REMAP-CAP Data Completion Guidelines

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1 Introduction

The following document provides guidance for the completion of the REMAP-CAP Case Report Form (CRF). Use the links below to navigate to data completion guidelines for each form of the CRF.

General Guidance
Eligibility Assessment
Baseline Form
Microbiology Form
Daily Data
Medication Administration Form
Consent
Discharge Form
Adverse Events and Serious Adverse Events
Protocol Deviations
Follow-up Forms
Biological Sampling Forms
Pregnancy Outcome Form
Appendices
Change log

2 Federation with ASCOT trial

In Australia and New Zealand, REMAP-CAP is federated with the ASCOT trial and both Platforms utilise a common CRF. The guidance in the following pages apply to both REMAP-CAP and ASCOT, unless otherwise specified.

3 Version History

This document is Version 15.1 of the REMAP-CAP Data Completion Guidelines. When viewed as a PDF, the date of export is shown in the heading and on the cover page.

A summary of changes and version history can be found here.

4 General Guidance

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- Trial database
- Contact
- Date and time format
- Rounding numerical data
- Study day definition
- General Definitions
    - Organ Failure Support

4.1 Trial database

The URL for the REMAP-CAP database (including eligibility assessment and eCRF) is: https://remapcap.spinnakersoftware.com

4.2 Contact

For clarification of any definition in this document, please contact your local regional project manager. For any database-related issues, please email info@remapcap.org.

4.3 Date and time format

Date format is *DD-MMM-YYYY* for all date data points in the CRF. For example, 2nd of February 2018 is written as 02-FEB-2018.

Twenty-four hour time format is to be used for all times that are entered. For example, 6:05 PM is entered as 18:05. Note that midnight is entered as 00:00 (i.e., there is no 24:00 hours).

If you do not know an exact time, estimate based on the available contextual information.

4.4 Rounding numerical data

If enough space is not provided in the CRF to enter a full numerical value as recorded, please round up or down as appropriate to fit the space available. Round the value up if the last digit is equal to or greater than (≥) 5, or round the measurement down if the last digit is less than (<) 5.

4.5 Study day definition

A study day is defined as a calendar day (i.e., 00:00 - 23:59). Study Day 1 is the day of randomisation, and starts at the time of randomisation. There is no Study Day 0.

> ⚠ Note that previous versions of the CRF have defined Study Days based on the 24-hour period that corresponded to ICU charts at the participating site. There is no need to update data for existing participants to reflect this new definition.

4.6 General Definitions

	Definition
Admission date and time	The date and time at which a patient physically arrives in a clinical location (e.g. acute hospital or ICU).
Discharge date and time	The date and time at which a patient physically leaves the clinical location to which they were admitted. If a patient has been "bed blocked" or is ready for discharge from a ward or ICU, but physically remains in the ward or ICU, then the patient is still defined as being admitted to an that location until they physically leave it. If a patient with an endotracheal tube or tracheostomy tube in situ is transported directly from ICU to a location outside of the acute hospital (e.g. home) for the purposes of palliation, and the patient remains under the continued care of the ICU team, they are considered to remain admitted to ICU. For such patients, ICU discharge is the date and time that the ICU team ceased to provide care for the patient.
Index hospitalisation	The admission to an acute hospital in which enrollment in this trial occurred. Includes transfers to other acute hospitals that represent a continuation of the same acute hospital admission.
Home	A place of residence in which an individual is living independently or with minimal assistance. This includes: • Individuals who are homeless / unhoused • An individual who is receiving 'hospital in the home' care in their usual residence • A individual who resides in University Halls of Residence or similar

	Definition
Nursing home or long-term care facility	A nursing home or long-term care facility refers to a residential facility that provides assistance with activities of daily living (e.g., dressing, bathing, toileting, eating) on a regular basis, due to chronic physical or mental conditions or disabilities. The following are not considered nursing homes / long-term care facilities: • Independent living in a retirement village • Hospital in the home • Residence in a hostel or rest home without assistance with activities of daily living
Rehabilitation hospital	A rehabilitation hospital includes: • An in-patient sub-acute rehabilitation facility, either within the same hospital or at a different location • A transitional living facility • Statistical discharge indicating change from acute to chronic care, whereby an in-patient is transferred to a unit that is geographically separate from acute hospital wards and managed by a separate team
Intensive Care Unit	An intensive care unit (ICU) is defined as a hospital unit that provides specialised care for critically ill patients. They may also be known as critical care units, or intensive treatment/therapy units (ITU). This includes High-Dependency Units (HDU) or other areas where patients are under the care of intensivists. During a pandemic, the definition of an ICU includes a repurposed area that is capable of providing ICU-level care (i.e., non-invasive ventilation with a sealed mask, invasive mechanical ventilation, or vasopressors via a continuous infusion).

