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# Non-invasive positive pressure ventilation mask to minimize mask leak and potential aerosolization leading to spread of virus such as COVID-19

## Research Protocol

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### BACKGROUND AND SIGNIFICANCE

Patients presenting to emergency departments and hospitals for various medical conditions often require non-invasive ventilation (breathing support). For example, a person with shortness of breath as a complication of COPD (chronic obstructive pulmonary disease) may be treated with a BiPAP machine, one type of non-invasive ventilation.

However, in the current environment of COVID-19, aerosols produced by a BiPAP machine in a COVID-19 positive patient pose serious potential harms to healthcare providers and other patients. All patients with similar symptoms to COVID-19 are presently treated as positive until definitive testing determines otherwise. The best test available for COVID-19 takes up to 4 hours to determine the patient's status, which is too long to delay application of BiPAP in a distressed patient. This could lead to either a delay in care or the need for invasive breathing measures (intubation), which requires intense resource utilization, may not be in line with a patient's goals of care, and could cause serious harms (i.e. infection, medication reactions, etc.) in patients who do not need it.

As well, the lack of BiPAP as an option in the clinician's arsenal leads to increased ventilator days that would previously have been bridged with a BiPAP machine. The use of a closed-loop BiPAP machine in which no expired air is released into the environment would solve these problems. Building off the experiences of a similar approach that was trialed in Italy in response to the COVID-19 crisis, this project will develop and test a novel BiPAP mask that reduces mask leaks and thus aerosolization.

Few studies have been done on the potential harm caused by aerosolization from non-invasive ventilation[1]. The data available suggest that caution must be taken with acute respiratory infection (ARI) patients when placing them on non-invasive ventilation such as CPAP or BiPAP due to excess risk to health care workers[1–4]. This advice is being heterogeneously applied during the recent COVID-19 pandemic, with some practitioners advocating the use of non-invasive ventilation[5].

There is a role for non-invasive ventilation in COVID-19 negative patients during the pandemic, although practitioners are reluctant to initiate these measures because of the slow speed, lack of reliability and

lack of availability of the viral swab confirming corona virus status. This study seeks to ensure that an easy-to-produce, specifically engineered mask and circuit has the ability to maintain non-invasive ventilatory support without aerosolizing viral particles. If successful, this will return an important tool to the clinician's arsenal.

Dr. Tarek Loubani has a history of success in the development and validation of high-quality, low cost medical devices that are manufactured and made publicly available through the Glia Project, a non-profit organization solely owned by Dr. Loubani. He has received several notable awards for his work including the Shuttleworth Foundation and Bassel Khartabil Fellowships.

Dr. Tarek Loubani has worked with the Division of Emergency Medicine, London Health Sciences, Inštitut za Razvoj Naprednih Aplikativnih Sistemov (IRNAS), Glia and others to bring to market the 3D printed Glia stethoscope, tourniquet and otoscope. Additionally, there are ongoing trials to validate and calibrate a 3D printed pulse-oximeter and electrocardiograms.

The need for a reduced-aerosolizing non-invasive ventilation mask was made apparent with the current pandemic. Dr. Loubani and a team of physicians spanning relevant specialties (emergency, anesthesia, internal medicine and critical care) across several hospital regions in Ontario (London, Toronto, Kingston) provide insight into device design. This work is a collaboration between the Division of Emergency Medicine, London Health Sciences (LHSC), Glia, Toronto General Hospital Advanced Perioperative Imaging Lab (TGH-APIL), University Health Network (UHN), McKenzie Health, and General Dynamics Land Systems (GDLS).

The Division of Emergency Medicine provides research support to this study. LHSC provides support in execution of this study. Glia provides logistical, Health Canada, open source development and 3D printing support. TGH-APIL provides device development and research support. McKenzie Health provides device development and research support. GDLS provides initial prototype design and laboratory testing to demonstrate the fit of the mask with reduced air leaks, adequate air flow, and ease of connection to ventilators.

Proof of this concept has occurred in the laboratory and clinical validation is being pursued.

## STUDY OBJECTIVE(S); INCLUDING SPECIFIC AIMS AND/OR HYPOTHESES

To validate that an easy-to-produce, specifically-engineered mask and circuit has the ability to maintain non-invasive ventilatory support while reducing aerosolization of viral particles

The primary objective of this study is to assess if the mask device leaks when attached to a patient's face in real-world use.

This outcome will be measured in two ways:

1. Through continuous recording of data from the ventilator (approximately every 3-10 seconds) of leak volume (L/min). This measurement is a normal output of modern ventilators.

2. Through interval checks of the seal by a respiratory therapist (RT), registered nurse (RN), or the most responsible physician (MRP).

