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1. Introduction

1.1 Basics of mechanical ventilation.

Humans' respiratory system or in simple terms breathing physiology is controlled via a complex network of receptors, sensors, and feedback loops. Important breathing sensors are located in the brain, heart, blood vessels, vascular network, and respiratory muscles including the diaphragm, and lung. The brain has two important respiratory sensors: one afferent sensor which triggers a breath and sends signals to the thoracic cage respiratory muscles to contract thereby triggering inhalation of surrounding air (Figure 1). The second efferent sensor gives signals to stop inhaling air and in turn, triggers the opposite reflex and facilitates exhalation of air. Physiologically, once a minimum volume of air (with oxygen) is inhaled, a feedback signal goes back to the brain from thoracic cage musculature to stop further inhalation and air (with carbon-di-oxide) is exhaled out passively (Loscalzo, 2022).

Normal physiological breathing may become abnormal in many clinical conditions or pathological states. Abnormality may range from complete inability to trigger normal breathing called “apnoea” to rapid breathing with excessive use of thoracic and diaphragm musculature leading to fatigue and tiredness called “tachypnoea”. Clinical situations like injury to the brain from spontaneous or road traffic trauma, stroke or drug intoxication may lead to apnoea or complete loss of normal spontaneous breathing. In comparison, situations like pneumonia, acute or chronic heart failure and sepsis where individuals may experience tachypnoea or fast breathing. Prolong tachypnoea may lead to rapid deterioration needing admission to hospital or critical care unit (Loscalzo, 2022). In clinical scenarios as described above where individuals lose either the complete ability to breathe for themselves or find it extremely challenging and painful, an artificial breathing system or mechanical ventilator can be instituted to rescue and stabilise such clinical scenarios by medical team. The institution of mechanical ventilator can be done by doctors with different backgrounds and clinical expertise.

Individuals who are found with apnoea will rapidly damage multiple organs due to falling oxygen levels in the blood. Within minutes individual will start to develop a coma with reduced consciousness. This occurs due to less oxygen reaching the

brain and causing damage to brain tissues. If this vicious cycle is not stopped in a timely fashion, it will lead to rapid death. In comparison, tachypnoea where patient's respiratory demand is high, and the body is unable to match required oxygen demands. In this scenario, the respiratory system will try to compensate initially with rapid breathing, but soon respiratory muscles will develop fatigue and will start accumulating lactate. Eventually, respiratory muscles including diaphragm will not be able to work effectively leading to a decrease in oxygen level resulting in damage to end organs and death.

1.2 Basic description of how mechanical ventilator works.

A mechanical ventilator is an artificial breathing system which gives oxygen and removes carbon dioxide from the lungs and is instituted temporarily till recovery of primary organ failure from initial insult occurs. Primary organ failure could be brain, heart, or lungs. A mechanical ventilator is connected to the patient via an endotracheal tube (ETT) which is placed inside the patient's trachea. ETT is connected to a mechanical ventilator through two plastic intermediary tubing's (Figure 2). Initial insertion and maintenance of ETT within the trachea is an extremely painful process, and this is achieved by giving initial bolus followed by continuous infusion of intravenous sedative and analgesic medications to maintain an artificial chemical coma state. The institution of mechanical ventilation can be done either by pre-hospital first responder doctors or paramedic team or it can be done within the hospital system by emergency department doctors or in critical care units by intensive care and anaesthesia doctors (Anon., 2024)

Individual patients will continue to receive treatment from a mechanical ventilator until there is either improvement in clinical condition or resolution of initial pathological insult or primary organ failure. During the entire duration of patients receiving treatment from the mechanical ventilator, ventilator settings are continuously manipulated by the clinical team based on individual patient requirements and pathological state with the aim of full separation from the ventilator. The liberation or separation process is reviewed daily by reducing artificially induced chemical coma, and separation is achieved when there is full recovery from primary insult.

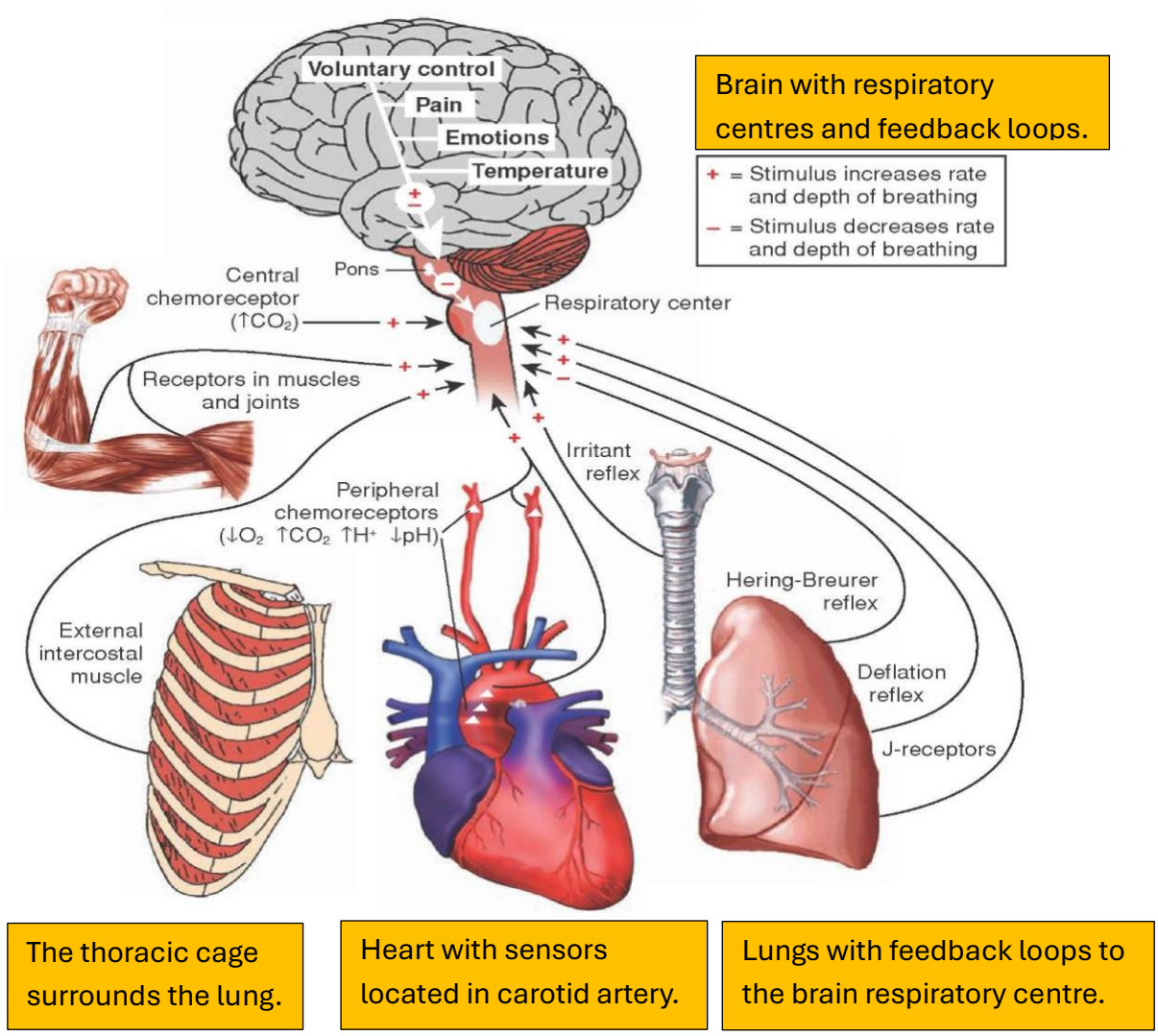

Figure 1: Diagram showing the location of the respiratory centre which is below pons (Pons is an area of the brain which regulates respiration). The respiratory centre is reactive to internal stimulations like voluntary control, pain, emotions, and temperature through a positive feedback loop. The respiratory centre receives afferent positive feedback from the lung through the deflation reflex, J-receptors, and External intercostal muscles and afferent negative feedback through the Hering-Breurer reflex. The respiratory centre also receives signals from irritant reflex located in the upper airway, afferent signals from muscles and joints as well as afferent signals from peripheral chemoreceptors located in the aortic arch. Peripheral chemoreceptors located in the aortic arch of the heart respond to low oxygen or hypoxemia, hypercapnia, acidosis and raised hydrogen ion concentration (Ref – Harrison Internal Medicine).

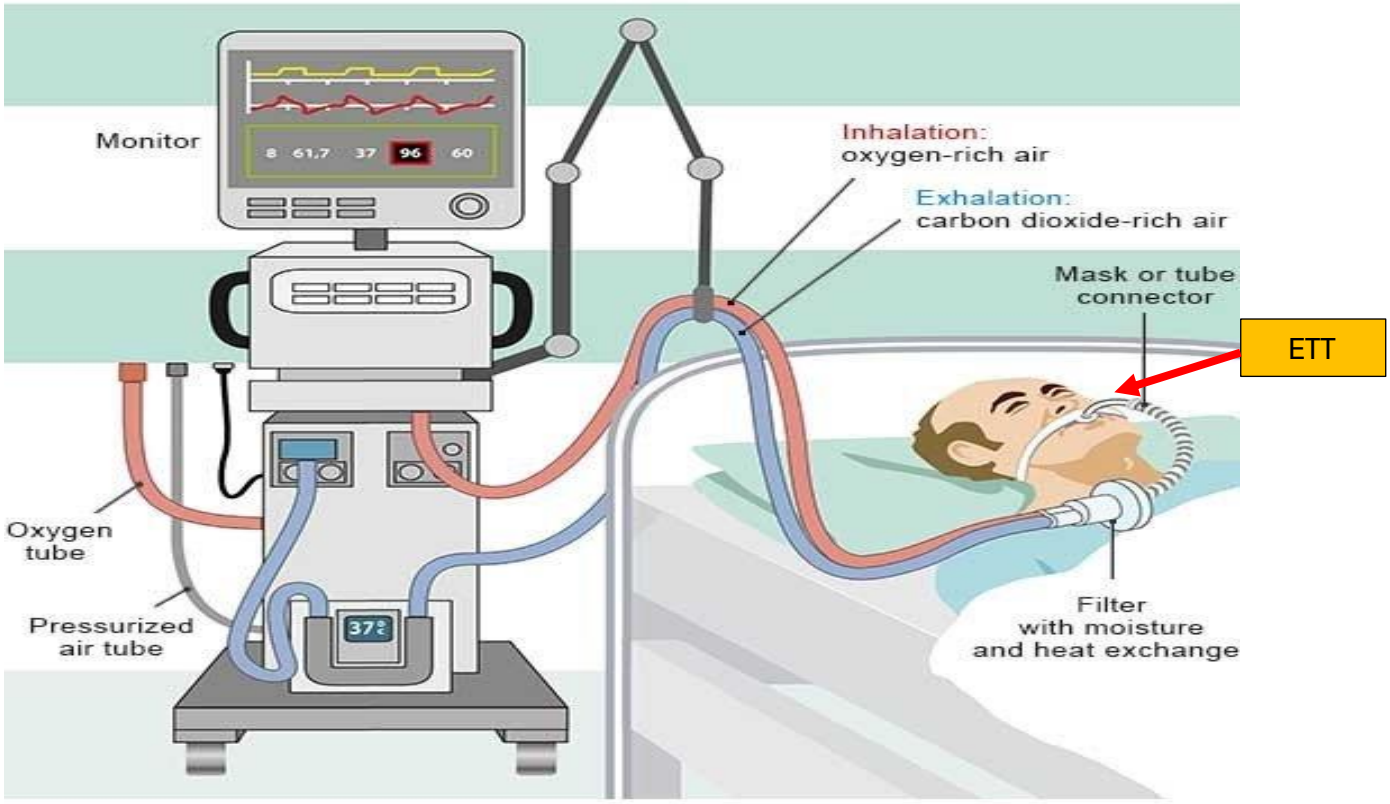

Figure 2: Diagram showing a mechanical ventilator which provides oxygen and removes carbon dioxide from critically ill patients. An endotracheal tube is passed into the patient's trachea and the mechanical ventilator is connected to the patient endotracheal tube using two tubes, a tube connector, and an exchange filter with the ability to store moisture and heat. The inhalation tube (Pink coloured) provides oxygen-rich air, and the exhalation tube (blue coloured) removes carbon dioxide-rich air. The ventilator monitor continuously shows all the usual ventilatory data points (Ref-https://www.informedhealth.org/how-does-mechanical-ventilation-work-during-an-operation.html).

1.3 Classification of Liberation failure rate.

Published data from prospective and retrospective registries and clinical studies clearly showcases that not all attempts to liberate patients from mechanical ventilators are successful. Liberation failure rates are low from around five to eight per cent in patients after elective surgery to as high as seventeen per cent in patients admitted to a medical intensive care unit after severe brain trauma and stroke (McConville, 2012).

Higher liberation failure rate is directly related to increased mortality and morbidity of patient (T, 2023). Beduneau has authored an international position paper on

liberation and have classified the liberation process into four categories (Beduneau, 2017). Categories are no weaning where weaning is not attempted at all due to patient death prior to the liberation attempt, simple weaning where the first attempt resulted in a termination of mechanical ventilation and successful weaning, difficult weaning where weaning was completed after more than one day but less than one week after the first attempt to liberate and prolonged weaning where weaning was still not terminated seven days after the first separation attempt. Patients with older age, cardiac and respiratory comorbidities and multiple organ failures on admission will usually fall under difficult or prolonged weaning.

1.4 Weaning decision-making and relation with patient outcome.

Routinely, the decision to liberate from the mechanical ventilator is made by a critical care medical team through simultaneous evaluation of multiple features like patient past medical history, and bedside physiological vitals like heart rate, blood pressure and mechanical ventilator variables. Other factors such as recovery status of primary organ failure, total duration of mechanical ventilator therapy, evaluation of all the medical or surgical treatment received, and any complications that have occurred from the day of admission. After reviewing and integrating all data points, the medical team makes the clinical decision whether to liberate patient from the mechanical ventilator or not. Clinical decisions are usually based upon combining previous eminence knowledge and simultaneous evaluation of bedside data points. As per published studies, patient outcomes and mortality will be higher if incorrect decisions are made and patients are removed from ventilators when they are not clinically ready. Also, the process of reinstitution of mechanical ventilators itself leads to complications like higher incidence of ventilator-associated pneumonia, complications from increased hospital and intensive care unit length of stay, and more doses and duration of antibiotics required to treat newly acquired infections (T, 2023).

Features such as neurological status measured by the Glasgow Coma Score (GCS) and sedation level scores measured with the Richmond agitation sedation scale (RASS) are probably the most important features (Mehta & Chinthapalli, 2019) (Page & McKenzie, 2021). A higher GCS score will ensure an awake patient with a strong airway reflex and cough strength, thereby minimising the chance of oral and airway

secretions trickling into the lungs and associated risk of aspiration pneumonia. Removing the ventilator in such scenarios when the GCS score is low will be associated with increased risk to patient as well as high chances of re-institution of mechanical ventilation.

Mechanical ventilatory features such as spontaneous breathing trial (SBT) is a process where ventilatory support is lowered to a minimum and patient ventilatory and physiological parameters are observed for a set duration. The duration of SBT could range from thirty minutes to one hour. Physiological variables like respiratory rate and oxygen level are monitored throughout the SBT process. Clinical bedside signs of SBT failure could be a rapid decrease or fall in the level of oxygen or increased respiratory rate which suggests the patient is not ready yet to come out from ventilatory support. Multiple successive failed SBT trials put patients into the category of difficult weaning thereby increasing the duration of intensive care and hospital stay. SBT failure could result from multiple reasons such as chronic cardio-respiratory illness or the persistence of primary organ failure. For ventilatory weaning to be successful, it is imperative that SBT outcome is included in final decision-making (Thille, 2022).

Lastly, an ETT cuff leak should be present. ETT cuff leak provides assurance that there is no upper airway oedema, and the patient will be able to breathe normally when ETT is removed. Removal of the tube inadvertently when airway oedema is present will lead to upper airway stridor and tachypnoea resulting in a decrease in patient oxygen level needing re-insertion of ETT and placing the patient on ventilator. There are several tests that could be done pre-emptively like the ETT cuff leak test which may help to predict upper airway oedema (Smith, et al., 2018).

1.5 Features related to weaning from mechanical ventilation.

Assessing patients' readiness to be liberated from the ventilator needs evaluation of multiple variables. These variables are categorized into the patient, mechanical ventilator, environment, and human factors. The importance of variables varies from patient to patient and not all factors are needed to be evaluated for every patient. For example, in patients with brain trauma, key patient variables for decision-making will be GCS score, quantitative estimation of airway secretion load and quantitative

estimation of cough strength as compared to patients with heart failure whereby passing SBT, quantification of severity of heart failure and negative ETT cuff leak test will be a key factor for successful liberation from mechanical ventilation.