	Definition

Illness Severity State	Within this Platform, participants are categorised as being in one of three illness severity states:
	• **Moderate** Illness Severity State, defined as hospitalised patients who:
	  • Are not receiving organ failure support, AND
	  • Are not in the Recovering State
	• **Severe** Illness Severity State, defined as hospitalised patients who:
	  • Are receiving qualifying organ failure support with one or more of:
	  • Invasive mechanical ventilation
	  • Non-invasive mechanical ventilation
	  • High-flow nasal oxygen
	  • Continuous infusion of vasopressors, inotropes or both
	  • Are not in the Recovering State
	• **Recovering** Illness Severity State, defined as hospitalised patients who:
	  • Are clearly recovering from their acute infection AND
	  • Are unlikely to require or receive a significant escalation in level of organ failure support for the remainder of their hospital admission

Reveal of allocation	• 'Reveal of allocation' refers to the time at which a given participant's randomised allocations to interventions within one or more domains is revealed or made available.
	• In many cases, the intervention(s) that the participant is allocated to will be revealed at the time of randomisation.
	  • This is termed '**immediate reveal** of allocation', and occurs when all information that is required to confirm a patient's eligibility for a domain is available at the time of randomisation.
	• In some circumstances, a patient's allocations within one or more domains may not be revealed until after additional information is provided. This is termed '**delayed** or **deferred reveal** of allocation'.
	  • **Deferred reveal** of allocation occurs when the patient's eligibility for a given domain can only be confirmed once further information becomes available (e.g. the results of microbiological testing, or the outcome for a request for consent).
	  • **Delayed reveal** of allocation refers to situations where a patient is not eligible for a given domain at the time of randomisation, but may become eligible at a later point pending further information becoming available, or a change in their condition.

4.6.1 Organ Failure Support

	Definition

Low intensity oxygen	• Low-intensity oxygen is defined as supplemental oxygen (FiO2 > 0.21) delivered at a rate below what constitutes high-flow oxygen therapy:
	  • Less than 30L/min (or less than 2L / minute / kilogram of body weight in children less than 15 kilograms)
	  • Greater than, or equal to, 30L/min (or 2L / minute / kilogram of body weight in children less than 15 kilograms), with an FiO2 < 0.4

High-flow oxygen	• High-flow oxygen is defined as oxygen delivered via nasal prongs or cannula using a specialised device with:
	  • a fractional inspired oxygen concentration of 0.4 or higher, and
	  • a flow-rate of at least 30L/min (or at least 2L /minute / kilogram of body weight in children less than 15 kilograms).

Non-invasive ventilation	• Non-Invasive Ventilation (NIV) includes:
	  • Continuous positive airways pressure (CPAP)
	  • Bi-Level Positive Airway Pressure (BiPAP)
	  • Non-Invasive Positive Pressure Ventilation (NIPPV)
	• NIV does not include CPAP or BiPAP used solely for the management of pre-existing obstructive sleep apnoea or other similar condition.

	Definition

Invasive mechanical ventilation	• Invasive mechanical ventilation includes any form of positive pressure ventilation above the expiratory pressure given during inspiration, delivered via an oral-tracheal, nasotracheal tube, or tracheostomy tube - with or without positive-end expiratory sureness (PEEP)
	• Invasive mechanical ventilation includes:
	  • Assist Control Volume support
	  • Assist Control Pressure support
	  • Synchronized Intermittent Mechanical Ventilation, volume control with or without pressure support
	  • Synchronized Intermittent Mechanical Ventilation, pressure control with or without pressure support
	  • Pressure support (with no or without mandatory breaths)
	  • Airway Pressure Release Ventilation
	  • Pressure Regulated Volume Control
	  • Adaptive Support Ventilation / Volume Support
	  • High-frequency Oscillation (Jet) ventilation
	  • Tube Compensation
	  • Other invasive mode
	• Invasive mechanical ventilation does not include:
	  • T-piece
	  • CPAP via TT (or endotracheal tube (ETT))
	  • Direct Tracheal/Tracheostomy Interface/Connection
	  • Swedish nose.