The patient will be in a monitored care setting (as per standard of care for non-invasive ventilation) and will be monitored by a RN, RT, and the MRP in collaboration with the study team.

Monitoring will not deviate from the standard of care, as seal checks are routinely conducted and leak volumes are routinely displayed. The only change is that the data each machine collects will not be deleted, but will be exported for use in this study.

Participants will be enrolled in the study for up to 24 hours of their BiPAP treatment after entering the study.

The secondary objective of the study is to assess markers of ventilation and perfusion in patients, including pH, pCO2, pO2, respiratory rate, heart rate and level of consciousness (via GCS).

These markers will be measured through routine vital signs monitoring (respiratory rate, heart rate and GCS) and an arterial or venous blood gas (pH, pCO2, pO2).

## METHODS

### Study Design

This study is an opportunistic prospective randomized controlled trial.

If experimental non-invasive ventilation masks are available in the patient's expected size, patients will be randomized to control masks or experimental. If experimental masks are not available, the patient will be consented and entered into the control arm. Patients who receive BiPAP or CPAP with the mask are assessed for several variables over time to ensure adequate treatment and assess leaks.

### Study Population

The study population will include patients in the Emergency Department or an in-patient in a monitored or ICU setting requiring non-invasive ventilation for respiratory distress or hypercapnia at both London Health Sciences Centre. This population will include both the Victoria Hospital site and University Hospital site. The local sample size is n=50.

### Inclusion Criteria:

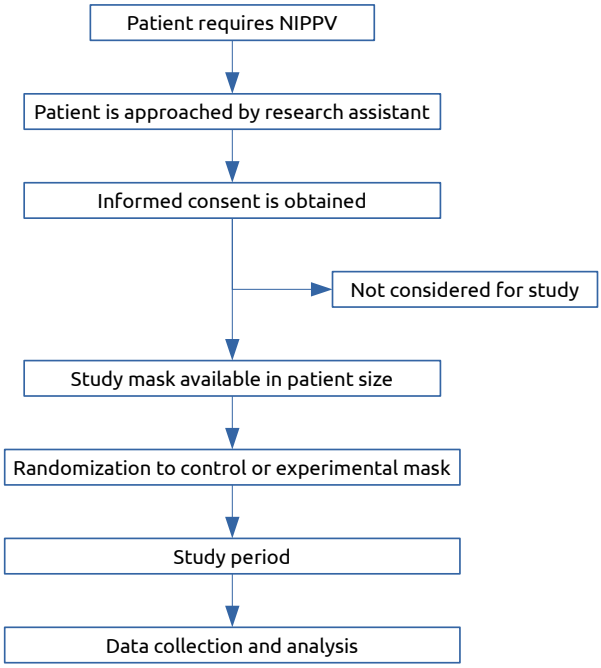
- Patient with respiratory failure due to primary pulmonary pathology.
- Patient who is selected for BiPAP or CPAP by the health care provider

### Exclusion Criteria:

- Age <18 years.

- Respiratory failure due to non-pulmonary pathology.
- Impaired consciousness (Glasgow coma scale <10).
- Patients with contraindications of NIV.
- Severe upper gastrointestinal bleeding.
- Chest trauma.
- Agitated or violent patient.

## Study Procedures




A patient may be enrolled in this study if they require BiPAP in the following circumstances:

1) Immediately on arrival to the emergency department

If a patient arrives to the emergency department through the waiting room or via ambulance, an emergency department MD will assess the patient to determine the most appropriate care. If non-invasive ventilation is the most appropriate course of action for this patient and they are unable to provide consent due to their current respiratory status, the SDM may provide consent or consent will be delayed until the SDM is available or the patient is able. There will be no delay in care in order to obtain consent.

The patient will be immediately taken to the designated negative pressure care area. The assigned registered nurse (RN), medical doctor {MD), and respiratory therapist (RT) will doff enhanced PPE and the patient will be hooked up to BiPAP using the MAIN Covid Mask.

The patient will be monitored closely by the assigned RN, RT, and MD. The health care team will immediately ensure that the patient is tolerating the mask and that their respiratory status is improving. This can immediately be observed by the patient's oxygen saturation level (Sp02) and respiratory rate. This patient would be hooked up to a cardiac monitor with continuous oxygen monitoring to ensure continued efficacy and no decline of the patient's condition.

If the patient decompensates or the device is proving to have significant air leaks, the patient will be switched to the appropriate support (e.g. intubation) based on the judgement of the most responsible physician (MRP).

2) At any time throughout their visit in the emergency department

If a patient arrives to the emergency department through the waiting room or via ambulance and the patient does not immediately require ventilatory support, the patient will be triaged and assessed according to their condition. If the patient has respiratory complaints, the physician will discuss the patient's goals of care. If noninvasive ventilation is part of the goals of care and appears imminent, consent for the study treatment will be obtained for future use if the patient condition worsens, indicating the need for non-invasive ventilation.