The percentage of liberation failure rate from mechanical ventilation was very high at the University Hospital of Wales adult critical care unit. The rate was ascertained through a prospective service evaluation project for six weeks which showcased a weaning failure rate of around twenty-seven percent. As compared to Internationally published data over last two decades, the liberation failure rate was two to two and a half times higher (McConville & Kress, 2012). The project's main aim was to find a crude ventilatory weaning failure rate which would act as a benchmark to institute future improvement strategies and was not designed to assess factors directly or indirectly affecting the failure rate.

1.5.1 Variables related to patient:

1. **Neurological status**: Individuals should have normal or near normal global brain function, in simple terms individuals should be able to open their eyes or move hands and legs during basic bedside neurological examination. Global brain function can be crudely measured using combination of GCS and RASS scoring system (Mehta & Chinthapalli, 2019) (Page & McKenzie, 2021). The rationale of having normal neurological status before liberating patients from mechanical ventilators is important, as normal brain function means the presence of normal airway reflexes and it will prevent inadvertent entry of stomach contents into the lungs. Liberating patients with poor brain function risks entry of stomach contents into the lungs giving patients aspiration pneumonia and increased risk of death. (Thille, et al., 2013)

2. **Sedation level**: Individuals need a continuous infusion of intravenous (directly injected into blood) medications to tolerate a breathing tube being placed within the trachea. This is done to blunt the pain reflex/pathway associated with the presence of a foreign body within the airway. As patients start to show signs of clinical improvement, the dose of sedative medications is lowered. The level of sedation is routinely assessed using a multiple-scoring system with the aim of achieving awake and interactive patients prior to attempting liberation from mechanical ventilator.

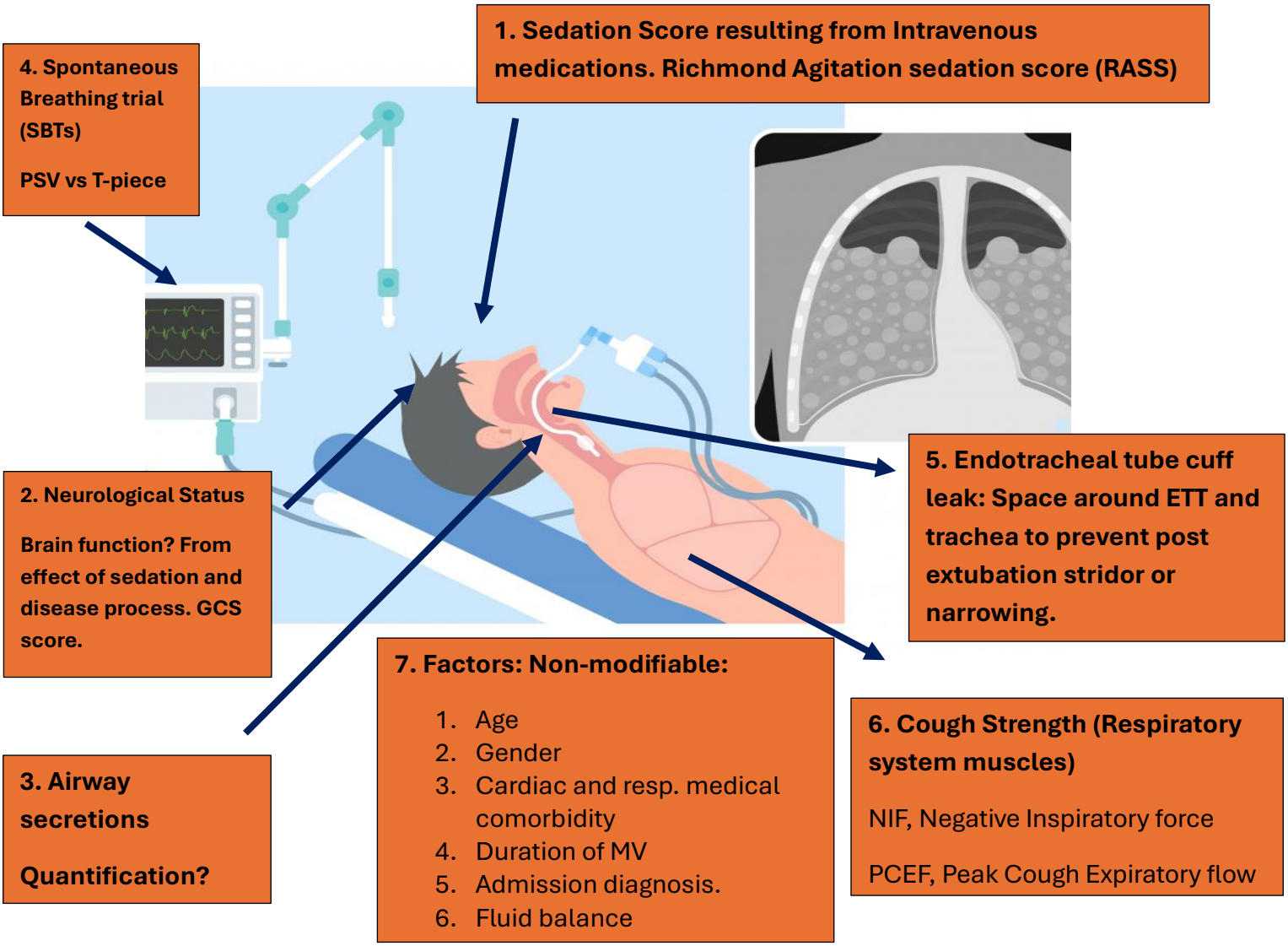

Figure 3: A pictorial representation of all the variables that need to be considered prior to liberating patients from mechanical ventilators. Variables are numbered from one to seven. 1 – Sedation score of patients when intravenous medications are stopped, 2 – Brain or neurological function at the time of evaluation using GCS score and RASS scoring system, 3 – quantification of airway secretions, 4- Spontaneous breathing trial result, 5- ETT cuff leak test result, 6- Quantification of cough strength and lastly, 7- Description of six non-modifiable factors.

3. **Endotracheal tube Cuff leak test:** Individuals who remain on a mechanical ventilator for a long time may develop airway swelling or oedema from the presence of ETT with its inflated balloon (ETT balloon acts as a foreign body). The presence of swollen or oedematous airway can be assessed by deflating ETT cuff by aspirating air through spring-loaded one-way valve. An inflated balloon normally acts as a sealant and prevents the trickling of oral and upper airway secretions into the lungs. If no air leaks out from around the ETT on aspirating air from one-way valve, it suggests the presence of oedematous or swollen airways. Removal of ETT on such

occasions may lead to stridor or upper airway obstruction, inability, or difficulty to breathe and rapid drop in oxygen levels. The risk of upper airway swelling increases as the duration of mechanical ventilation increases (Smith, et al., 2018).

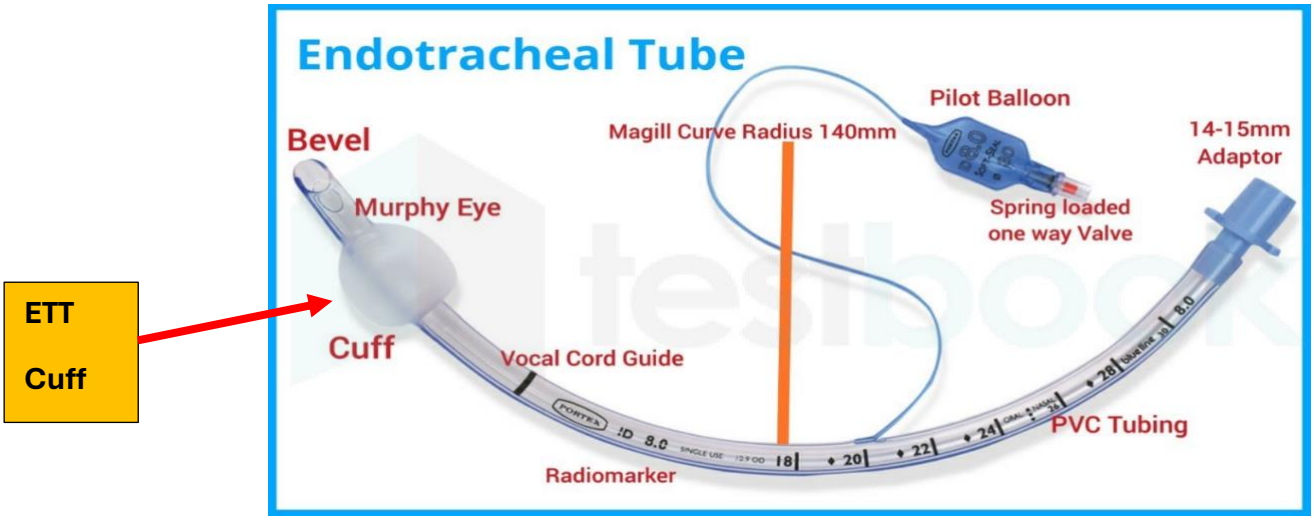

Figure 4: A regular Endotracheal tube (ETT) with different labelled parts. ETT cuff is situated at the end of the tube and highlighted with a red arrow. Spring-loaded pilot balloon allows the clinical team to both fill and remove air from the ETT cuff.

4. **Airway secretions from lower respiratory tract**: A normal individual will be able to cough out oral and upper and lower lung secretions effectively. Normally such secretions are neither excessive in quantity nor in thickness. In comparison, for patients who are recovering from critical illness and now need to be liberated from the mechanical ventilator, their secretions will be both excessive as well as thick in consistency. Many research studies have given recommendations and proposed guidance for objective assessment of both the volume as well as consistency of secretions. Medical teams who are considering liberating patients from ventilators need to take both factors into consideration before removing the breathing machine. (Thille, 2020).

5. **Cough strength**: Breathing is normally divided Into two phases:

1) Inspiration or inhaling surrounding air is an active process and occurs largely by contraction of the diaphragm and external intercostal muscles.

2) Expiration or exhaling inspired air is a passive process and occurs through the relaxation of the diaphragm and contraction of internal intercostal muscles. The

ability of any individual to cough and remove secretions normally depends upon the strength of the diaphragm. The diaphragm being the largest muscle involved in respiration gets weaker as individuals spend more time on mechanical ventilators and it is extremely important to assess cough strength prior to removing the mechanical ventilator. Objective assessment of diaphragm can be done via multiple techniques like measurement of peak cough expiratory flow (PCEF), negative inspiratory flow (NIF) etc. These measurements are done whilst the patient is still connected to a ventilator. Patients who are liberated from mechanical ventilators with poor cough strength will experience a slow inspissation of secretions within the lung resulting in less oxygen transfer and the necessity to reinstitute mechanical ventilator. Such instances are more common in patients admitted after pneumonia and brain trauma (Thille, 2020).

6. **Non-modifiable factors:**

A) **Age and gender:**

Age and gender are the two commonest non-modifiable factors that are needed to be considered for weaning decision making. Failure on not being able to remove the breathing machine is more common in the older population as compared to the younger population. This occurs mainly due to the lower percentage of skeletal muscles in the older population and the slow anabolic phase or recovery after sustaining injury. Also, the female gender has a propensity to have a higher failure rate as they have less proportion of skeletal muscles and a smaller diaphragm as compared to the male gender (McConville & Kress, 2012).

B) **Medical and surgical comorbidity:**

Patients who have medical conditions like Asthma and Chronic obstructive pulmonary disease (COPD) generally spend more time on mechanical ventilators and are difficult to liberate. Lung physiology in such a scenario is chronically deranged and adds an extra layer of complexity to decision-making. Lungs are generally overinflated with a flatter diaphragm which makes attempting liberation extremely challenging. Other cardiovascular conditions like acute or chronic heart failure are associated with similar challenges (McConville & Kress, 2012).

C) **Fluid balance:**

Positive fluid balance or net positive cumulative fluid balance during critical care stay is associated with multiple organ failures and poor outcome. It directly limits and hampers the ability to improve lung function and remove breathing machine. Positive fluid balance is associated with an increased risk of resistant infections and sepsis as well as kidney failure. Individuals spent more time in critical care with positive fluid balance resulting in excessive deconditioning of respiratory muscles. It is imperative for the clinical team to daily assess the fluid status and either aim to limit excess fluid or withdraw fluids using water tablet medications(Beduneau, 2017).

D) **Duration of Mechanical ventilation:**

Duration of mechanical ventilation is also a key factor to consider prior to ventilator liberation. As individuals spend more time on mechanical ventilator, many additional complications start to accumulate like ventilator-associated pneumonia (VAP), other organ failures involving the heart and kidney, excess protein catabolism, and weakness of skeletal musculature to name a few. All the above factors directly lead to excessive dependence on ventilators and the inability of individuals to breathe without assistance. It is imperative for the clinical team to daily evaluate fitness or readiness to come off from breathing machine as daily evaluation of readiness has been reported to reduce time on mechanical ventilator (T, 2023).

E) **Admission Diagnosis:**

Admission clinical diagnosis is an important factor and may help in estimating the approximate duration of mechanical ventilation. Individuals admitted with brain trauma are likely to spend months as compared to days for patients who are put on mechanical ventilators after elective surgery.

1.5.2 Features related to mechanical ventilator:

A mechanical ventilator acts as a bridge to recovery, provides oxygen and removes carbon dioxide until primary insult is resolved and treated. Since the discovery of mechanical ventilators, there have been many tests developed which may forecast the suitability for patients to come off from ventilator. The tests have been broadly

categorised as spontaneous breathing trial (SBT). These tests are broadly separated into either temporary disconnection of ETT from the ventilator for thirty minutes or reduced assistance from the ventilator to the lowest levels without disconnecting ETT. During these temporary SBT manoeuvres, clinical team assess patients' respiratory performance using set criteria like oxygen level, respiratory rate per minute, pain while breathing or dyspnoea score and others. Multiple patient-related data points are collected, and the decision is made whether patients have passed or failed the test. These tests are broadly categorized under the name of spontaneous breathing trials (SBT).

1.5.3 Environmental and human features:

Environmental and human factors are also important and integral to the right decision-making. Environmental factors in which clinical teams are working such as weather, light and noise can indirectly influence human performance and decision making. Intensive care ergonomics such as bed location and position, distance between two beds, general critical care infrastructure, extubation equipment availability and location of equipment are other key factors that may play a role in decision-making. Environmental factor's weightage in liberation decision-making will vary from institution to institution.

Human factors on the other hand refer to elements like human behaviour, capabilities, limitations, and interactions. This can be translated to critical care medical teams' capability to integrate all physiological and ventilatory variables and to make an individualized and measured decision rather than using historical eminence knowledge. It is also imperative for clinicians to continuously update knowledge with new published evidence that is coming through and inculcate them in daily practice and decision making. This will provide the best chance to have a successful weaning outcome. Some of the human factors that may negatively impact right decision-making are continuous distractions at work and decision tiredness. It is important that clinical team make decision after going through an agreed weaning protocol whereby no important feature is missed. The decisions are continuously audited, and a process is laid down for continuous learning and feedback.