Vasopressor or inotrope	• A vasopressor is a pharmaceutical agent that causes vasoconstriction, thereby increasing blood pressure.
	• An inotrope is a pharmaceutical agent that increases myocardial contractility.
	• Examples of inotropes and vasopressors include:
	  • Adrenaline / epinephrine
	  • Noradrenaline/ norepinephrine
	  • Dobutamine
	  • Dopamine
	  • Metamarinol (Aramine, Metaradrine, Metaramin, Pressonex)
	  • Levosimendan (Simdax)
	  • Milrinone (Primacor)
	  • Vasopressin (Pitressin)
	  • Phenylephrine
	  • Ephedrine

	Definition

Renal replacement therapy	• Renal Replacement Therapy (RRT) includes any form of:
	  • continuous hemofiltration, haemodialysis or haemodiafiltration
	  • Intermittent haemodialysis
	  • Slow Low Efficiency Dialysis (SLED)
	  • Peritoneal dialysis

5 Eligibility Assessment

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- Eligibility Assessment
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5.1 Eligibility Assessment

This page provides guidance for the completion of the eligibility assessment for REMAP-CAP, including pages that are completed post-randomisation to reveal allocation within a given domain (i.e. 'domain reveal' pages). The eligibility module of the trial database is dynamic, and the questions that are displayed will vary based on which domains and interventions the patient is being assessed for.

Always check that you are logged into the correct location / hospital in the study database before screening a patient. Patients entered into test sites cannot be migrated to live sites.

5.1.1 Consent to screen

Field / Question	Definition	Applies to
Is there agreement to enter screening information to determine this patient's eligibility for this trial	• Select '**Yes**' if there has been sufficient confirmation, in relation to the requirements in this jurisdiction, to collect and retain screening information. • If you are unsure about requirements in your jurisdiction, contact your Regional Coordinator.	Locations where consent / agreement is required to screen a patient for eligibility
Can screening information be entered without agreement from patient or proxy, as approved by your ethics committe	• Select '**Yes**' if there has been sufficient confirmation, in relation to the requirements in this jurisdiction, to collect and retain screening information as determined by the ethics committee, if agreement is not obtained from the patient or proxy. • If you are unsure about requirements in your jurisdiction, contact your Regional Coordinator.	Locations where consent / agreement is required to screen a patient for eligibility
Who was the agreement provided by	• Select the response option that best represents who has provided agreement to enter screening information in order to determine the patient's eligibility for this trial. • If you select '**other**', you will be asked to specify who provided agreement. ◦ Succinctly describe the relationship of the individual to the patient. Do not enter the individual's name.	Locations where consent / agreement is required to screen a patient for eligibility

5.1.2 Demographic information

Field / Question	Definition	Applies to
Patient age	• Enter the patient's age in years. • If exact age is unknown, enter estimated age. • Do not round age to the nearest year. For example, if the patient is 30 years and 11 months, enter 30 years. • If a patient is less than one year old, enter '0' (zero)	All patients

Field / Question	Definition	Applies to
Infant age	• Enter the patient's age in months. • If exact age is unknown, enter estimated age. • For patients aged 28-30 days old, enter "**1**" month • Do not round up to the nearest month. For example, if a patient is 4 months and 3 weeks, enter 4 months.	Patients who are aged 2 years or younger
Sex at birth	• Sex at birth is determined by physical sexual characteristics at the time of birth, not by gender identity. • For intersex patients (i.e. individuals born with sex characteristics that do not fit typical binary definitions for male or female bodies, including sexual anatomy, reproductive organs, hormonal patterns, and/or chromosome patterns), select the gender that they most identify with.	All patients
Date and time of hospital admission	• Enter the date and time that this patient first presented from the community to an emergency department (ED) for this acute illness. • If the patient was transferred from another hospital, record the date and time that they presented to the first hospital's ED. • If the patient presented to an ED multiple times prior to this hospital admission, enter the date and time that the patient presented to the ED and was subsequently admitted as an in-patient for this hospital admission. • If the patient was admitted directly from an outpatient clinic, enter the date and time that they were formally admitted to the hospital. • If you are unsure of the time that the patient first presented to ED, enter 01:00 on the day of admission.	All patients
Date and time of ICU admission	• Enter the date and time at which a patient physically arrived in the ICU.	Patients located in an ICU or paediatric ICU