3) At any time during their hospital admission

When a patient is admitted to the hospital, the admitting consultant or resident discusses the patient's goal of care and code status. At this time, if the patient agrees to non-invasive ventilation and its use appears imminent, consent may be obtained should the patient's condition worsen and require non-invasive ventilation.

The direct measurement of aerosols is non-trivial. However, aerosols travel in air, and so air leak is a necessary condition for aerosolization. This study measures air leaking around a mask as approximated by air leaking out of a circuit as an indirect measurement of aerosolization.

## DATA COLLECTION

Demographic Data: age, sex, height, weight, presence or absence of dentures, presence or absence of facial hair

Metabolic Data: arterial or venous blood gas measurements ($pC0_2$, pH, $HC0_3$, and $p0_2$), vital signs (body temperature, pulse, respirations, blood pressure, oxygen saturation).

Note: no additional blood work beyond standard patient care will be required for the study.

Non-invasive Ventilation Data: Ventilation technique, IPAP, EPAP, leak volume per minute, mask fit, patient tolerance of mask.

Adverse events Data: From initiation to completion of non-invasive ventilation using the standard or non-aerosolizing mask, any reports of : nasal or oral bleeding, pneumothorax, ulcers, and free text for other concerns.

Note: The electronic medical record (Power chart) will be accessed to review this data

**All data will be tracked by the DSMC to ensure safety of patients. Where possible, the committee will analyze data to ensure patients are ventilating as expected by compiling and reviewing all bloodwork results found in the blood gases.**

## DATA ANALYSIS

Data will be entered directly into a study-specific LibreOffice database (The Document Foundation, Berlin, Germany). All data analyses will be performed using R (R Foundation, Vienna, Austria). All identifying patient data will be kept separate from study data. LibreOffice and R are two pieces of Open Source software that will be run locally on study computers and store all data to the LHSC P: drive. A LibreOffice database is stored in an ODS (Open Document Spreadsheet) file. It is a storage format akin to Microsoft Excel's XLSX format. LibreOffice Calc is the software used to create the database, and is an Open Source Software (OSS) equivalent of Microsoft Excel.

Data from the BiPAP machine (IPAP, EPAP, L/min of leak) are collected nearly continuously (every 3-10 seconds depending on machine) on the ResMED 150 or similar machine. An alarm will sound on the machine if leak volume exceeds standard of care. The leak volume will be reviewed with data analysis after the duration of BiPAP or at 24 hours. Data will be transferred from this machine to a local computer for entry into the above database.

For Data Analysis, the means and standard deviations of the Glasgow coma scale (GCS), respiratory rate, heart rate, pH, $PaCO_2$, and $PaO_2$ will be calculated for each time period.

Participants will be assigned a subgroup of control or experimental depending on which mask the patient received. These two subgroups will be compared using an analysis of variance (ANOVA) to detect differences between outcome parameters. A subgroup analysis will also be taken based on COVID-19 culture status regardless of the type of respiratory failure. This analysis will be performed with an ANOVA on the outcome parameters.

The critical importance of mask leaking means that these data will be displayed as a sum of all incidents. As these are binomial, a subgroup and time comparison will also be carried out using a generalized linear model of the binomial family (logistic regression). Leak volumes will be compared with an ANOVA.

As there is a real or perceived conflict of interest, Dr. Tarek Loubani will not be involved in any data analysis.

## ETHICS AND PRIVACY

The research team will seek approval from Western Health Sciences Research Ethics Board.

All data collected will be maintained on the LHSC "P" Drive in a password protected folder. Investigators will only look at or analyze data on LHSC computers. Hard copies will be stored in a locked filing cabinet in a secured location. Data will be coded with unique identifiers and the master list containing any identifiers will be stored separately from the collected data.

There will be no additional information stored on any external hard drives, laptops, or portable devices.

This study data will be retained for 15 years as per Health Canada policy. After this 25 year period, paper records secured in a locked filing cabinet at LHSC will be destroyed according to institutional protocols, which includes placing the records in locked, confidential shredding bins. The bins are then collected by an outsourced company (Shred-It) and the contents are shredded. Computer and electronic records will be encrypted and secured for 25 years and then all study files will be destroyed according to institutional protocols of data deletion including clearing all memory sticks. This will be done in consultation with the IT department for current protocols.

## PLANS FOR DISSEMINATION OF FINDINGS

The source code for the device, anonymized data from the study, and preprints will be stored in a local repository and submitted for publication.

The investigators will also disseminate findings through mass media and peer-reviewed publication.

## References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