1.6 Predictive Models as decision tool to reduce weaning failure rate:

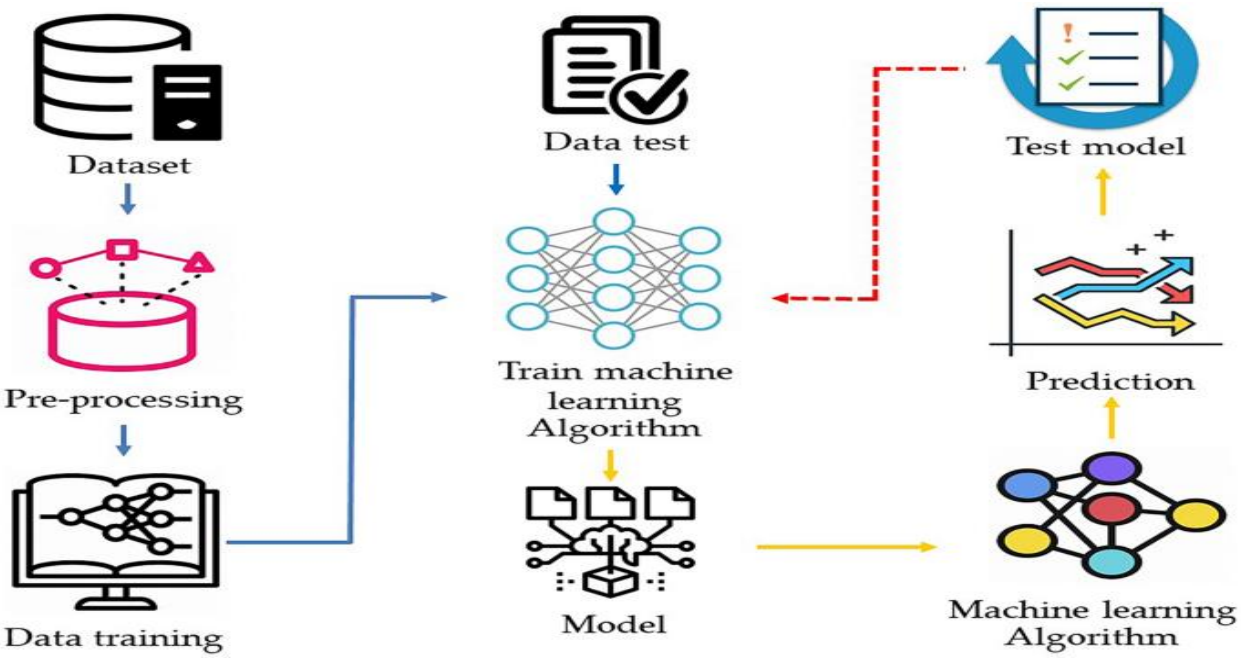

Figure 5: Example of how a machine learning algorithm is designed and developed using datasets. First datasets undergo pre-processing where raw data is cleaned to make it suitable for further analysis. Data is then trained using pre-processed data to create a machine learning algorithm.

Predictive modelling utilizes advanced statistical models to integrate large complex input variables to produce output. As described above, multiple variables are required to be assessed on every patient to make decision on ventilator liberation. Predictive models are developed using either retrospective or prospectively collected data. Data is initially analysed to make sure missing values are imputed, outliers are detected and treated, standardization of numerical features are done, classes are balanced to address the class imbalance and removal of irrelevant or redundant features is achieved with aim to improve model performance. Aim is to use techniques like principal component analysis to reduce the number of features while preserving important feature (Anon., n.d.). After pre-processing is achieved, clean data is then separated into training and validation sets. This process of data separation can be done multiple times to improve the internal validity of the model. The performance of the model can be evaluated using multiple metrics like accuracy, precision, sensitivity, F-score, Receiver Operating Characteristic (ROC) and area under the curve (AUC). Choosing the right evaluation metric is crucial for

understanding how well a predictive model generalizes to unseen data and aligns with the specific objectives of the analysis.

Routinely, clinical teams making weaning decisions are required to integrate multiple variables and data points to arrive at conclusion. This integration can be challenging for a busy clinical team and may result in a higher weaning failure rate. This is probably the main limitation as humans may find it difficult to remember and/or integrate all variables in a systematic fashion to arrive at clinical decisions. In comparison, a predictive modelling tool would analyse all variables and provide the clinical team with a probability decision risk score. This score can be easily integrated into final clinical decision-making. Clinical acceptance and clinical use of such modelling tools will depend upon the openness of the chosen variable as well as algorithm used to calculate probability score.

1.6.1 Planning and designing of my predictive model; a new approach.

Multiple published studies have designed weaning predictive tools using either single centre retrospective data or a single centre available open data resource. Most of the published models are also not validated prospectively to be used at the frontline In rapid clinical decision making. After reviewing the already published data on weaning modelling and learnings from it, this project will first aim to design a standardized weaning pathway where important weaning related variable details are collected prospectively. Data collected via this process will be over a one-to-two-year time-period. Primary aim will be to have large data sets and many patients physiological and ventilatory variables which will help to strengthen the model. Prospective data will then be analysed using a tool to develop a predictive weaning decision tool. This tool will be validated in multiple critical care settings to improve external validity. Developing tools in this fashion will avoid all the following: 1) selection bias, 2) recall bias, 3) missing variables with poor data quality, 4) Inaccurate and imputed data points, and 5) poorly established causality between cause and effect with limited validity and generalizability. Existing prediction tools lack inclusion of all important weaning related features and none of the tools use the ETT cuff leak test. My model and stepwise approach will address all existing gaps in designing a weaning model.

1.6.2 Impact of Predictive Modelling Tool in taking weaning decision.

If a predictive modelling tool has high sensitivity and specificity, it will be able to predict or make correct and informed decisions in most clinical circumstances. The impact of such decision-making will have direct and indirect benefits. Direct benefits will be reduced risk of ventilator-associated pneumonia (VAP), decreased incidence of other organ failures like heart, kidney and brain, reduced requirement of cumulative sedative medications dose, reduced critical care and hospital length of stay as well as mortality and morbidity. Financial savings will be for individuals in the insurance-based healthcare system, and public organisations in cases where the public healthcare system operates. The impact will also be global as prediction tools with good external validity can be used internationally, especially in low- and middle-income countries. It will also have good patient and family experience.

Currently, such tools are not being developed in this fashion and this will be the first attempt in designing such innovative model.

2. Literature Review

2.1 How the literature search on machine learning models and ventilator weaning were done.

PubMed database was searched using following Mesh (Medical Subject Headings) terms:

1. “Machine learning (ML)” and “Ventilator weaning”, gave 27 results.

2. “Artificial Intelligence (AI)” and “Ventilator Weaning”, gave 62 results.

3. “Machine learning (ML)’ and “ventilator weaning” and “feasibility”, gave 1 result.

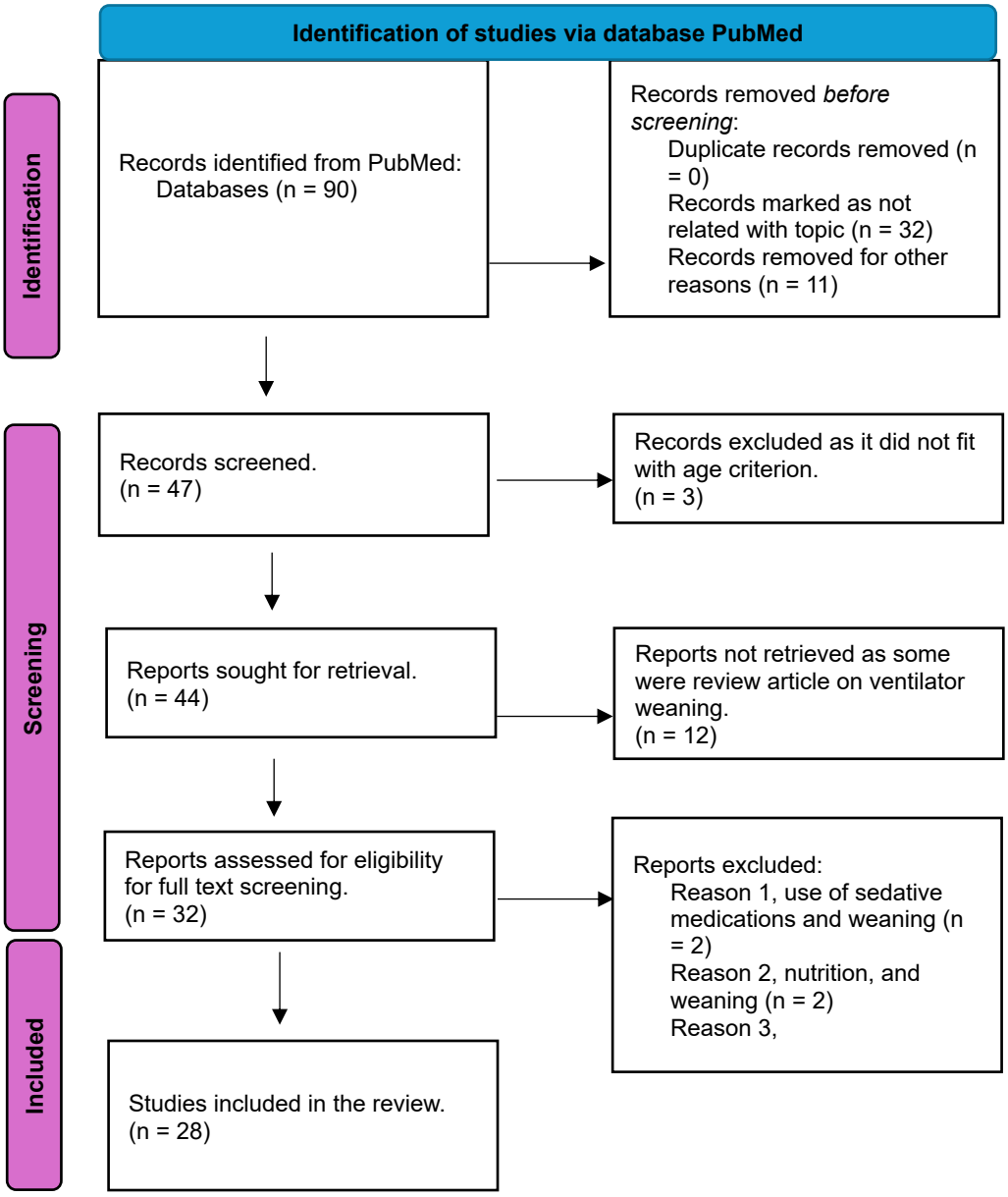

Figure 9: PRISMA Flowchart: PubMed database was searched using Mesh terms “Ventilator weaning”, “machine learning”, “AI”, and “feasibility”. Twenty-eight results were studied in the end out of a total of ninety studies. (Page, 2021).

In total, ninety studies were evaluated, and twenty-eight studies were included in the final descriptive analysis. The criterion for inclusion were adult patients aged more than eighteen years and ML or AI tools used to help with weaning from mechanical ventilation. It is also very clear that the future direction of healthcare is continuously and rapidly evolving, and the use of big data analytics using ML algorithms may help clinicians at the bedside to make better-informed decisions. Many concepts and nuances have come up on using machine learning tools to design weaning models during the review of twenty-eight published literature (Page, 2021) and they are described as follows from 2.2 to 2.8.

2.2 Strength and weakness of machine learning tools to develop weaning prediction models (S, 2020).

Almost all studies used highly complex ML algorithm and principles to aid in ventilatory weaning. Some of the examples are as follows:

Qing Pan et al used the XBoost statistical tool to predict extubation failure using a comprehensive breathing variability index (Pan, 2023). Similarly, Takanobu Otaguro et al used Light GBM (Light Gradient-Boosting Machine) and XGBoost (Extreme Gradient Boost) to predict weaning success or failure by using more than twenty-five patients and ventilatory variables (Takanobu, 2021). Both the above ML tools use regression, classification, and ranking problems and perform complex mathematical algorithms. Po-Hsun Huang et al used another complicated statistical tool, an extended classifier system with a real-valued input (XCSR) model to help with ventilatory weaning (Huang, 2022). The ML tool was trained using forty-three variables and used a complicated computational rule-based ML method that combined exploration and ML components. Some of the computational and statistical models used were highly complex and beyond the capacity to be understood by an average clinical team. In comparison, some of the strengths of using ML tools are as follows:

1. **Scalability**: ML tools can handle large datasets efficiently, allowing for the processing of massive amounts of information in reasonable time frames (Watson, 2019). Flavia Torrini et al performed a systematic review and meta-analysis involving sixty-seven studies using patient cohort data of 26,847 participants. Bayesian multivariable meta-analysis tools were used which led to the identification of twelve variables as risk factors for weaning failure. These variables were distributed into three areas namely patient comorbidities, acute disease severity and some patient characteristics involving circulatory, respiratory, and neurological features (Torrini, 2021).

2. **Adaptability**: ML tools can adapt and improve further over time as they are exposed to more data, making them suitable for dynamic and changing environments. Juliette Menguy et al developed a prospective data warehousing project using a dynamic prediction AI model using a single feature like heart rate variability during an SBT. This model had features of continuous adaptability and ongoing learning as more and more prospective data were included in the model (Menguy, 2023).

3. **Automation, prediction, and forecasting**: ML models automate repetitive tasks such as data pre-processing, feature selection and model training, freeing up human resources for more complex and creative tasks. Also, ML can make accurate predictions and forecasts based on historical data, providing valuable insights for decision-making.

4. **Continuous learning**: ML models can continuously learn from new data, enabling them to stay relevant and up to date in real-time scenarios.

5. **Cost-effective**: Once trained, ML models can perform tasks at a lower cost compared to traditional methods, especially for tasks requiring high computational resources.

ML tools also have some weaknesses and the most common are whereby the clinical team is unable to understand the model complexity fully. AI using ML tools is often seen as a black box because it can produce complex outputs without providing a clear explanation of how it reached those conclusions. This lack of transparency

can lead to concerns about trust, accountability, and bias. Watson et al developed a model using complex algorithms, some clinicians felt it to be a black box and hesitated to use it to make clinical decisions at the bedside (Watson, 2019). Several factors contribute to this perception (Zednik, 2021) and are as detailed below.

1. **Complexity of Models**: Many AI models, especially deep learning models, involve numerous layers and parameters, making it difficult for clinicians to understand how inputs are transformed into outputs.

2. **Data Dependency**: AI models are trained on vast amounts of data, and their outputs are heavily influenced by the quality, diversity, and biases present in that data. Without transparency into the training data, it's challenging to understand why a model makes certain decisions.

3. **Algorithmic Opacity**: Some AI algorithms, such as deep neural networks, operate in ways that are not easily interpretable by humans. The internal workings of these algorithms can be highly complex and difficult to decipher.

To mitigate the black box problem in AI, several approaches can be under-taken and these are as follows:

1. **Interpretability techniques**: Researchers are developing methods to make AI models more interpretable, such as feature importance analysis, attention mechanisms, and model-agnostic techniques like LIME (Local Interpretable Model-agnostic Explanations) and SHAP (Shapley Additive exPlanations). These features are key to be included in any future models.

2. **Transparency and documentation**: AI developers can improve transparency by documenting their models, including information about the data used for training, the model architecture, and any post-training modifications.

3. **Ethical guidelines and regulations**: Governments and industry organizations can establish guidelines and regulations that promote transparency, accountability, and fairness in AI development and deployment.

4. **Bias detection and mitigation**: AI developers should actively identify and address biases in their models and data, employing techniques such as bias audits, fairness constraints, and diverse dataset collection.

5. **Education and awareness**: Increasing awareness among users and stakeholders about the limitations of AI models and the importance of transparency and interpretability can help foster trust and mitigate concerns about black-box AI.

6. **Explainable AI and real-time applications**: Kai-Chih Pai used explainable ML models to predict extubation in critically ill patients (Pai, 2022). An explainable AI model was developed using multiple variables at the domain feature as well as individual level. Model performance was more than 90%. Explainable AI helps the clinical team to develop confidence to use the model at the front line. Similarly, real-time model applications where results are built within day-to-day clinical workstreams can also improve the weaning rate. Ying-Jen Chang et al developed a real-time - assisted system to predict either immediate weaning from the ventilator after lung resection surgery or the need for critical care admission and delayed weaning from the ventilator (Chang, 2021). It was built using many pre-operative variables. AI model was able to predict whether patients were able to wean after the surgery or not. It had good satisfaction scores from both senior and junior anaesthesia colleagues' users as well as objectively quantified time saved by anaesthesiologists in doing pre-operative assessment before surgery. By implementing the above strategies, developers and users can work together to address the black box problem in AI and build a more trustworthy and responsible predictive tooling system.

2.3. Models developed using single-centre vs multi-centre data.

Models that were trained on retrospective data from a single centre have wide-ranging issues and these are elaborated as below.

A) **Limited generalizability** – Results from a single centre may not apply to broader populations or different settings, as they may not adequately represent the diversity of patient demographics, healthcare practices or regional variations. Kuo-Yang Huang and co-authors developed a weaning prediction model using time-series

ventilator-derived parameters only (Kuo-Yang, 2023). The model was developed using retrospectively collected ventilatory variables without any physiological or medical history data. Model predictability was developed using a random forest with an area under curve (AUC) of 0.976. Similarly, Jinchul Kim et al developed a ML model using the MIMIC-4 database. Two key predictors that came out of the Kim model were anion gap and lactate, both are very generic physiological factors and higher values signify a stressed physiological system and low values signify stability or an unstressed system (Kim, 2023). Issues with such a model development process are lack of generalizability and limits to wider adaptation.