5.1.3 Platform Eligibility

Field / Question	Definition	Applies to
Does the patient have acute infection of the respiratory tract	• Select '**Yes**' if the treating clinician believes there is recent-onset infection that involves one or more sections of the upper or lower respiratory tract. • Includes exacerbation of chronic infection. • Excludes infection of the middle ear or sinuses, including the mastoids.	All patients
Is death deemed imminent and inevitable during the next 24 hours	• Select '**Yes**' if the senior treating clinician believes that there is no reasonable possibility of the patient surviving the next 24 hours.	All patients

Is the patient, their substitute decision maker, or their primary treating clinician committed to some active treatment	• Select '**No**' if a decision has been made to withhold clinical treatment (or intensity of treatment) that would otherwise be indicated for the patient's current severity of illness. For example:
	  • if the patient is hypotensive and a vasopressor will not be commenced or, if already commenced, the current dose will not be increased.
	  • if the patient has a clinical indication for intubation, but a decision has been made not to intubate them.
	• This <u>does not</u> include where a decision has been made that a future escalation of intensity of treatment, beyond the current level that is being received, is inappropriate.
	• This criterion seeks to exclude those patients where supportive comfort measures are being provided. Patients who are planned for active ward management with a clear aim to improve survival, even if intensive care unit level support is not being offered, should still be included.
		All patients

Field / Question	Definition	Applies to

Is the patient expected to be discharged from this hospital admission today or tomorrow	• Select '**Yes**' if the patient is expected to be discharged from hospital later today, or any time tomorrow.
	• If there is an intention to transfer the patient to another hospital today or tomorrow:
	  • Select '**Yes**' if the receiving hospital is not participating in this trial
	  • Select '**No**' if the receiving hospital is participating in this trial. Where appropriate, discuss participation with the receiving hospital, particularly with respect to domain and intervention compatibility.
		All patients

Has this patient been enrolled into this Platform within the last 90 days	• If the patient is known to have received an allocation in this trial, or in another trial that is analysed in the same statistical model as this trial, within the last 90 days, select '**Yes**'.
	  • Examples include the ASCOT trial in Australia and New Zealand.
	  • If you are unsure about whether another trial will be analysed in the same statistical model as this trial, contact your Regional Project Manager.
	• This question will appear in locations where it is permissible to re-randomise a patient to the same Platform after 90 days have passed since the previous randomisation.
	• Select '**No**' for patients who have been:
	  • Screened for eligibility for participation in this trial within the last 90 days, but not randomised
	  • Included in the trial registry, but not randomised
	  • Randomised in the Moderate State during this hospitalisation, and are now being reassessed to receive additional allocations in the Severe State.
		Locations where re-randomisation within this Platform is permitted after 90 days

Field / Question	Definition	Applies to

Has the patient been enrolled into this Platform before	• If the patient is known to have received an allocation in this trial, or in another trial that is analysed in the same statistical model as this trial, at any time, select '**Yes**'.
	  ◦ Examples include the ASCOT trial in Australia and New Zealand.
	  ◦ If you are unsure about whether another trial will be analysed in the same statistical model as this trial, contact your Regional Project Manager.
	• This question will appear in locations where it is not permitted to ever re-randomise a patient to the same Platform.
	• Select '**No**' for patients who have been:
	  ◦ Previously screened for eligibility for participation in this trial but not randomised
	  ◦ Included in the trial registry, but not randomised
	  ◦ Randomised in the Moderate State during this hospitalisation, and are now being reassessed to receive additional allocations in the Severe State.
		Locations where re-randomisation within this Platform is not permitted

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5.1.4 Illness Severity State

