normally produce F1 components were used for manufacturing reusable CPAP devices to meet the global demand for the device.

Supporting the National Health Service through industrial partnerships

In April 2020, the Department of Health and Social Care ordered 10,000 CPAP devices (**S3**), completed within "*15 days from the confirmation of order*" (Managing Director of Motorsports, Formula 1) (**S3**), with UCL leading on the [TEXT REMOVED FOR PUBLICATION]. Production was conducted at the Brixworth Formula 1 Northamptonshire factory at a maximum rate of up 1,000 devices a day (**S4**). Partnering with automotive logistics company G-TEM, CPAP kits were distributed across more than 125 NHS hospitals in England, the devolved nations, crown dependencies and overseas territories. The General Secretary of the European Society of

Intensive Care Medicine highlights that CPAPs enabled large UK hospitals to offer "*life-saving treatments to patients in a timely fashion…take critically ill patients from local trusts*", and "*prevented many patients from being exposed to the risks of sedation and mechanical ventilation"* (**S2**).

Not only has the UCL team enabled "*rapid mass production.. to be distributed speedily*' across many UK hospitals (Chief Executive at UCLH), but also '*the device has been a game changer in the management of a very large number of COVID-19 patients with respiratory insufficiency…in the United Kingdom*" (**S2**). During the second wave response for Covid-19, 60 devices were provided to both University Hospital Lewisham and Queen Elizabeth Hospital Woolwich. According to the Consultant in Intensive Care Medicine at University Hospital Lewisham, "*within 2 or 3 minutes of consumables being assembled*', patients could benefit from the UCL innovation and there were "*no reported patient clinical incidents during the time these devices were used"* (**S2**). The availability of the UCL-Ventura CPAPs contributed to "*reduction in secondary harm caused by mechanical ventilation and associated organ dysfunction*' by reducing rate of invasive mechanical ventilation by over 50%" (**S2**).

There has been a marked shift in clinical practice across the UK since the beginning of the pandemic with far greater use of CPAP as hospitals recognised this was both an effective strategy and, crucially, spared stretched intensive care resources for the most critically ill. From March to June 2020, use of mechanical ventilation fell by 26% for equally sick patients, intensive care stay has halved for survivors, and mortality fallen by a quarter (**S5**).

International collaborations to improve healthcare systems and patients' outcomes

By mid-April 2020, to contribute to the global humanitarian effort, the consortium released blueprints of the full design and manufacturing instructions at zero-cost to support in-country manufacture. As of December 2020, these designs have been requested over 3440 times and access has been given to over 1900 teams from 105 countries around the world (**S6**). Over 20 countries (including India, Mexico, Pakistan, Peru, Paraguay and South Africa) have succeeded in extensive local manufacture and hospital deployment of the UCL device.

Professor Shipley and the team worked with in-country teams, particularly through the Department of International Trade and Foreign, Commonwealth and Development Office to provide support to local teams spanning technical and manufacture, supply chains, regulation (working with the MHRA), and clinical guidance. By the end of December 2020, over 400 devices were manufactured in Peru, in use in more than 40 hospitals across the country, with the demand for invasive ventilators decreasing by around 50% (**S7**). Locally manufactured devices are also helping patients in countries including India, South Africa, Colombia and Mexico. Some of the 500 devices manufactured in Pakistan have been donated to neighbouring countries – including 50 to Tajikistan – as part of a humanitarian effort (**S7**). Two leading Australian automotive firms, Walkinshaw Automotive Group and Premcar partnered together to assist Australian healthcare system by manufacturing UCL CPAPs to local hospitals (**S7**). Mercedes-Benz South Africa have donated 500 UCL-Ventura devices to 90 government hospitals in the Eastern Cape province (**S7**).

Following extensive engagements with government departments, Professor Shipley and her team partnered with the International Medical Education Trust (IMET2000) to deliver CPAPs for use in Palestine (5 hospitals) and Uganda (2 hospitals) (**S7**). Working on a non-profit basis, the UCL team has fundraised to cover basic manufacturing and supply costs of the CPAP kits for those most in need globally, for example raising over GBP25,000 to send more UCL-Venturas to Palestine.

Professor Shipley and the team continue to assist with knowledge transfer by providing technical and manufacturing support to in-country teams, particularly on the mechanics and engineering design of the UCL-Ventura CPAPs, and their operation in diverse clinical settings. The UCL team have delivered extensive knowledge transfer activities, for example clinical

training programmes (to over 600 doctors and nurses in Palestine, through IMET2000 and Medical Aid for the Palestinians) (**S7**), translated learning videos, online webinars and Q&A advice. Such activities have helped health workers to understand the engineering concept and functionality of such a "*simple, yet complex medical tool*" (health worker at Hugo Chavez Hospital, Palestine) (**S8**). YouTube videos on the operation of the UCL-Ventura alone have received over 58,000 views (**S9**). The UCL team has received widespread global coverage through the likes of BBC News, Times, Al Jazeera, Sky Sports, La Vanguardia (Spain) (**S4**).

In recognition of the efforts, the team received the Royal Academy of Engineering's President's Special Award for Pandemic Services and engineering co-lead Professor Tim Baker was awarded an MBE for services to healthcare in the UK and abroad. The team is working with policymakers to maximise the learnings from the project and was featured in the government's report on The 4th Industrial Revolution Response to COVID-19, which commends the relationship between UCL Mechanical Engineering and Mercedes AMG HPP for providing "*unprecedented manufacturing capability, whilst maintaining high precision and an ability to respond at pace*" (**S10**).

5. Sources to corroborate the impact

S1. Lord Agnew Kt, DL, House of Lords
S2. NHS Senior Leads CPAP & UCL team Letter of performance (General Secretary European Society of Intensive Care Medicine; Chief Executive and Professor of Medicine UCLH; Consultant in Intensive Care Medicine, University Hospital Lewisham)
S3. Managing Director of Motorsports at Formula 1
S4. UCL CPAPs Selected News Feature
S5. ICNARC COVID report
S6. Map of approved CPAP orders by country
S7. CPAPs in:
South America- Peru
Africa- South Africa ;Uganda
Asia and Middle East- Palestine, Pakistan
S8. Walkinshaw Automotive Group and Premcar assist with Covid-19 treatment
S9. YouTube Channels showing total number of views for videos related to UCL CPAPs
S10. The Fourth Industrial Revolution Response to COVID-19