B) **Bias –** Single-centre study is more liable to selection bias, where the characteristics of the patients at that centre may not be representative of the broader population. Rong-Cheng Xie et al developed a model to predict ventilatory weaning in post-cardiac surgery patients. The model was developed in a single centre and was based upon variables such as the proportion of male patients, EuroSCORE-2, operation time, pump time, bleeding during operation and brain natriuretic peptide values (Xie, 2024). Model AUC was 0.880 for the training dataset and 0.753 for the validation test. Very narrow patient inclusion is characteristic as the model was developed using a post-cardiac surgery patient cohort, and model validation was done using single centre data which limits model use as well as adds huge bias. Similarly, Yang-Han Lin et al developed an AI model to improve the weaning outcome of patients with mechanical ventilation admitted to the medical intensive care unit. Fourty-nine variables were used to develop an AI model which was integrated within routine daily clinical decision-making. The model resulted in a reduction in extubation failure rate, shorter mechanical ventilation time, and reduced hospital, and ICU length of time (Yang-Hin, 2024).

C) **Statistical power** – Single-centre studies may have reduced statistical power limiting their ability to detect significant effects or associations.

D) **Specialized cases** – Some single centres have a concentration of specific medical conditions or treatments limiting the generalizability of findings to another clinical condition. Lucas M Fleuren et al developed a ML model in patients admitted with COVID-19 pneumonia, a very specialized disease aetiology. The model had

good prediction capability and some of the variables like body mass index (BMI) and duration of mechanical ventilation were key features leading to better weaning prediction. The main limitation of the study was the inclusion of just one clinical state limiting wider usage (Fleuren, 2021).

E) **Equity** – Single-centre study may raise ethical concerns about equitable access to participation and potential biases In the study population.

F) **Cross-validation** – Multi-centric studies will provide cross-validation with improvement in predictive power as well as generalizability.

Also, single-centre studies may still provide valuable insights, especially in exploratory or hypothesis-generating research. However, their findings should be evaluated and cross-validated in more diverse populations before wider adaptations. In comparison, multicentric studies involve researchers and institutions from different geographical locations or settings which allows for more wider and diverse participant pool enhancing generalizability. Sample size is usually larger as well as participant recruitment adding diversity which can improve the statistical power and applicability of study results. Multicentric studies can easily validate findings across different populations and settings, enhancing the robustness and reliability of research outcomes. The study can be replicated across centres which adds credibility to study conclusions. The findings are often more applicable to real-world settings due to the diversity of study population, it can help better understand and account for variability in outcomes due to different practices, environments or patient characteristics and this method is widely used to run clinical trials.

2.4. Combination vs single variable predictive modelling:

Seyedmostafa Sheikhalishahi et al designed a predictive model to wean patients from mechanical ventilation using a single ventilator variable. The investigator designed a modelling tool using retrospective MIMIC-4 (Medical Information Mart for Intensive Care -4) and e-ICU (electronic intensive care unit) databases (Sheikhalishahi, 2024). Positive end-expiratory pressure (PEEP) was used as a single ventilatory variable to guide weaning. The model had an area under

receiver operator curve (AUROC) of 0.84. Similarly, Renata Baltar da Silva et al performed an exploratory analysis where heart rate variability was used to predict mechanical ventilation weaning. The rationale behind this was higher heart rate variability during SBT was associated with higher success and in comparison, lower variability was associated with weaning failure. Weaning patients from a ventilator is a complicated process that needs consideration and evaluation of multiple variables from both the patient and the ventilator (da Silva, 2023). Other variables such as cardiac and respiratory comorbidities as well as laryngeal oedema are key factors in achieving success. Developing a model using a single variable involves using that variable as the predictor or independent variable to predict another variable or dependent variable. This approach is often a starting point in data analysis and can provide insights into the relationship between variables.

In comparison, model using multiple features ranging from patient physiology, ventilator as well as past medical history were also used to predict weaning success or failure. Qin-yu Zhao used nineteen variables to derive a prediction weaning model which had AUC of 0.803 only (Qin-Yu, 2021). Similarly, Chung-Feng Liu et al used forty-five variables and developed a two-stage weaning model with an area under curve of 0.90. Developing a ML model using several independent features to predict a target dependent variable which is successful weaning prediction. This approach allows for capturing more complex relationships and potentially improving the accuracy of the predictions compared to using a single variable. ML models using multiple variables are also more robust with better predictability (Chung-Feng, 2022).

2.5. Models developed for an individual disease or clinical condition:

Kuang-Ming Liao et al developed a weaning model in three stages for patients admitted to respiratory care centres. ML or AI algorithms were used in already available clinical variables to develop models during the first stage. In the second stage, the AI model was further developed into an innovative prediction system to assist clinical teams, and lastly impact of the AI tool was then analysed at the bedside. Twenty-six features were used to develop the AI model and it included ventilator data, demographics, and physiological data. The AI prototype model was then integrated with interactive functions to be used by clinicians in an

interactive dashboard. Dashboard was able to predict probability at set time intervals with good results. The biggest limitations of the model were that it was developed in a very small and very specific cohort of patients namely patients admitted in respiratory care centres which reduced model generalizability and external validity in a wider cohort of patients (Liao, 2022).

Similarly, Wei-Teing Chen et al developed a model using a patient cohort admitted to a sub-speciality of cardiac intensive care unit. Twenty-eight variables were used to predict extubation success or failure and seven variables were included in the final support vector machine (SVM) model. Seven variables namely expired tidal volume, expired minute ventilation, heart rate, peak pressure, pH, age and set ventilatory rate were able to predict extubation success within twenty-four hours of critical care admission. This study again recruited patients from a very specific location of patients admitted to the cardiac intensive care unit, the study was not validated as well as lacked generalizability to a wider critical care patient cohort (Chen, 2022). Both studies had major limitations of lacking external validity and wider generalizability to consider clinical use.

2.6. Ethical challenges with development of machine learning models:

1. **Bias and fairness**: The prediction model may involve biases that may be inherent in the training data such as demographic biases or historical inequalities. Failing to correct such biases can perpetuate unfairness and discrimination when the model is applied.

2. **Transparency and Interpretability**: Models that heavily rely on complex opaque algorithms may be difficult to interpret, leading to challenges in understanding and explaining their decisions. Lack of transparency can raise concerns about accountability and trustworthiness. Examples of complex algorithms which were used to develop the weaning model are as follows:

A) Hung-Ju Kuo et al developed a weaning model using an artificial neural network (ANN). ANN consists of interconnected neural networks, known as artificial neurons, organized in layers. The layer typically includes input layers, one or more hidden layers and an output layer. It may sometimes get very difficult for the clinical team to

understand the model development phase which limits wider clinical application (Hung-Ju, 2015).

B) Zhixuan Zeng et al developed a recurrent neural network (RNN) model for dynamic prediction of the extubation failure risk in patients with invasive mechanical ventilation. This model was developed retrospectively using a publicly available large MIMIC-4 database. The model was able to update results every four hours and used eighty-nine features including patient demographics, clinical features such as GCS, blood biochemistry and others. Features were divided into static and dynamic, and the model was validated multiple times. RNN model adapted to changing clinical data during mechanical ventilation and provided real-time guidance for extubation. The two biggest drawbacks were, 1) RNN complex algorithm and how it used static and dynamic variable indices to arrive at weaning prediction. The algorithm was so complex that it may limit clinical use and adaptability to use at the front line, and 2) The Model was developed using a retrospective database and not prospectively validated (Zeng, 2022)

3. **Data privacy and security**: Models are usually developed using sensitive and personal data during training. Ensuring privacy and security of data throughout the model development process is critical to protect individuals' rights and prevent unauthorized access.

4. **Algorithmic dependence**: A model developed using specific conditions or data sources may reveal its dependence on certain algorithmic patterns or methodologies. Understanding and mitigating this dependence is important to prevent unintended consequences or vulnerabilities.

5. **Equitable access and impact**: A model should consider ensuring equitable access and impact across different user groups or populations. The model should be designed in a way that benefits all stakeholders fairly and does not exacerbate existing disparity.

6. **Regulatory compliance**: Adhering to relevant laws, regulations, and ethical guidelines is paramount during the model development process. Compliance helps

mitigate legal risks and ensures responsible development and deployment of ML models.

2.7. Model developed using retrospective data versus prospectively validated model.

Antuani Rafael Baptistella et al developed and validated an extubation predictive score (ExPreS) index. ExPreS scoring system was developed using multiple variables namely Rapid shallow breathing index (RSBI) during SBT, dynamic lung compliance, duration of Invasive mechanical ventilation, estimated Glasgow coma score, haematocrit, serum creatinine and neurological assessment. Variables were a combination of respiratory and non-respiratory factors associated with extubation outcome. Once the model was prepared, it was then prospectively applied and validated in eighty-three patients with a success rate of 97.6%. The model also created an ExPreS scoring system with a score of more than 59 is associated with high success, 45-58 is associated with intermediate and less than 44 is associated with low success. The model was validated prospectively and performed well during front-line clinical application. One of the bigger strengths of any model is external validation as well as wider generalizability as it reinforces confidence among users (Baptistella, 2021) and clinical teams. In comparison, the model developed using retrospective data either publicly available or otherwise risks accruing significant bias with poor external validity.

2.8. Features of an Ideal Ventilator Weaning Model.

1. Model is developed using a combination of patient physiological variables, dynamic ventilator variables during SBT, laryngeal oedema as well as patient past cardio-respiratory medical history.

2. The model is developed by collecting data prospectively in a large subset of patients with varying primary reasons for invasive mechanical ventilation.

3. The final model is then externally validated and made generalizable to a wider cohort of patients.

4. The model is dynamic with output included within a clinical information system or an electronic patient record.

5. The model is adaptive and undergoes continuous reinforced learning to optimize predictability.

3. Methodology

3.1 Introduction

The methodology should be a comprehensive approach that combines rigorous prospective data analysis with strategic planning to achieve the primary aim of reduction in the weaning failure rate for all patients admitted to the critical care unit. It is important to use both quantitative and qualitative research methods to gain a holistic understanding of the problem at hand and develop actionable insights. The methodology should be such that it allows to adapt to changing circumstances and incorporate feedback throughout the process. It should also be open to ensure transparency and alignment, ultimately driving effective decision-making and delivering tangible results. Improve upon the current liberation failure rate, may be achieved through a transparent process in two stages:

3.2 First stage: A qualitative quality improvement strategy

A qualitative quality improvement strategy with four stages and two double diamonds. The double diamond design model is represented by two diamond shapes, indicating a process of divergent and convergent thinking. The first diamond represents the stage of defining the problem, and the second diamond represents the stage of defining the solution. The problem phase is further separated into the discovery phase where the actual problem is extensively discovered and analysed using divergent thinking. In the define phase problem is evaluated extensively using data captured during the discovery phase. The problem phase is followed by the solution phase, which is divided into the development and delivery phases. Analysis and learning as per data captured during the problem phase are further developed with the aim to deliver on to the clinical area. (Anon., n.d.).

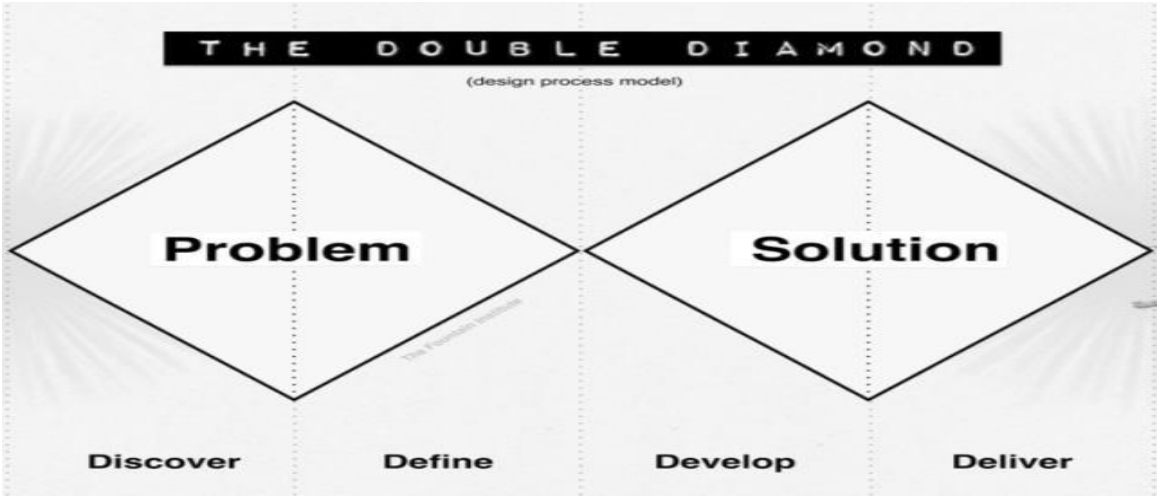

Figure 6: Four separate stages on a double diamond quality improvement phase. Discover phase to define the problem using divergent thinking, define to narrow down on key problems using convergent thinking. The solution phase is then divided into the developing and delivery phases. The develop phase is the steps that are developed as a solution and finally deliver phase is where solutions are delivered, and impact is assessed.

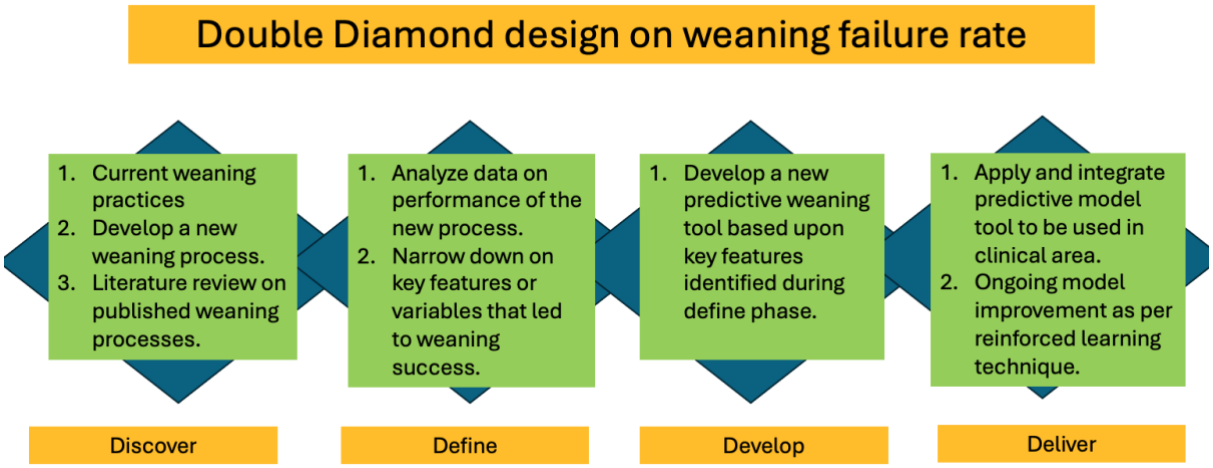

Figure 7: Description of double diamond design on weaning failure. It is divided into four steps, 1) Discover phase – Defining current weaning practices and literature review to develop a new weaning process 2) Define phase – Analyse data on the performance of the new process with statistical identification of key weaning features 3) Develop a new predictive modelling tool using key variables, and lastly 4) Apply and integrate the tool in day-to-day clinical decision making.

3.2.1 Double diamond design process in relation to weaning failure.

Figure seven explains the double diamond approach and processes that will be required at every stage.

1. **Discover:** In this phase, the aim will be to describe existing weaning practices at the local unit level with the aim to capture all nuanced decision-making. During this stage, there will be no direct interference with front-line clinicians with the aim of discovering the problem scope in detail. Data will be collected on weaning failure rate, steps used by the medical team to make clinical decisions and subsequent impact on patients like rate of aspiration pneumonia, hospital, and critical care duration of stay. Simultaneously, a detailed published literature review will be undertaken to extract important extubation variables that have led to successful weaning. Based upon initial data collection and literature review, a new multi-disciplinary weaning process will be established to arrive at a final weaning decision. This step is key as it will establish a very standard baseline among the clinical team. Standardisation will avoid variation and will help to better apply statistical tools in the define phase to narrow down on key variables/features.

2. **Define**: During this phase, evaluation is performed of the new multi-disciplinary weaning process. Data is analysed using ML statistical tools to identify key variables that are directly or indirectly impacting upon weaning success or failure.

3. **Develop**: A new predictive modelling tool is developed using statistically significant variables identified during the define phase. The modelling tool will undergo strict testing to establish validity and generalizability.

4. **Deliver**: To deploy new predictive modelling tools and then test them within the clinical environment. A continuous and ongoing analysis of the established pathway will be undertaken to fine-tune the whole process based on any new evidence or feedback from the existing process.