Field / Question	Definition	Applies to

Is the patient currently receiving oxygen support	Select the option that best describes the patient's current level of oxygen support at this time:
	• **None**: the patient is not receiving any oxygen support with a fraction of inspired oxygen (FiO_2) greater than 0.21
	• **Low-intensity oxygen therapy**: the patient is receiving oxygen support (FiO_2 > 0.21) that is:
	  ◦ delivered at a flow rate of less than 30 L/min (or less than 2 L/min/kg in children weighing less than 15 kilograms), or
	  ◦ with an FiO_2 of less than 0.40, delivered at any flow rate
	• **High-flow oxygen:** see General Definitions
	• **Non-invasive ventilation**: see General Definitions
	• **Invasive mechanical ventilation**: see General Definitions
		All patients

Is the patient currently receiving a continuous vasopressor and/or inotrope infusion	• At the time of eligibility assessment. • If the patient is receiving one or more vasopressor agents or inotrope agents, or both, as an on-going infusion, select '**Yes**'. • If the patient is receiving only intermittent doses of a vasopressor or inotrope, even if administered frequently, select '**No**'. • Vasopressors and inotropes are defined in General Definitions	All patients

Field / Question	Definition	Applies to

When did the patient commence the current period of organ failure support	• Enter the date and time that the patient first commenced the current period of qualifying organ failure support.
	• The current period of organ failure support is defined as the commencement of any of the following organ failure supports that have continued without interruption until now.
	  ◦ High-flow oxygen
	  ◦ Non-invasive ventilation
	  ◦ Invasive mechanical ventilation
	  ◦ Vasopressors or inotropes administered via continuous infusion
	• Where a patient has moved between different modalities of organ failure support without interruption, the date and time that this period of organ failure support was commenced corresponds to the date and time that the *initial* organ failure support was commenced.
	  ◦ For example, if a patient receives non-invasive ventilation and is then moved to high-flow oxygen without interruption, enter the date and time of commencement of the non-invasive ventilation.
	• If a patient is receiving more than one modalities of organ failure support (e.g. invasive ventilation and vasopressors), enter the date and time that the first of these therapies was commenced.
	• "Interruption" of organ failure support <u>does not</u> include:
	  ◦ Temporary cessation of organ failure support for procedures, logistical reasons, etc. where there is an intention to reinstate the organ failure support as soon as possible.
	  ◦ Cessation of organ failure support without the aim of recommencing, but where the cessation of the organ failure support has resulted in clinical deterioration requiring recommencement of the organ failure support within one hour. An example is failed extubation.
	• Where organ failure support was first commenced prior to the index hospitalisation, enter the date and time of hospital admission.
		Patients who are receiving specified organ failure support(s) at time of screening

Field / Question	Definition	Applies to
	• For patients who receive one of the specified organ failure supports as usual therapies at home prior to this acute illness, commencement of organ failure support is the date and time that the patient's level of support was first increased beyond their usual level of support during this acute hospital admission. • This may be evidenced by a clinically significant increase in FiO_2, PEEP, flow rate, or frequency of administration.	
Has the patient received invasive mechanical ventilation during this hospital admission	• Includes invasive mechanical ventilation during a previous ICU admission during this acute hospital admission. • Invasive mechanical ventilation is defined in General Definitions. • Invasive mechanical ventilation provided in the operating room or for a procedure does not meet this criteria. • If the patient is receiving long-term invasive ventilation, select '**Yes**' only if there is a significant increase in intensity of provision of invasive mechanical ventilation (e.g. a clinically significant increase in FiO_2, PEEP, or inspiratory support).	Patients who are not receiving any oxygen support, and are not receiving vasopressors or inotropes via continuous infusion
Is the patient now clearly recovering from their acute infection	• Select '**Yes**' if, in the opinion of the treating clinician, the patient is now recovering from their acute infection, as evidenced by improvement in physiological measurements and clinical assessment. • Select '**No**' if the trajectory of the patient's illness is still considered to be uncertain.	All patients

Field / Question	Definition	Applies to
Do you expect the patient to require a significant escalation in intensity of organ failure support during the remainder of their hospital admission	• Select '**No**' if the treating clinician considers that it is unlikely that the patient will require an escalation in their current level of organ failure support • Escalation may include: increased level of ventilatory support (e.g. FiO_2, flow rate, or PEEP); escalation to more intensive modality of ventilatory support (e.g. from non-invasive to invasive mechanical ventilation); increased dose of vasopressors or inotropes; or increased frequency of application • This question relates to the *requirement* of an increased level of organ failure support, not whether it will be provided. If it is considered possible that the patient may require a higher intensity of organ failure support answer '**Yes**', even if a decision has been made that provision of intensity of treatment, beyond the current level that is being received, is inappropriate.	All patients