3.2.2 Discovery phase

Whilst the discovery or description phase aims to explore existing practices, there is a need to first standardise certain elements of weaning pathway. This standardisation will be achieved through undertaking a combination of literature review and mapping current weaning decision-making criteria. Standardisation of the process will be narrowed down to three stages involving nursing staff, physiotherapists, and the medical team. The process will involve the assessment of

patients using objective criteria in a structured format. The three stages are described as follows:

Stage 1 – Nursing team led:

A) Spontaneous Awakening Trial (SAT):

Continuous infusion of sedative drugs should be slowly reduced to achieve a patient-specific awakening from a chemical coma. Appropriate analgesia and other intravenous medications to manage agitation should be prescribed to avoid the need for re-sedation where possible. Planning to liberate the patient from the ventilator should start a day or few hours before. For patients who have been identified by the medical team as appropriate for planned extubation the next morning, nurse-led bedside interventions are as follows:

Enteral feeding through gastric tube is to be stopped at 0400 (if applicable) on the planned day of ventilator weaning, add 10% dextrose intravenously to replace calories if on Insulin. Enteral feeding is stopped early to minimise the risk of aspiration pneumonia.

Discussion with the medical team regarding the plan for analgesia (Medication to prevent pain from the ETT) and use of appropriate medication for managing agitation to avoid re-introduction of sedative medications where possible. Between 0400 and 0830 sedation medications are to be optimised with further decrease in dose to achieve a safe awakening from the chemical coma.

Stage 2 - Physiotherapy team led:

Physiotherapy staff will liaise with the medical team to confirm patients are being considered for liberation from mechanical ventilation. The physiotherapy team will also liaise with the bedside nursing team to optimize sedation and will perform many tests in a systematic fashion to assess readiness to come off from the ventilator. Assessments and tests done will be mainly as follows:

A) **Spontaneous Breathing Trial (SBT):**

SBTs are performed to evaluate whether the patient can breathe without ventilatory assistance. Suggested SBT settings can be either using pressure support ventilation where the patient is connected to a ventilator and ventilatory assistance is reduced or a T-piece where the ventilator is disconnected completely for thirty minutes to one hour, and respiratory and patient physiological features are measured.

The criteria for SBT 'failure' are: Below are some of the criteria which may help to differentiate between SBT success and failure.

The respiratory rate is more than thirty-five to forty for five minutes.

Increased use of neck accessory muscles.

SpO2 (Oxygen saturation) is less than ninety percent with FiO2 (fraction of inspired oxygen) more than fifty percent.

Heart rate >140 beats per minute or >25% above baseline.

Systolic blood pressure >180mmHg (millimetres of mercury).

Sudden cardiac arrhythmias.

Worsening agitation, anxiety, or depressed mental state.

Apart from SBT, other factors that are important to successfully achieve extubation include neurological status, quantitative assessment of secretion load and cough strength. It is therefore imperative to concomitantly perform other extubation indices as they provide objective evidence to inform the decision-making process. Not all tests will be required to be performed on every patient type.

B) **Peak Cough Expiratory Flow (PCEF):**

This manoeuvre aims to provide an objective assessment of cough strength. The procedure is undertaken by asking the patient to cough or observe a spontaneous cough. If the patient is unable to follow instructions to cough, 2 millilitres of saline can be instilled via the endotracheal tube to elicit a cough. If the PCEF is more than sixty litres per minute, it is very effective, and the patient can now be considered to have passed the test.

C) **Occlusion pressure at 100 milliseconds (P0.1):**

This is a test of respiratory or breathing drive and is therefore non-volitional. It is the negative pressure that occurs 100 milliseconds (0.1 seconds) after a spontaneous inspiratory effort has been detected. Patients who remain on ventilators for many days to weeks lose the capability to perform synchronised breathing activity when attempting to decrease ventilatory assistance. This is reflected in a higher breathing drive which requires targeted training.

D) **Maximum Inspiratory Pressure (MIP) or Negative Inspiratory Force (NIF):**

This manoeuvre aims to provide an objective assessment of inspiratory muscle strength. It is the negative deflection in pressure during active, maximal effort to breathe during an expiratory hold manoeuvre. This manoeuvre is performed whilst the patient is still connected to a mechanical ventilator.

E) **Neurological status:**

A patient must be able to maintain an open and patent airway following extubation. In addition, the inability to respond to basic commands is associated with a high probability of extubation failure. The patient will be asked to squeeze their hand and track with their eyes. It is recognised, however, that this assessment is very crude and may not be appropriate for some patients with neurological injuries.

F) **Secretion load:**

Although this is a subjective assessment, the presence of excess or copious respiratory secretion is associated with weaning failure. Patients with moderate to abundant secretions may be more than eight times as likely to fail extubation than those with mild or no secretions. The frequency of endotracheal suctioning required, and volume of secretion load should be discussed with the bedside nursing staff.

Extubation risk stratification: Following assessment using the above features, patients will be stratified into 'low, moderate or high' risk for extubation.

Stage 3 – Medical team led:

G) Endotracheal tube (ETT) cuff leak test

To perform this test, it is imperative to pre-warn the patient as deflation of the ETT cuff will elicit discomfort and may trigger a coughing bout. The first step is to perform an oral cavity, posterior pharynx, ETT and subglottic port suctioning, The ETT cuff is deflated with the aim of ascertaining audible leak and deficit of expired tidal breath. An expired tidal breath deficit of more than 110-130 ml has good specificity to rule out upper airway oedema. If the patient has failed a cuff leak test, it is imperative to begin treatment prior to performing a repeat test.

Two treatments that have been proven to help with decreasing airway oedema are as follows:

1. **First line**: Dexamethasone 6.6 mg 4 hrs prior to extubation attempt if the patient has multiple risk factors (pre-emptive), a second dose of 6.6mg dexamethasone can be given if stridor is present post-extubation.

2. Second line: 2.5 ml of 1% epinephrine via Aerogen vibrating mesh nebuliser (VMN).

The aim will be to collect objective data for all three phases, as well as final weaning clinical decisions.

Roll-out Process: Roll-out will be in a phased manner till all members of the multi-disciplinary team had a chance to read the new guidance. Multi-professional collaboration will be key to ensure all stages are completed in a timely manner and data collected as per plan.

Table 1: Three stages of liberation assessment by multi-disciplinary team.

Three stages and MDT members roles in liberation from mechanical ventilation.		
STAGE 1	Spontaneous Awakening Trial (SAT) 1. If Yes, Sedation titration to an acceptable and safe level to achieve spontaneous awakening trial and spontaneous breathing on ventilator.	NURSING TEAM
STAGE 2	Physiotherapist led assessment of multiple weaning indices: 1. Perform spontaneous breathing trial (SBT) 2. Other extubation indices objective measurements based upon individual patient physiology, - Cough strength with Peak cough expiratory flow. - Respiratory drive with Occlusion pressure at 100 milliseconds (P 0.1) - Inspiratory Muscle strength using data from maximal inspiratory strength or Negative Inspiratory force. 3. Objective assessment of neurological status by measuring Glasgow coma score and using simple basic commands, 4. Objective assessment of secretion load and categorization into mild, moderate, or copious secretion load. 5. Data collection of stage 2 and 3 variables.	PHSIOTHERAPY TEAM
STAGE 3	Medical team led endotracheal tube cuff leak assessment, 1. Perform ETT cuff leak test. Initiate appropriate treatment if multiple risk factors are present or no cuff leak. Medical team led final decision on liberation from MV, 1. Review from medical team on all data points captured as above and making final decisions on whether to liberate patients from ventilator or not.	MEDICAL TEAM

Data Collection

Objective data for all stages will be collected in a standardised format, first on a paper proforma followed by the transfer of data onto a secured electronic system.

Data will be collected by members of the physiotherapy team. The aim of the data collection proforma will be to capture data for all stages, and these are as follows –

1. Age.

2. Body mass index (BMI).

3. Gender – Male or female.

4. Primary and secondary reason for critical care admission.

5. Past medical history like diabetes, hypertension, chronic cardio-respiratory diseases like asthma and chronic obstructive pulmonary disease (COPD).

6. Date of institution of invasive mechanical ventilation.

7. Number of failed extubation since the institution of invasive mechanical ventilation.

8. Sedation scores namely Richmond agitation sedation scale (RASS) when sedative medications were stopped.

9. SBT attempted or not, if yes what were the physiological variables like respiratory rate, heart rate, rapid shallow breathing index (RSBI), dynamic lung compliance, partial pressure of oxygen and carbon dioxide during RSBI? Did the patient pass the SBT or not and record that information as yes or no?

10. Extubation indices to be completed at the end of SBT like occlusion pressure at hundred milliseconds (P0.1), Maximum inspiratory pressure (MIP) and peak cough expiratory flow (PCEF).

11. Quantify airway secretions load objectively into mild, moderate, and severe.

12. Objectively record the neurological status of patients using the Glasgow coma score.

13. Endotracheal tube cuff leak present or absent.

14. Outcome on the weaning decision as extubated or not at that moment as well as within 72 hrs.

3.2.3 Define:

The first phase will unify and standardize the whole liberation pathway. Crude data from the first phase will be used to assess overall performance and the impact of the new process on the liberation success rate. It will also provide guidance on how to optimize the process further through either the addition or removal of any variable. This will be done as per the double-diamond approach of divergent and convergent thinking. Standardizing the process initially and collecting a standard dataset will go a long way in removing inconsistencies in the weaning approach used by colleagues, will address missing values and outliers that might be difficult to evaluate in future and may also make the prediction model extremely unstable. Data will also be analysed for inconsistencies or any potential for improvement.

Data will be described using descriptive statistics. Common descriptive statistical tools like mean, mode, median, range, proportion and standard deviation will be used to summarize and describe the important characteristics of the dataset. A pre- and post-analysis of the process will be performed. Pre-analysis will involve the calculation of the baseline weaning failure rate before the introduction of a new process.

Some of the examples of how data will be defined are as follows:

1. Mean age of study participants.

2. Mean BMI.

3. Gender distribution in percentage.

4. Number of days on mechanical ventilation, presented as mean.

5. Percentage of patients who were successful weaned from the ventilator through this process.

Primarily, the aim of data analysis will be to objectively quantify the weaning failure rate as well as identify the key variables that helps in differentiating between weaning success or failure. Variables that may help to differentiate between success and failure might be a combination of features involving patients, ventilator parameters and past medical history. It can also be an isolated single feature. Such variables will then be used to develop a predictive modelling tool in the next phase.

3.2.4 Develop:

In this phase, a predictive modelling tool to liberate patients from mechanical ventilators will be developed. Figure 8 shows steps on how a prediction model can be developed. Before developing any prediction model, it is important to ensure certain key characteristics are in place to increase the model's effectiveness and reliability.

1. **Clear Objective**: Define the specific problem the prediction model aims to solve and the desired outcome. A well-defined objective helps in selecting appropriate features, variables, and evaluation metrics. In this case, the primary aim is to reduce the weaning failure rate.

2. **Quality Data**: High-quality data is essential for building an accurate prediction model. Ensure the data is clean, relevant, and representative of the problem domain. Address missing values, outliers, and inconsistencies in the data pre-processing stage. Ensure data is collected after optimising decision variance and a set standard is established.

3. **Variable Selection**: Identify the relevant features (input variables) that will have a significant impact on the prediction. Correct and ideal feature selection helps in reducing dimensionality, improves model performance, and avoids overfitting. Narrowing on variable selection can come from an extensive literature search on the topic as well as in-depth knowledge of the clinical problem at hand.

4. **Data Splitting**: Divide the dataset into training, validation, and test sets. The training set is used to train the model, the validation set is used to tune hyperparameters and evaluate model performance during development, and the test

set is used to assess the final model's generalizability. Datasets can be trained through two ML principles – Supervised and Unsupervised machine learning.

4a) **Supervised machine learning:**

Supervised ML is a type of ML where the algorithm is trained on labelled data. This means the input data is paired with the correct output, allowing the algorithm to learn the mapping between the input and output variables. The goal is for the algorithm to learn to predict the output accurately for new unseen data based on the patterns it learned during the training. Common supervised learning tasks include regression techniques. Output data could be weaning failure rate and regression techniques can be applied to identify input factors which are leading directly to weaning success.

4b) **Unsupervised machine learning:**

Unsupervised ML is a type of ML where the algorithm is trained on unlabelled data. Unlike supervised learning, there are no predefined labels or output associated with the input data. Instead, the algorithm learns to identify patterns, structures, or relationships within the data on its own. It plays a crucial role in exploratory data analysis, pattern recognition and data pre-processing tasks. The main goals of unsupervised learning include:

A) **Clustering:** Grouping similar data points together based on their intrinsic characteristics. Common algorithmic tools like k-means clustering are useful.

B) **Dimensionality reduction**: Reducing the number of features or variables in the data while preserving its important information.

C) **Anomaly reduction**: Identifying unusual or anomalous patterns in the data that deviate from normal behaviour. Anomaly detection algorithms aim to distinguish outliers or anomalies from most of the data.

Unsupervised learning tools will be less useful as the input and output variables are already known.

5. **Evaluation Metrics**: Choose appropriate evaluation metrics based on the nature of the prediction problem (e.g. R-squared for regression). Select metrics that align with the initial objectives and priorities.

Outcome metrics like weaning failure rate will be a key metric to measure.

6. **Model Selection**: Select the appropriate prediction model based on the problem requirements, data characteristics, and available resources. Consider various algorithms (e.g., logistic regression) and choose the one that best fits the problem domain and data. Logistic regression is used for binary tasks, where the output variable has only two possible outcomes (e.g., yes/no). It models the probability that an input belongs to a particular class using the logistic function, which maps any input value between zero and one. If the probability is above a certain threshold, the input is classified as belonging to one class; otherwise, it is classified as belonging to another class.

7. **Validation Strategy:** Implement proper validation techniques such as cross-validation to assess the model's performance and generalizability. Validate the model on multiple datasets to ensure its robustness.

8. **Interpretability and Explainability**: Ensure the prediction model is interpretable and explainable, especially in domains where decision-making transparency is critical. Understandable models are easier to trust and deploy in real-world scenarios.

Addressing these key characteristics will help to build a strong foundation for developing a reliable and effective prediction model in weaning patients from mechanical ventilation. Developing a generalizable prediction model needs detailed planning as well as meticulous execution of all steps in a linear fashion.

The prediction model to correctly predict liberation from a mechanical ventilator will need a large dataset and routinely collected important key variables. If variables are collected without any error or with minimal missing values, it improves model development and performance. Application of supervised learning tools and models

like logistic regression to narrow down key variables with better predictability and ability to validate tools for better model performance and generalizability.

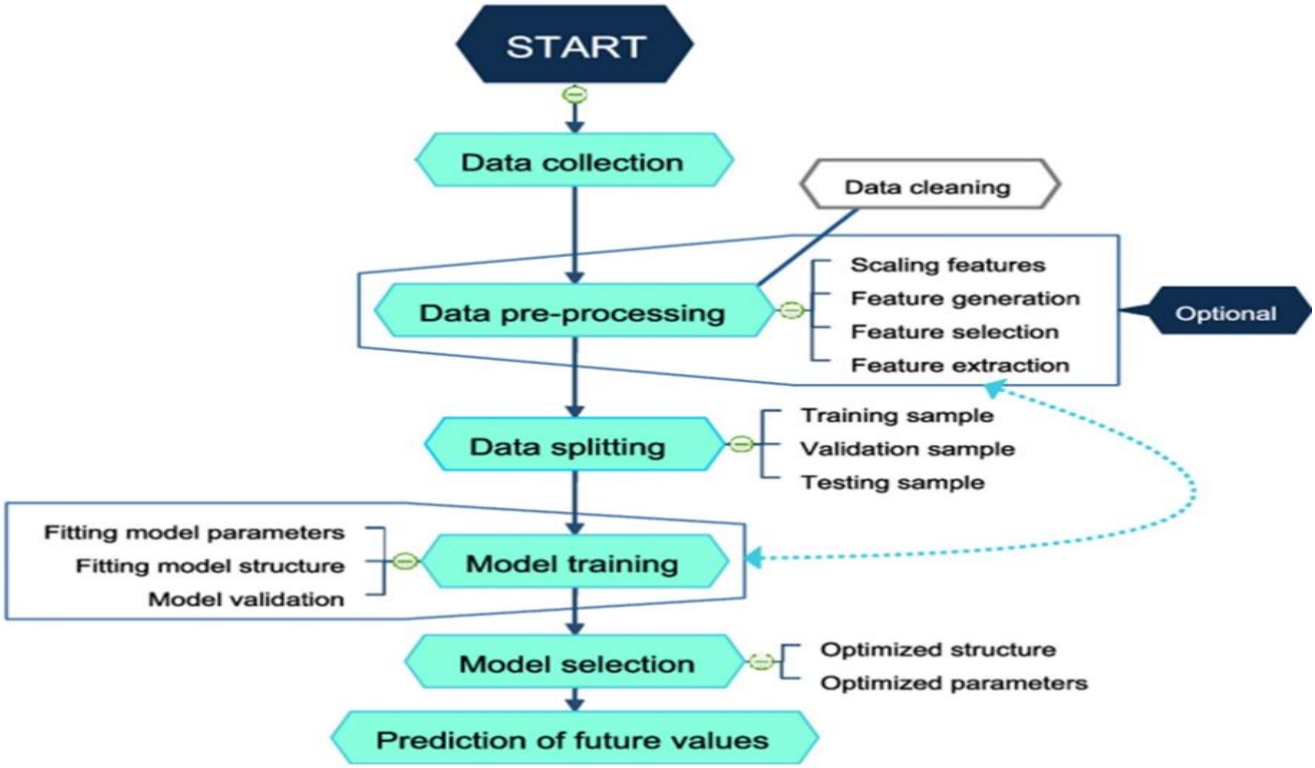

Figure 8: Process and steps involved in building a prediction model. The first step is data collection, followed by data pre-processing. Data is first cleaned using multiple tools. After data pre-processing, data is then split into training, validation, and test sets. The model is then trained using multiple features like model fitting and model validation. After training is done, the model is then selected and used clinically to perform future predictions.