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5.1.5 Patient, Pathogen and Disease Characteristics

Field / Question	Definition	Applies to
Where was the respiratory tract infection acquired	Select the option that best reflects where the patient's respiratory tract infection is believed to have been acquired: • **Community-acquired:** acute infection acquired outside of the hospital and manifesting within 48 hours of hospital admission • **Hospital-acquired:** acute infection not incubating at the time of hospital admission and manifesting more than 48 hours after hospital admission	All patients

Field / Question	Definition	Applies to
Does the infection involve the lower respiratory tract	• Select '**Yes**' if the patient's respiratory tract infection involves the lower respiratory tract. • Select '**No**' if the patient's respiratory tract infection only involves the upper respiratory tract. • Lower respiratory tract is defined as infection of the airways below the level of the larynx, including tracheitis, bronchitis, bronchiolitis, and pneumonia. • Upper respiratory tract is defined as infection of the airways at the level of the larynx and above, excluding isolated otitis media or mastoiditis.	All patients
Is pneumonia present	• Select '**Yes**' if the patient has radiological evidence of new onset infiltrate consistent with infection. • In patients with pre-existing radiological changes, select '**Yes**' only if there is evidence of new infiltrate	All patients

What is the date of onset of clinical features of this acute respiratory tract infection	• Enter the date that the patient first experience the symptoms of this acute respiratory tract infection.
	• Symptoms may include coughing, sore throat, headache, nasal discharge or congestion, feeling feverish or having chills, aches or pains of the muscles or joints, and fatigue.
	• Use all available information to estimate the date of first symptom onset. For example:
	  ◦ If medical notes indicate that the patient was admitted with a "five-day history of cough", then enter the date five calendar days prior to the date of hospital admission.
	  ◦ If the patient or a family member states that the patient has had a fever for "around 3 or 4 days" prior to coming to hospital, enter the calendar date four days prior to the date of hospital admission.
	• Symptoms may first occur before or after admission to hospital.
	• If the patient does not have any signs or symptoms of acute respiratory tract infection at this time, select '**patient is asymptomatic**'
	• If no information is available to estimate a date of symptom onset, select '**not recorded**'.
		All patients

Field / Question	Definition	Applies to

Does the patient have a known condition resulting in immune suppression, or have they received treatment resulting in immune suppression	• Select '**Yes**' if the patient has an underlying immunodeficiency or has received immunosuppressive therapy.
	• Immunosuppressive therapy is defined as:
	  • Currently receiving, or has received in the last three months, non-biological oral immune modulating drugs (e.g., methotrexate > 25 mg/ week, azathioprine > 3.0 mg/kg/day, or 6-mercaptopurine > 1.5 mg/kg/day)
	  • Currently receiving, or has received within the past three months, immunosuppressive chemotherapy
	  • Received any form of chemotherapy in the last four weeks.
	  • Allogenic haematopoietic stem cell transplantation within the last 12 months, or at any time if given as on-going treatment for chronic GVHD
	  • CAR-T cell treatment within the last 12 months
	  • receiving, or has received within the past 12 months, immunosuppressive biological therapy (e.g., alemtuzumab, ofatumumab, or rituximab)
	  • Organ transplantation recipients
	  • Receiving other targeted cancer treatments which can affect the immune system, such as protein kinase inhibitors or PARP inhibitors
	  • Receiving radiotherapy, including Myeloablative radiotherapy (e.g. prior to a stem cell transplant) or high-dose radiotherapy for lung cancer
	  • Receiving high-dose steroid treatment (e.g., > 15 mg/kg methylprednisolone or equivalent for > 5 days)
	  • Receiving long-term steroid treatment (e.g., > 20 mg/day of a systemic steroid)
	• Immunosuppressive disease defined as the patient having one or more of the following diseases that are sufficiently advanced to suppress resistance to infection (excludes malignancy which has been in remission for five years or more)
	  • Acquired Immunodeficiency Syndrome (AIDS)
	  • Acute leukaemia (including high-risk MDS)
	  • Lymphoma
	  • Myeloma
		All patients

Field / Question	Definition	Applies to

	• Metastatic cancer
	• Any other disease that is sufficiently advanced to suppress resistance to infection, for example:
	  • Primary or inherited immune deficiency syndromes, including B cell deficiencies (such as Bruton agammaglobulinemia), T cell deficiencies (such as Wiskott Aldrich disease), or combined deficiencies (such as Common Variable Immunodeficiency).
	  • Secondary immune deficiency syndromes requiring treatment with regular IV immunoglobulin.
	  • Aplastic anaemia or other causes of chronic neutropenia or neutrophil dysfunction.	