3.2.5 Deploy:

Deployment of a prediction modelling tool will be the last step in the double-diamond approach. Once a prediction model is prepared, it will be tested and deployed in a clinical environment. The performance of the new model will be continuously monitored whilst being used in a clinical environment. The tool and subsequent process will be agile to include any new variable or features that will further boost weaning predictability of model.

4. Results

4.1 Stepwise development of prediction model.

The development of a predictive model will be reported as per the TRIPOD-AI checklist (Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis Or Diagnosis – AI) (Collins, 2024). Collins and co-authors published a recent stepwise guidance on how to report and publish any new model development in a systematic fashion. Following is a description on how this model once developed will be published.

1. **Title**: A feasibility study for developing a predictive learning model to reduce liberation or weaning failure rate from mechanical ventilator in critically ill patients admitted to the adult Intensive care unit.

2. **Introduction**: On initial service evaluation, the liberation or weaning failure rate within the adult critical care unit at the University Hospital of Wales were found to be high. The aim is to develop a prediction model using prospective local patient data, which will include demographic details as well as patient physiological and ventilatory features. The adult critical care unit is a tertiary referral centre for a variety of services and pathways. It does not cater for patients admitted after cardiac surgery and individuals with ages less than sixteen years. The model will aim to include all patients who are admitted to the adult critical care unit, and the treating clinical team are planning to separate the patient from the breathing machine. The predictive model once developed will be used by the clinical team or critical care consultants and applied prospectively to help with decision making on ventilator separation. The model will not include any patients with ages less than sixteen years and patients will be included from any social or ethnic background.

3. **Objectives**: The study will aim to develop a prediction learning model on ventilator weaning using prospective data. Once the model is developed, it will be validated by the clinical team by making weaning decisions in collaboration with the predictive model result as well as using clinical acumen.

4. **Methods:** Routine care data will be used to train and develop a predictive model. As there is no clinical information system or electronic patient record, the model can only be developed prospectively. The project will be undertaken as a service evaluation as no patient randomisation will take place. The study will start from 1st February 2024 and will run for one to two year or until all patients are recruited. The study will take place at the University Hospital of Wales adult critical care unit, a secondary care healthcare setting. All patients who are being weaned from the ventilator will be included in the study. No patient follow-up is designed as part of the study. Routine data like patient demographic details, number of days on mechanical ventilator, ventilatory variables like dynamic compliance, fraction of inspired oxygen during spontaneous breathing trial, reason for mechanical ventilation, and past medical history will be collected.

5. **Outcome**: The primary outcome is to decrease the weaning failure rate from mechanical ventilator; this will be achieved by first developing a predictive modelling tool and then using it in combination with clinical acumen and analytical knowledge for all decision-making related to weaning for all patients. The aim is to run a study over one to two years initially to develop the model followed by one year to validate the model locally. During the period of validation and clinical use, data will be collected on percentage of weaning failure rate, impact of the model in reducing the failure rate as well as clinical team satisfaction survey. The process of blinding will not be applied at any stage.

6. **Predictors**: The prediction model will be built upon multiple variables. The selection of variables is based on features that were used in already published literature, along with new features that were added based on clinical judgment and using recent clinical research literature. Predictors are divided into the following categories:

A. **Demographics and Past medical history**: Age, Gender, History of any cardio-respiratory pathology.

B. **Disease-related**: Duration of mechanical ventilation, fluid balance, a primary disease that led to the institution of mechanical ventilation namely pneumonia, brain trauma stroke or heart failure.

C. **Mechanical ventilation related**: Dynamic lung compliance and PaO2 (Partial pressure of arterial oxygen saturation) over FiO2 (Fraction of Inspired Oxygen from the ventilator) ratio during SBT.

D. **Patient-related**: Cough strength, respiratory secretions load, ETT cuff leak test, sedation level score during SBT.

E. **Post-extubation variables**: Incidence of weaning failure rate, reasons for extubation, rate of secondary infection post-extubation failure, or any other complications.

Predictor data collection will not be blinded. All the models published until now have described the importance of variables based on data analysis of retrospective electronic patient records. This will be the first feasibility study where important and routine variables related to weaning and extubation will be collected prospectively to develop a liberation prediction model.

7. **Study sample size**: The aim is to prospectively include all consecutive patients for one to two years who have been scheduled to be liberated from the ventilator and admitted to University hospital of Wales adult critical care unit. The adult critical care unit admits approximately thirteen to fifteen hundred patients annually and seventy percent of such patients are admitted needing mechanical ventilators. The aim will be to collect data for nearly five to six hundred patients over a two-year period. Data sets will be separated into training, validation, and testing sets. If the prospectively collected data is limited, a K-fold cross-validation technique is used. The training set is further divided into K subsets, one of is used for validation and the other, the K-1 subset, is used for training. After K repetitions of this process, wherein each repetition, a different validation subset is used, the best model is chosen and assessed versus the test set. Sensitivity, specificity, area under curve, F-factor and accuracy will be calculated using multiple ML models like logistic regression (LR), Random forest (RF), support vector machine (SVM), Categorical boosting (CatBoost), eXtreme Gradient boosting (XGBoost), light gradient boosting machine (LightGBM). If there are any missing data, it will be imputed using statistical tools.

8. **Analysis**: Data will be separated into training and testing datasets. The model will be developed with an output aim of decreasing liberation failure rate and input variable of use of multiple patient, demographic and ventilator data. Variables or hyperparameters will be given individual points based on clinical importance and the model will be validated using statistical tools. R or Python programming will be used to run all statistical tools. The output will be defined as the probability of extubation success or failure. Once the model is developed, the aim will be to validate it further in other sub-speciality of critical care settings like cardiothoracic. External validation will boost model generalizability and ease of adaptation in wider and different critical care sub-speciality. Supervised ML will be used for the regression of a new observation based on a training set. Deep learning and artificial neural networks are considered more advanced or sophisticated forms of machine learning algorithms. Neural networks mimic the nervous system by constructing neural layers such as input, output, and in-between hidden layers. Deep learning can be categorized as neural networks with multiple hidden node layers, making the network size larger and allowing the model to be accurate. The model once developed should be able to provide predictions that are close to the training set observations; otherwise, the model is underfitted. On the other hand, ML models should be generalized beyond the scope of the training set or an overfitted model.

9. **Open Science**: The feasibility project is approved by the Cardiff and Vale University Health Board quality improvement team as a service evaluation project with waving off individual participant consent. The project has no source of funding yet established but an application will be submitted to NIHR (National Institute for Health and Care Research) to bid for some innovation funds. There is no conflict of interest between any study investigators. The study protocol and data sets have been approved by the information governance team and data will be collected on the redcap IT digital system. The study protocol has been registered as a LIMON (Liberation from Invasive Mechanical ventilatiON) project. Application to register study was submitted to Cardiff and Vale quality and audit team and it has been approved for two years from the date of start of study. Collected data will be stored in both physical paper format as well as in digital redcap IT system. Anonymised data will be made available to any investigator in

future after an appropriate request has been made through proper information governance channels. Codes that are developed during the analytical phase will be stored securely within or outside the Redcap platform and can be shared with any other investigator for scrutiny.

10. **Results**: The total number of participants included in the final analysis will be described including the outcome of extubation success and failure. This will be described through a summary diagram. The study period will be described in detail, including all the participant's characteristics and key variables. Description of details on missing data, total sample size, modelling tools used and any statistical difference between features. If there is missing data, what tools were used for imputation and whether any impact of such tools on the final model? Prediction model development will be described in detail including ML or deep learning tools used for the development and validation. A process on how training and testing datasets were developed, sensitivity, specificity, confidence interval, and area under the curve for all ML tools.

11. **Discussion:** In the discussion part, describe a model which can predict extubation success and failure with the highest statistical probability. Discuss the merits of results, any imputation used, feature selection and how this study has fared as compared to another already published study. Discuss model validation, limitations, and generalizability and what could be further done to improve upon research in this field.

4.2 Result of an initial service evaluation project done at University hospital of Wales, Cardiff

An initial service evaluation was done to objectively define burden of weaning failure rate on the critical care unit. This was undertaken for a period of four weeks. The data showed that weaning failure rate was around twenty-seven percent. This process helped to collect baseline data on problem burden. The data was analysed in detail to evaluate on what were the main reasons that led to weaning and extubation failure. It was then followed by introduction of a new guidance and weaning process which was based upon extensive literature review as well as learning from initial data collection. This new process was then disseminated widely

across multi-disciplinary team for imbedding new learning. A re-audit was done to evaluate the effect of new weaning process. Re-audit was done only on some areas of critical care unit. The results of the new audit showcased marked reduction in incidence of weaning failure rate. In total, 23 weaning assessments were included in the initial analysis with liberation failure rate of only 6.25%. In comparison, colleagues who did not use such process has a weaning failure rate of 17.4%. Similarly, attempted extubation in critical care area where this process was not started also showed a significant higher weaning failure rate of 22.7%. These results show signal that new weaning process is robust which has resulted in decrease in failure rate, but it needs larger data sets to arrive at any firm conclusion. Early results only support undertaking a large feasibility study to develop model.

Table 2: Results of 23 patients who undergone extubation as per new weaning process.

Outcome	Total	Reason for reintubation or not extubated.	%
Extubated	16		
Re-intubated	1	Secretion load, FiO_2 requirement.	6.25
Not extubated	6	2 SBT criteria not met. 1 failed SBT. 2 low GCS. 1 wait until morning.	

Table 3: Result of patients who were extubated within critical care zone where new process was launched but due to varying reasons decided not to follow new weaning process.

Outcome	Total	Reason for reintubation	%
Extubated	23		
Re-intubated	4 (+1 more than 72 hours)	4 increased FiO_2 requirement, secretion load and cough	17.4

Table 4: Result of patients who were extubated in critical care zone where process was not launched.

Outcome	Total	Reason for reintubation	%
Extubated	22		
Re-intubated	5	2 increased FiO_2 requirement, secretion load and cough 2 T2RF and agitation 1 Stridor	22.7

5 Discussion:

The adult critical care unit at the University Hospital of Wales, Cardiff is one of the largest tertiary hospitals in Wales. The proportion of patients needing advanced airway support or mechanical ventilation is nearly seventy per cent of all critical care admissions, which equates to nearly nine hundred to thousand patients admitted annually. The critical care unit is a tertiary referral centre for many specialized pathways like trauma, neurosurgery, haematology, and cardiology. Patients are put on mechanical ventilator for a variety of clinical conditions or pathological states. Some of the common conditions like pneumonia and heart failure top the list of indications for the institution of mechanical ventilation.

Local clinicians in the past were evaluating patients for weaning readiness without any established pathway or protocol. There was a wide variation in steps undertaken by clinical team and individuals to reach a defined weaning endpoint and most of the patients were unable to achieve successful weaning. Also, currently in Wales there is no digital electronic patient record (EPR) or clinical information system which prospectively collects all the patient clinical data in one place. Lack of EPR affects retrospective evaluation of routinely collected patient features as well as ability to make any improvement. Some of the features like patient demographics and past medical history are collected in different national electronic system which is transcribed from the admission proforma or booklet for the unit. Ventilatory and physiological variables are directly transcribed from monitors onto a large “ICU chart”, which is changed every twenty-four hours. Similarly, data on neurological state, cough strength and ventilatory parameters are all located in different silos, some on paper charts and some recorded digitally. Location of data in multiple silos is a major issue and probably the primary reason for a higher weaning failure rate.

Collating all information on features in a structured and streamlined process with added input from a validated predictive modelling tool will go a long way in reducing the current weaning failure rate. Models will be developed using local patient cohorts which hopefully will provide higher internal validity.

Also, extubation or liberation failure rate in general has a significant impact on not only the patient but the wider healthcare system as well. Some of the patient and hospital impact are described as below-

Impact on the patient:

1. Extubation failure rate directly increases patient mortality and morbidity. Successive failure rate adds to cumulative critical care mortality.

2. Increased rate of ventilator associated pneumonias and antibiotic usage, more incidence of other organ failure namely renal and circulatory failure needing dialysis and other supportive treatment.

3. Increased critical care unit and hospital stay.

4. Delayed recovery from primary illness and poor quality of life on hospital discharge.

5. Increased need for rehabilitation program and rehabilitation duration before discharge.

Impact on Hospital:

1. Increased bed occupancy rate.

2. Higher cumulative treatment cost.

3. Increased duration of ICU and hospital stay.

4. Impact on availability of beds and timely admission for new patients.

So, based on the wide-ranging impact on both patients and institutions, extubation decisions must be made after exhaustive evaluation of all clinical and ventilatory

features for all patients individually. Use of predictive modelling tool in collaboration with clinical acumen may improve the probability of successful extubation in general.

Models that have been published are developed until now using large language ML algorithms like artificial neural networks and convoluted neural networks, they all use complicated statistical tests and analysis to derive conclusions. Most of the published models have been developed using retrospective electronic patient records (EPR) using routinely collected patient and ventilatory features. Some of the retrospective data have either come from open-source published hospital records like MIMIC-2 and MIMIC-3 or have come from single-centre studies from hospitals in China and Taiwan. Features used for creating models were diverse and ranged from evaluating single variables like heart rate variability to multiple features which included patient demographics, past medical history, and ventilatory and physiological variables. Retrospective studies by inherent nature are prone to biases like recall or selection bias, as they rely on existing data rather than controlled and randomised experiments. They are also limited in their ability to establish causation due to the design of experiments being purely observational. One model was also integrated with clinical information systems or electronic patient records. Integration helped clinicians to see how weaning predictions were changing on an hourly basis and inculcated confidence among clinicians to use the modelling tool and included probability results in clinical decision-making. It is also imperative to explain the ML or AI model and how it was developed transparently. If the model is not thoroughly explained, interpretable or understood by users, it can be problematic leading to distrust.

Also, some of the statistical tools used to develop prediction models like deep neural networks and convoluted neural networks have multiple hidden layers between the input and output layers. They are capable of learning complex patterns and representations from data, making them highly effective for tasks, but equally, they are incredibly complex to understand and sometimes they can be difficult to interpret. Such complex models also require large datasets to derive results. It is also important to validate model results prospectively in different healthcare settings

to have robust external validation and wider generalizability. Such measures were lacking in many published models.

This feasibility modelling development study is designed to overcome some of the limitations as seen in already published literature. This feasibility study is designed after reviewing high-impact literature to first narrow down on features that are key for extubation decision-making. Important features will then be structured and introduced in clinical area to be used prospectively. Result of decision making will then be prospectively recorded. The aim is to have a large set of data with a variety of patients included within it ranging from neuro-trauma to lung failure and other disease cohorts. Once data is recorded, a large language machine-learning model will be used to analyse recorded data. It is expected that a combination of features will be able to predict success or failure with high accuracy. The model will then be applied prospectively in different clinical environments as well as in other centres to improve generalizability. Development of model in this way will avoid any limitations as learned from previous published studies and will be able to help with designing a robust model with high external validity and accuracy.

6. Conclusion

Success of any healthcare innovation or intervention not only depends upon sound scientific knowledge but also upon analysis of prospective or retrospective healthcare datasets. Nowadays, there are advanced statistical ML models which may help to better differentiate between what is important variable versus noise within the datasets. The aim of the feasibility study is to build a novel weaning model prospectively using key ventilatory, physiological and other patient related variables. The literature review demonstrated that many such studies are designed in the past with varying outcomes and largely most studies were not even externally validated. Also, many models were developed using retrospective rather than prospective data. This feasibility prediction model will be developed after undertaking a novel quality improvement methodology to optimise basic process of ventilatory weaning first. An interim analysis showed that there was reduction in weaning failure rate from twenty-seven percent to around seven percent. This result was positive and provides huge confidence that the final model will be clinically useful with high validity and accuracy. Also, clinical adaptation of new process gives confidence that prospective data collection will be of improved quality and suitable to build an effective ML model. There will be less data quality issues and assumptions made during the development of model which will improve sensitivity and specificity of predicting weaning success or failure.