What is the patient's SpO_2	• Enter the documented saturation of peripheral oxygen measured closest to the time of screening (now).	All patients who are not receiving invasive mechanical ventilation
What is the patient's PaO_2	• Enter the partial pressure of oxygen (PaO_2) measured on the most recent Arterial Blood Gas (ABG) analysis while the patient was invasively mechanically ventilated. • If more than one ABG was drawn, use the most recent sample. • Record the result and select the appropriate unit of measurement (mmHg or kPa).	Patients who are receiving invasive mechanical ventilation
What is the corresponding FiO_2	• The fraction of inspired oxygen (FiO_2) (range 0.21 -1.0) the patient was receiving at the time that the ABG used to record the patient's PaO_2 in the previous question was obtained, or at the time that the SpO_2 was recorded.	All patients

Field / Question	Definition	Applies to
What is the corresponding PEEP	• The Positive End Expiratory Pressure (PEEP) in cmH_2O that the patient was receiving at the time that the ABG used to record the patient's PaO_2 and FiO_2 was obtained. • If the patient was receiving invasive mechanical ventilation using APRV mode at the time that the ABG was obtained, select '**patient receiving APRV**'.	All patients receiving invasive ventilation
Does the patient have bilateral opacities on chest imaging that are not fully explained by effusions, lobar or lung collapse, nodules, cardiac failure, or fluid overload	• Select '**Yes**' if the patient has one or more regions of interstitial and/or alveolar (air space) opacity on a plain chest x-ray or Computed Tomography Scan (CT scan) that is consistent with being caused by infection. • For patients with pre-existing radiological changes, there should be evidence of new infiltrate (consolidation) before answering '**Yes**'.	All patients
Is the patient's respiratory tract infection the primary contributor for their requirement for this organ support	• Select '**Yes**' if, in the opinion of the treating clinician, the patient's respiratory tract infection is the primary contributor for their current level of respiratory support. • Answer '**No**' if their current level of respiratory support is due primarily to other reasons. • Not primarily attributable to acute heart failure, fluid overload, or pulmonary embolism (PE)	All patients
What is the likelihood that bacterial respiratory tract infection is contributing to this acute illness	• Select the response option that best represents the likelihood that a bacterial infection is contributing to this patient's acute respiratory tract infection. • The likelihood of bacterial infection is defined primarily by clinical assessment plus any microbiological data available, acknowledging that, for bacterial infection or co-infection, results from commonly used microbiological testing strategies may take a significant time (e.g., culture) and have low sensitivity.	All patients

Field / Question	Definition	Applies to
What is the likelihood that the following viral pathogens are contributing to this acute illness	• For each of the specified viral pathogens, indicate the likelihood that they are contributing to the patient's acute illness at this time. • Excludes positive tests for a pathogen which are not considered to represent active infection. For example, a patient who has recently recovered from SARS-CoV-2. • **Confirmed:** the pathogen has been confirmed with microbiological testing, and is considered to be contributing to the patient's acute illness at this time. • **Suspected but not confirmed**: microbiological testing has not been performed, or has been performed but the results are not yet available, but the treating clinician considers the pathogen to be a likely diagnosis based on clinical assessment and supporting evidence. • **Not suspected:** the pathogen is not suspected by the treating clinician. Microbiological testing for the pathogen has not been performed and will not be performed. • **Tested and not detected:** microbiological testing has been performed and has tested negative for the pathogen.	All patients

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5.1.6 Domain Eligibility

Field / Question	Definition	Applies to
What was the date and time of the first known intravenous antibiotic administered for this illness	• Date and time the patient received the first intravenous (IV) dose of an antibiotic for this illness (including if given in the community, if known). • If no IV antibiotic has been administered, select '**not given**'. • If unsure of the time that the first IV antibiotic was administered, enter 01:00 (1 am) on the day you know that an IV antibiotic was administered. • If the patient was transferred from another hospital, enter the date and time that they were given an IV antibiotic in the transferring hospital, if known. • Only information that is easily available should be used (e.g., documented medical notes and observations).	Patients being assessed for the Antibiotic Domain