The weaning model developed through this way will contribute significantly to the existing body of knowledge in the field of ML on ventilator weaning and will also have positive impact on clinical area related to ventilator weaning. Once model is developed, aim should be to apply model across critical care subspecialities like cardiothoracic surgery or trauma, as well as in different countries to improve external validity. A perfect ML algorithm built using TRIPOD-AI guidance will go a long way in providing support to clinical teams in day-to-day clinical decision making.

In conclusion, our feasibility study will explore designing a new ML model to reduce weaning failure rate from mechanical ventilation in critically ill adult patients. Interim analysis provided good signal with improved weaning outcome and will help to design a new ML weaning model with no inherent limitations.

7. References

1. Loscalzo et al. (2022) ‘Harrison’s Principles of Internal Medicine, 21st ed. (Dyspnoea, Chapter 37, Pg 263).
2. Loscalzo et al. (2022) ‘Harrison’s Principles of Internal Medicine, 21st ed. (Coma, Chapter 28, Pg 183).
3. https://en.wikipedia.org/wiki/Mechanical_ventilation.
4. McConville, J.F. and Kress, J.P. (2012) ‘Weaning Patients from the Ventilator’, The New England journal of medicine, 367(23), pp. 2233–2239. Available at: https://doi.org/10.1056/NEJMra1203367.
5. PHAM T, HEUNKS L, BELLANI G, MADOTTO F, ARAGAO I, BEDUNEAU G, GOLIGHER EC, GRASSELLI G, LAAKE JH, MANCEBO J, PEÑUELAS O, PIQUILLOUD L, PESENTI A, WUNSCH H, VAN HAREN F, BROCHARD L, LAFFEY JG, 2023. Weaning from mechanical ventilation in intensive care units across 50 countries (WEAN SAFE): a multicentre, prospective, observational cohort study. lancet Resp Med, (11), pp. 465-476.
6. Béduneau, G. et al. (2017) ‘Epidemiology of Weaning Outcome according to a New Definition. The WIND Study’, American journal of respiratory and critical care medicine, 195(6), pp. 772–783. Available at: https://doi.org/10.1164/rccm.201602-0320oc.
7. Mehta, R. and Chinthapalli, K. (2019) ‘Glasgow coma scale explained’, BMJ (Online), 365, pp. l1296–l1296. Available at: https://doi.org/10.1136/bmj.l1296.
8. Page, V. and McKenzie, C. (2021) ‘Sedation in the Intensive Care Unit’, Current Anesthesiology Reports, 11(2), pp. 92–100. Available at: https://doi.org/10.1007/s40140-021-00446-5.
9. Thille, A.W. et al. (2022) ‘Spontaneous-Breathing Trials with Pressure-Support Ventilation or a T-Piece’, The New England journal of medicine, 387(20), pp. 1843–1854. Available at: https://doi.org/10.1056/NEJMoa2209041.
10. Smith, S.E., Newsome, A.S. and Hawkins, W.A. (2018) ‘An Argument for the Protocolized Screening and Management of Post-Extubation Stridor’, American journal of respiratory and critical care medicine, 197(11), pp. 1503–1505. Available at: https://doi.org/10.1164/rccm.201711-2364LE.

11. McConville, J.F. and Kress, J.P. (2012) ‘Weaning Patients from the Ventilator’, The New England journal of medicine, 367(23), pp. 2233–2239. Available at: https://doi.org/10.1056/NEJMra1203367.
12. THILLE, A.W., RICHARD, J.-C.M. and BROCHARD, L. (2013) ‘The Decision to Extubate in the Intensive Care Unit’, American journal of respiratory and critical care medicine, 187(12), pp. 1294–1302. Available at: https://doi.org/10.1164/rccm.201208-1523ci.
13. Thille, A.W. et al. (2020) ‘Role of ICU-acquired weakness on extubation outcome among patients at high risk of reintubation’, Critical care (London, England), 24(1), pp. 86–86. Available at: https://doi.org/10.1186/s13054-020-2807-9.
14. https://www.designcouncil.org.uk/our-resources/the-double-diamond/
15. https://www.sas.com/en_gb/insights/articles/analytics/a-guide-to-predictive-analytics-and-machine-learning.html
16. Page, M.J. et al. (2021) ‘The PRISMA 2020 statement: an updated guideline for reporting systematic reviews’, BMJ (Online), 372, pp. n71–n71. Available at: https://doi.org/10.1136/bmj.n71.
17. Pan, Q. et al. (2023) ‘Comprehensive breathing variability indices enhance the prediction of extubation failure in patients on mechanical ventilation’, Computers in biology and medicine, 153, pp. 106459–106459. Available at: https://doi.org/10.1016/j.compbiomed.2022.106459.
18. OTAGURO TAKANOBU ET AL, 2017. Machine Learning for Prediction of Successful Extubation of Mechanical Ventilated Patients in an Intensive Care Unit: A Retrospective Observational Study. J Nippon Med Sch, 88(5), pp. 408-17.
19. Huang, P.-H. et al. (2022) ‘Toward Evaluating Critical Factors of Extubation Outcome with XCSR-Generated Rules’, Bioengineering (Basel), 9(11), pp. 701-. Available at: https://doi.org/10.3390/bioengineering9110701.
20. Torrini, F. et al. (2021) ‘Prediction of extubation outcome in critically ill patients: a systematic review and meta-analysis’, Critical care (London, England), 25(1), pp. 391–391. Available at: https://doi.org/10.1186/s13054-021-03802-3.
21. Menguy, J. et al. (2023) ‘Defining predictors for successful mechanical ventilation weaning, using a data-mining process and AI’, Scientific reports,

13(1), pp. 20483–20483. Available at: https://doi.org/10.1038/s41598-023-47452-7.

22. Vollmer, S. et al. (2020) ‘Machine learning and AI research for patient benefit: 20 critical questions on transparency, replicability, ethics, and effectiveness’, BMJ (Online), 368, pp. l6927–l6927. Available at: https://doi.org/10.1136/bmj.l6927.
23. Watson, D.S. et al. (2019) ‘Clinical applications of machine learning algorithms: beyond the black box’, BMJ (Online), 364, pp. l886–l886. Available at: https://doi.org/10.1136/bmj.l886.
24. Zednik, C. (2021) ‘Solving the Black Box Problem: A Normative Framework for Explainable AI’, Philosophy & technology, 34(2), pp. 265–288. Available at: https://doi.org/10.1007/s13347-019-00382-7.
25. Pai, K.-C. et al. (2022) ‘Explainable machine learning approach to predict extubation in critically ill ventilated patients: a retrospective study in central Taiwan’, BMC anesthesiology, 22(1), pp. 351–351. Available at: https://doi.org/10.1186/s12871-022-01888-y.
26. Chang, Y.-J. et al. (2021) ‘A Real-Time AI-Assisted System to Predict Weaning from Ventilator Immediately after Lung Resection Surgery’, International journal of environmental research and public health, 18(5), pp. 2713-. Available at: https://doi.org/10.3390/ijerph18052713.
27. Kuo-Yang Huang et al. (2023) ‘Developing a machine-learning model for real-time prediction of successful extubation in mechanically ventilated patients using time-series ventilator-derived parameters’, Frontiers in medicine, 10. Available at: https://doi.org/10.3389/fmed.2023.1167445.
28. Kim, J. et al. (2023) ‘Machine Learning Algorithms Predict Successful Weaning From Mechanical Ventilation Before Intubation: Retrospective Analysis From the Medical Information Mart for Intensive Care IV Database’, JMIR formative research, 7, pp. e44763–e44763. Available at: https://doi.org/10.2196/44763.
29. Xie, R.-C. et al. (2024) ‘Development and validation of a clinical prediction model for early ventilator weaning in post-cardiac surgery’, Heliyon, 10(7), pp. e28141–e28141. Available at: https://doi.org/10.1016/j.heliyon.2024.e28141.

30. Fleuren, L.M. et al. (2021) ‘Predictors for extubation failure in COVID-19 patients using a machine learning approach’, Critical care (London, England), 25(1), pp. 448–448. Available at: https://doi.org/10.1186/s13054-021-03864-3.
31. YANG-HAN LAN ET AL, 2024. The intervention of AI to improve the weaning outcomes of patients with mechanical ventilation: Practical applications in the medical intensive care unit and the COVID-19 intensive care unit: A retrospective study. 103(12), pp. 37500.
32. Sheikhalishahi, S. et al. (2024) ‘Predicting Successful Weaning from Mechanical Ventilation by Reduction in Positive End-expiratory Pressure Level Using Machine Learning’, PLOS digital health, 3(3), pp. e0000478–e0000478. Available at: https://doi.org/10.1371/journal.pdig.0000478.
33. da Silva, R.B. et al. (2023) ‘Heart rate variability as a predictor of mechanical ventilation weaning outcomes’, Heart & lung, 59, pp. 33–36. Available at: https://doi.org/10.1016/j.hrtlng.2023.01.007.
34. Qin-Yu Zhao et al. (2021) ‘Development and Validation of a Machine-Learning Model for Prediction of Extubation Failure in Intensive Care Units’, Frontiers in medicine, 8. Available at: https://doi.org/10.3389/fmed.2021.676343.
35. Chung-Feng Liu et al. (2022) ‘An AI system to predict the optimal timing for mechanical ventilation weaning for intensive care unit patients: A two-stage prediction approach’, Frontiers in medicine, 9. Available at: https://doi.org/10.3389/fmed.2022.935366.
36. Liao, K.-M. et al. (2022) ‘Development of an Interactive AI System for the Optimal Timing Prediction of Successful Weaning from Mechanical Ventilation for Patients in Respiratory Care Centers’, Diagnostics (Basel), 12(4), pp. 975-. Available at: https://doi.org/10.3390/diagnostics12040975.
37. Chen, W.-T. et al. (2022) ‘A Simple Algorithm Using Ventilator Parameters to Predict Successfully Rapid Weaning Program in Cardiac Intensive Care Unit Patients’, Journal of personalized medicine, 12(3), pp. 501-. Available at: https://doi.org/10.3390/jpm12030501.
38. HUNG-JU KUO, 2015. Improvement in the Prediction of Ventilator Weaning Outcomes by an Artificial Neural Network in a Medical ICU. Respiratory Care, 60(11), pp. 1560-9.
39. Zeng, Z. et al. (2022) ‘Interpretable recurrent neural network models for dynamic prediction of the extubation failure risk in patients with invasive

mechanical ventilation in the intensive care unit', BioData mining, 15(1), pp. 21–21. Available at: https://doi.org/10.1186/s13040-022-00309-7.

40. Baptistella, A.R. et al. (2021) 'Prediction of extubation outcome in mechanically ventilated patients: Development and validation of the Extubation Predictive Score (ExPreS)', PloS one, 16(3), pp. e0248868–e0248868. Available at: https://doi.org/10.1371/journal.pone.0248868.
41. Collins, G.S. et al. (2024) 'TRIPOD+AI statement: updated guidance for reporting clinical prediction models that use regression or machine learning methods.

8 Appendices

APPLICATION FOR ETHICAL APPROVAL

RESEARCH STUDENTS This form is to be completed by the student within **SIX** months for full-time students and **TWELVE** months for part time students, after the commencement of the research degree or following progression to Part Two of your course. Once complete, submit this form via the ***MyTSD Doctoral College Portal*** at (https://mytsd.uwtsd.ac.uk). This document is also available in Welsh.
RESEARCH STAFF ONLY All communications relating to this application during its processing must be in writing and emailed to pgresearch@uwtsd.ac.uk , with the title 'Ethical Approval' followed by your name.
STUDENTS ON UNDERGRADUATE OR TAUGHT MASTERS PROGRAMMES should submit this form (and receive the outcome) via systems explained to you by the supervisor/module leader.

In order for research to result in benefit and minimise risk of harm, it must be conducted ethically. A researcher may not be covered by the University's insurance if ethical approval has not been obtained prior to commencement.

The University follows the OECD Frascati manual definition of **research activity**: "creative work undertaken on a systematic basis in order to increase the stock of knowledge, including knowledge of man, culture and society, and the use of this stock of knowledge to devise new applications". As such this covers activities undertaken by members of staff, postgraduate research students, and both taught postgraduate and undergraduate students working on dissertations/projects.

The individual undertaking the research activity is known as the "principal researcher".

Ethical approval is not required for routine audits, performance reviews, quality assurance studies, testing within normal educational requirements, and literary or artistic criticism.

Please read the notes for guidance before completing ALL sections of the form.

This form must be completed and approved prior to undertaking any research activity.
Please see Checklist for details of process for different categories of application.

SECTION A: About You (Principal Researcher)

1	Full Name:		Manish Pandey			
2	Tick all boxes that apply:		Member of staff:	☐	Honorary research fellow:	☐
	Undergraduate Student	☐	Taught Postgraduate Student	☒	Postgraduate Research Student	☐

3	Institute/Academic Discipline/Centre:	University of Wales Trinity Saint David
4	Campus:	Lampeter
5	E-mail address:	2113361@student.uwtsd.ac.uk
6	Contact Telephone Number:	
	For students:	
7	Student Number:	2113361
8	Programme of Study:	MSc Digital Transformation for Health and Social Care
9	Director of Studies/Supervisor:	Phillip Scott/Edward Conley

SECTION B: Approval for Research Activity

1	Has the research activity received approval in principle? (please check the Guidance Notes as to the appropriate approval process for different levels of research by different categories of individual)	**YES**	☒	**NO**	☐
				Date	
2	If Yes, please indicate source of approval (and date where known): ***Approval in principle must be obtained from the relevant source prior to seeking ethical approval***	Research Degrees Committee	☐		
		Institute Research Committee	☐		
		Other (write in) Cardiff and Vale University health Board.	☒	**11/01/2024**	

SECTION C: Internal and External Ethical Guidance Materials

	Please list the core ethical guidance documents that have been referred to during the completion of this form (including any discipline-specific codes of research ethics, location-specific codes of research ethics, and also any specific ethical guidance relating to the proposed methodology).

	Please tick to confirm that your research proposal adheres to these codes and guidelines. You may add rows to this table if needed.	
1	**UWTSD Research Ethics & Integrity Code of Practice**	☒
2	**UWTSD Research Data Management Policy**	☒
3	UK policy framework for health and social care research	☒

SECTION D: External Collaborative Research Activity

If there are external collaborators then you should gain consent from the contact persons to share their personal data with the university. If there are no external collaborators then leave this section blank and continue to section E.

1	Institution	N/A				
2	Contact person name					
3	Contact person e-mail address					
4	Is your research externally funded?		**YES**	☐	**NO**	☐
5	Are you in receipt of a KESS scholarship?		**YES**	☐	**NO**	☐
6	Are you specifically employed to undertake this research in either a paid or voluntary capacity?	Voluntary	**YES**	☐	**NO**	☐
7		Employed	**YES**	☐	**NO**	☐
8	Is the research being undertaken within an existing UWTSD Professional Learning Partnership (APLP)?	If YES then the permission question below does not need to be answered.	**YES**	☐	**NO**	☐
9	Has permission to undertake the research has been provided by the partner organisation?	(If YES attach copy) If NO the application cannot continue	**YES**	☐	**NO**	☐

Where research activity is carried out in collaboration with an external organisation

10	Does this organisation have its own ethics approval system?	**YES**	☒	**NO**	☒
	If Yes, please attach a copy of any final approval (or interim approval) from the organisation (this may be a copy of an email if appropriate).				

QI project - approved

Hi Manish,

A project has now been approved and can be accessed in Your QI Projects within the Quality Improvement section on the AMaT system.

Project title: Liberation from Invasive Mechanical ventilatiON (LIMON)

SECTION E: Details of Research Activity

1	Indicative title:	A feasibility study for developing a predictive learning model to reduce liberation failure rate from breathing machine/ventilator in critically ill patients admitted to Intensive care unit.		
2	Proposed start date:	01-03-2024	Proposed end date:	01-05-2024
	Introduction to the Research (maximum 300 words per section) **Ensure that you write for a <u>Non-Specialist Audience</u> when outlining your response to the points below:** *Purpose of Research Activity* *Proposed Research Question* *Aims of Research Activity* *Objectives of Research Activity* Demonstrate, briefly, how **<u>Existing Research</u>** has informed the proposed activity and explain *What the research activity will add to the body of knowledge* *How it addresses an area of importance.*			
3	**Purpose of Research Activity** Patients admitted to hospitals with acute organ failure may need breathing machine to support acutely failing organs. This is achieved by passing an endotracheal tube down the trachea and connecting it to breathing machine through an intermediary plastic tubing's between the endotracheal tube and breathing machine or ventilator. Breathing machine provides oxygen and removes carbon-dioxide and also provides rest to the body until primary illness or insult is resolved. Patients are given sedative medications to tolerate the endotracheal tube placed inside the trachea. Patients may then remain on breathing machine for days to weeks till the acute insult is resolved.			

	Once patient start showing early signs of recovery, doctors will stop sleep medications and start to awaken the patients with the aim to remove tube and disconnect patient from breathing machine. On most occasions, the liberation of patients from breathing machine is successful and occasionally patient may fail the process needing reinstitution of breathing support. Currently, decision to liberate patients from breathing machine are taken by clinician/doctors using combination of routinely available demographic, clinical and ventilatory variables. The liberation failure rate using above approach is high in the Intensive care unit at University hospital of Wales leading to direct and indirect harm, increasing length of ICU and hospital stay and increasing mortality and morbidity. A prospective quality Improvement project is designed where data will be collected prospectively for all patients undergoing the process of liberation with aim to develop a predictive modelling tool to facilitate and support doctor decision making at the bedside.
4	**Research Question** A feasibility study to develop a predictive modelling tool using patient demographic, clinical and breathing machine data variables to help with decision making in liberating patients from mechanical ventilation.
5	**Aims of Research Activity** A feasibility study on developing a tool to help with predicting success or failure in liberating patients from mechanical ventilation.
6	**Objectives of Research Activity** 1. A novel decision prediction tool to help in liberating patients from breathing machine rather than eminence knowledge. Once tool is validated and clinically adapted, it may help to achieve following objectives over time, 2. Reduce ongoing direct and indirect patient harm from higher liberation failure rates. 3. Reduce duration of ICU and hospital stay.

	Proposed methods (maximum 600 words)
7	The project will be run as a quality improvement project named “LIMON (**L**iberation of patients from **I**nvasive **M**echanical ventilati**on**)” where prospectively non-patient identifier information and routine data will be collected for all patients who are scheduled to be liberated from Invasive Mechanical ventilation. Collected data will be routine like patient demographic (e.g, age, and gender), clinical variables like days on artificial breathing machine and some breathing machine variables. Data will be prospectively collected for 2-3 months to enable development of a clinical prediction modelling tool. Data will be stored electronically on AMAT system.
	Location of research activity Identify all locations where research activity will take place.
8	Adult Intensive Care Unit, University Hospital of Wales, Cardiff.
	Research activity outside of the UK If research activity will take place overseas, you are responsible for ensuring that local ethical considerations are complied with and that the relevant permissions are sought. Specify any local guidelines (e.g. from local professional associations/learned societies/universities) that exist and whether these involve any ethical stipulations beyond those usual in the UK (provide details of any licenses or permissions required). Also specify whether there are any specific ethical issues raised by the local context in which the research activity is taking place, for example, particular cultural and/or legal sensitivities or vulnerabilities of participants. If you live in the country where you will do the research then please state this.
9	N/A *(this box should expand as you type)*

10	Use of documentation not in the public domain: Are any documents **NOT** publicly available?	**NO**	☐
		YES	☒
11			

	(this box should expand as you type)

	Does your research relate to one or more of the seven aims of the Well-being of Future Generations (Wales) Act 2015?	YES	NO
12	A prosperous Wales	☐	☒
13	A resilient Wales	☐	☒
14	A healthier Wales	☒	☐
15	A more equal Wales	☐	☒
16	A Wales of cohesive communities	☐	☒
17	A Wales of vibrant culture and thriving Welsh language	☐	☒
18	A globally responsible Wales	☐	☒
19	If YES to any of the above, please give details:		
	Reduction in failure rate will lead to earlier discharge of patient from ICU and hospital and helping patients to lead a healthier life.		

SECTION F: Scope of Research Activity

	Will the research activity include:	YES	NO
1	Use of a questionnaire or similar research instrument?	☐	☒
2	Use of interviews?	☐	☒
3	Use of focus groups?	☐	☒
4	Use of participant diaries?	☐	☒
5	Use of video or audio recording?	☐	☒
6	Use of computer-generated log files?	☐	☒
7	Participant observation with their knowledge?	☐	☒
8	Participant observation without their knowledge?	☐	☒
9	Access to personal or confidential information without the participants' specific consent?	☐	☒
10	Administration of any questions, test stimuli, presentation that may be experienced as physically, mentally or emotionally harmful / offensive?	☐	☒
11	Performance of any acts which may cause embarrassment or affect self-esteem?	☐	☒
12	Investigation of participants involved in illegal activities?	☐	☒
13	Use of procedures that involve deception?	☐	☒
14	Administration of any substance, agent or placebo?	☐	☒
15	Working with live vertebrate animals?	☐	☒
16	Procedures that may have a negative impact on the environment?	☐	☒
17	Other primary data collection methods. Please indicate the type of data collection method(s) below.	☒	☐
	Details of any other primary data collection method: Routinely collected non patient identifier data like age and gender. Rest are clinical and ventilator data.		

If NO to every question, then the research activity is (ethically) low risk and **may** be exempt from **some** of the following sections (please refer to Guidance Notes).

If YES to any question, then no research activity should be undertaken until full ethical approval has been obtained.

SECTION G: Intended Participants

If there are no participants then do not complete this section, but go directly to section H.

	Who are the intended participants:	**YES**	**NO**
1	Students or staff at the University?	☐	☒
2	Adults (over the age of 18 and competent to give consent)?	☒	☐
3	Vulnerable adults?	☐	☒
4	Children and Young People under the age of 18? (Consent from Parent, Carer or Guardian will be required)	☐	☒
5	Prisoners?	☐	☒
6	Young offenders?	☐	☒
7	Those who could be considered to have a particularly dependent relationship with the investigator or a gatekeeper?	☐	☒
8	People engaged in illegal activities?	☐	☒
9	Others. Please indicate the participants below, and specifically any group who may be unable to give consent.	☐	☒
	Details of any other participant groups: (this box should expand as you type)		

	Participant numbers and source Provide an estimate of the expected number of participants. How will you identify participants and how will they be recruited?	
10	How many participants are expected?	It is a prospective quality improvement project over a period of 2-3 months. Adult Intensive Care at UHW, Cardiff admits 1200 patients per year, 70% of them are intubated prior to admission. Crude mortality rate in ICU is ~40%, leaving behind 30% or ~350 patients eligible to participate over one year. So, Over a period of 2-3 months, aim will be to collect data for consecutive 90-100 eligible patients.

11	Who will the participants be?	Critical ill patients admitted to Intensive care unit at University hospital of Wales, Cardiff.
12	How will you identify the participants?	Any patient scheduled to be liberated will be flagged up for participation in the QI project on very morning.

	Information for participants:	**YES**	**NO**	**N/A**
13	Will you describe the main research procedures to participants in advance, so that they are informed about what to expect?	☐	☐	☒
14	Will you tell participants that their participation is voluntary?	☐	☐	☒
15	Will you obtain written consent for participation?	☐	☐	☒
16	Will you explain to participants that refusal to participate in the research will not affect their treatment or education (if relevant)?	☐	☐	☒
17	If the research is observational, will you ask participants for their consent to being observed?	☐	☐	☒
18	Will you tell participants that they may withdraw from the research at any time and for any reason?	☐	☐	☒
19	With questionnaires, will you give participants the option of omitting questions they do not want to answer?	☐	☐	☒
20	Will you tell participants that their data will be treated with full confidentiality and that, if published, it will not be identifiable as theirs?	☐	☐	☒
21	Will you debrief participants at the end of their participation, in a way appropriate to the type of research undertaken?	☐	☐	☒
22	If NO to any of above questions, please give an explanation			
	(this box should expand as you type)			

	Information for participants:	**YES**	**NO**	**N/A**
24	Will participants be paid?	☐	☐	☒
25	Is specialist electrical or other equipment to be used with participants?	☐	☐	☒
26	Are there any financial or other interests to the investigator or University arising from this study?	☐	☐	☒
27	Will the research activity involve deliberately misleading participants in any way, or the partial or full concealment of the specific study aims?	☐	☐	☒

28	If YES to any question, please provide full details
	(this box should expand as you type)

SECTION H: Anticipated Risks

	Outline any anticipated risks that may adversely affect any of the participants, the researchers and/or the University, and the steps that will be taken to address them. If you have completed a full risk assessment (for example as required by a laboratory, or external research collaborator) you may append that to this form.		
1	Full risk assessment completed and appended?	Yes	☐
		No	☒
2	**Risks to participants** For example: sector-specific health & safety, emotional distress, financial disclosure, physical harm, transfer of personal data, sensitive organisational information		

	Risk to participants: None	*How you will mitigate the risk to participants:*
3	If research activity may include sensitive, embarrassing or upsetting topics (e.g. sexual activity, drug use) or issues likely to disclose information requiring further action (e.g. criminal activity), give details of the procedures to deal with these issues, including any support/advice (e.g. helpline numbers) to be offered to participants. Note that where applicable, consent procedures should make it clear that if something potentially or actually illegal is discovered in the course of a project, it may need to be disclosed to the proper authorities	
	N/A *(this box should expand as you type)*	
4	**Risks to the investigator** For example: personal health & safety, physical harm, emotional distress, risk of accusation of harm/impropriety, conflict of interest	
	Risk to the investigator: None *(this box should expand as you type)*	*How you will mitigate the risk to the investigator:* *(this box should expand as you type)*
5	**University/institutional risks** For example: adverse publicity, financial loss, data protection	
	Risk to the University:	*How you will mitigate the risk to the University:*

	None	*(this box should expand as you type)*
6	**Environmental risks** For example: accidental spillage of pollutants, damage to local ecosystems	
	Risk to the environment: None	*How you will mitigate the risk to environment:* N/A *(this box should expand as you type)*

	Disclosure and Barring Service			
	If the research activity involves children or vulnerable adults, a Disclosure and Barring Service (DBS) certificate must be obtained before any contact with such participants.	**YES**	**NO**	**N/A**
7	Does your research require you to hold a current DBS Certificate?	☐	☒	☐
8	If YES, please give the certificate number. If the certificate number is not available please write “Pending”; in this case any ethical approval will be subject to providing the appropriate certificate number.			

SECTION I: Feedback, Consent and Confidentiality

1	**Feedback** What de-briefing and feedback will be provided to participants, how will this be done and when?
	N/A

2	**Informed consent** Describe the arrangements to inform potential participants, before providing consent, of what is involved in participating. Describe the arrangements for participants to provide full consent before data collection begins. If gaining consent in this way is inappropriate, explain how consent will be obtained and recorded in accordance with prevailing data protection legislation.
	This project will be done as QI and no informed consent is required.
3	**Confidentiality / Anonymity** Set out how anonymity of participants and confidentiality will be ensured in any outputs. If anonymity is not being offered, explain why this is the case.
	Only non-patient information identifier (non-PII) data will be used to develop prediction model.

SECTION J: Data Protection and Storage

	Does the research activity involve personal data (as defined by the General Data Protection Regulation 2016 "GDPR" and the Data Protection Act 2018 "DPA")?	**YES**	**NO**
1	***"Personal data"*** *means any information relating to an identified or identifiable natural person ('data subject'). An identifiable natural person is one who can be identified, directly or indirectly, in particular by reference to an identifier such as a name, an identification number, location data, an online identifier or to one or more factors specific to the physical, physiological, genetic, mental, economic, cultural or social identity of that natural person. Any video or audio recordings of participants is considered to be personal data.*		No
	If YES, provide a description of the data and explain why this data needs to be collected:		
2	*(this box should expand as you type)*		
	Does it involve special category data (as defined by the GDPR)?	**YES**	**NO**

3	***"Special category data"*** *means sensitive personal data consisting of information as to the data subjects' –* *(a) racial or ethnic origin,* *(b) political opinions,* *(c) religious beliefs or other beliefs of a similar nature,* *(d) membership of a trade union (within the meaning of the Trade Union and Labour Relations (Consolidation) Act 1992),* *(e) physical or mental health or condition,* *(f) sexual life,* *(g) genetics,* *(h) biometric data (as used for ID purposes),*		No
	If YES, provide a description of the special category data and explain why this data needs to be collected:		
4	*(this box should expand as you type)*		

	Will data from the research activity (collected data, drafts of the thesis, or materials for publication) be stored in any of the following ways?	**YES**	**NO**
5	Manual files (i.e. in paper form)?	☐	☒
6	University computers?	☐	☒
7	Private company computers?	☐	☒
8	Home or other personal computers?	☐	☒
9	Laptop computers/ CDs/ Portable disk-drives/ memory sticks?	☐	☒
10	"Cloud" storage or websites?	☐	☒
11	Other – specify: Hospital QI AMAT system which is a secured system runs on hospital cloud server and allows to store data.	☒	☐
12	For all stored data, explain the measures in place to ensure the security of the data collected, data confidentiality, including details of backup procedures, password protection, encryption, anonymisation and pseudonymisation:		
	Project data will be stored on hospital run AMAT system. There will be no patient identifier information (PII) collected as part of the project. It is a password encrypted platform and only Principal project leads can access the system, platform runs on secure hospital server.		

	Data Protection		
	Will the research activity involve any of the following activities:	**YES**	**NO**
13	Electronic transfer of data in any form?	☒	☐
14	Sharing of data with others at the University outside of the immediate research team?	☐	☒
15	Sharing of data with other organisations?	☐	☒

16	Export of data outside the UK or importing of data from outside the UK?	☐	☒
17	Use of personal addresses, postcodes, faxes, emails or telephone numbers?	☐	☒
18	Publication of data that might allow identification of individuals?	☐	☒
19	Use of data management system?	☐	☒
20	Data archiving?	☐	☒
21	If YES to any question, please provide full details, explaining how this will be conducted in accordance with the GDPR and Data Protection Act (2018) (and any international equivalents, where appropriate):		
	(this box should expand as you type)		
22	List all who will have access to the data generated by the research activity:		
	Manish Pandey, PI for the project. *(this box should expand as you type)*		
23	List who will have control of, and act as custodian(s) for, data generated by the research activity:		
	Data owned by Cardiff and Vale University health Board. *(this box should expand as you type)*		
24	Give details of data storage arrangements, including security measures in place to protect the data, where data will be stored, how long for, and in what form. Will data be archived – if so how and if not why not.		
	Data will be stored on hospital AMAT system (QI project system), it will be stored for one year after project ends and then data will be archived. *(this box should expand as you type)*		
25	Please indicate if your data will be stored in the UWTSD Research Data Repository (see https://researchdata.uwtsd.ac.uk/). If so please explain. (*Most relevant to academic staff)*		
	No *(this box should expand as you type)*		
26	Confirm that you have read the UWTSD guidance on data management (see https://www.uwtsd.ac.uk/library/research-data-management/)	**YES**	☒
27	Confirm that you are aware that you need to keep all data until after your research has completed or the end of your funding	**YES**	☐

SECTION K: Declaration

	The information which I have provided is correct and complete to the best of my knowledge. I have attempted to identify any risks and issues related to the research activity and acknowledge my obligations and the rights of the participants**.**

		Manish Pandey	**Date: 28-01-2024**

For STUDENT Submissions:

			Date:

For STAFF Submissions:

			Date:

Checklist: Please complete the checklist below to ensure that you have completed the form according to the guidelines and attached any required documentation:

	I have read the guidance notes supplied before completing the form.
	I have completed **ALL RELEVANT** sections of the form in full.
	I confirm that the research activity has received approval in principle
	I have attached a copy of final/interim approval from external organisation (**where appropriate**)
	I have attached a full risk assessment (where appropriate) *ONLY TICK IF YOU HAVE* ***ATTACHED A FULL RISK ASSESSMENT***
	I understand that it is my responsibility to ensure that the above named research activity will meet the University's Research Ethics and Integrity Code of Practice.
	I understand that before commencing data collection all documents aimed at respondents (including information sheets, consent forms, questionnaires, interview schedules etc.) must be confirmed by the DoS/Supervisor, module tutor or Academic Director.

RESEARCH STUDENTS ONLY

Once complete, submit this form via the **MyTSD Doctoral College Portal** at (https://mytsd.uwtsd.ac.uk).

RESEARCH STAFF ONLY

All communications relating to this application during its processing must be in writing and emailed to pgresearch@uwtsd.ac.uk , with the title 'Ethical Approval' followed by your name.

STUDENTS ON UNDERGRADUATE OR TAUGHT MASTERS PROGRAMMES should submit this form (and receive the outcome) via systems explained to you by the supervisor/module leader.