Field / Question	Definition	Applies to

Do you suspect methicillin-resistant staphylococcus aureus (MRSA) infection	• Methicillin-resistant staphylococcus aureus (MRSA) is defined as a staphylococcus aureus that is resistant to any of the following antibiotics:
	  • methicillin
	  • oxacillin
	  • dicloxacillin
	  • nafcillin
	  • flucloxacillin
	• Patients with suspected MRSA infection are eligible for randomization to the Antibiotic and Macrolide Duration Domains, however an additional agent active against MRSA should be administered.
		Patients being assessed for the Antibiotic Domain

Is standard empiric antibiotic therapy for community acquired pneumonia appropriate	• Select '**Yes**' if bacterial infection is considered a strong possibility and standard empiric antibiotic therapy is appropriate. • Standard empiric antibiotic therapy for community-acquired pneumonia (CAP) is defined as: antibiotic therapy regarded as clinically appropriate before the potential availability of microbiological tests that allow guided antimicrobial therapy in accordance with local guidelines. • Consider if therapy with alternative antibiotics is indicated (e.g. colonisation with resistant organism, immunosuppression, known results of microbiological testing). • The Antibiotic Domain allocates patients to various options that are regarded as acceptable standard empiric antibiotic therapy, noting that some additional agents can be added (e.g. vancomycin for MRSA), but not substituted, to ensure appropriate empiric therapy for each patient.	Patients being assessed for the Antibiotic Domain

Field / Question	Definition	Applies to

Reason that empiric antibiotic therapy is not appropriate	• Select the response options that best describe why empiric antibiotic therapy for CAP is not considered to be appropriate.
	• More than one option may be selected.
	• **There is sufficient microbiological information to guide specific antibacterial therapy**
	  • A microbiological result is available which indicates targeted antibacterial therapy, such as culture with sensitivities or polymerase chain reaction (PCR) of a known typical or atypical (e.g. Legionella) bacterial pathogen. A positive test for influenza is not regarded as sufficient microbiological information to guide specific antibacterial therapy. If this is selected, you will be asked to specify what information is available to guide antibacterial therapy.
	• **Febrile neutropenia or significant immunosuppression**
	  • Includes organ or bone marrow transplantation, human immunodeficiency virus (HIV) Infection with cluster of differentiation 4 (CD4) cell count <200 cells/μL, systemic immunosuppression, long term systemic corticosteroids). This does not include neutropenia that is being attributed to the CAP (e.g., neutropenia secondary to severe sepsis).
	• **Suspected infection with resistant bacterial (other than MRSA) where empiric agents in this domains would not be expected to be active**
	  • Includes cystic fibrosis, bronchiectasis or other chronic suppurative lung disease where infection with Pseudomonas may be suspected.
	• **Suspected or proven serious concomitant infection** (e.g., meningitis)
	• **Suspected melioidosis (during melioidosis season, according to local guidelines)**
	  • Defined as the monsoonal period according to local guidelines, in sites located in tropical areas.
		Patients being assessed for the Antibiotic Domain, if empiric antibiotic therapy is not considered appropriate

Field / Question	Definition	Applies to

Will the patient commence or continue (if already commenced) any of the following medications	• Other than as an allocated therapy within this Platform.
	• Select any of the listed medications that have been prescribed or will be prescribed for immediate commencement.
	• **A systemic corticosteroid**
	  ◦ Includes only systemic corticosteroids administered enterally or parenterally
	  ◦ Examples include systemic corticosteroids for the treatment of COVID-19 infection, continuation of long-term therapy, bronchospasm, or septic shock
	• **An antiviral active against influenza, other than oseltamivir or baloxavir**
	  ◦ Examples include zanamivir or peramivir
	• **Imatinib, or another tyrosine kinase inhibitor targeting the same pathway as imatinib**
	  ◦ Other tyrosine kinase inhibitors targeting the same pathway as imatinib include dasatinib, nilotinib, ponatinib
	• **Tocilizumab**
	• **Baricitinib**
	• **None** of the listed medications have been commenced or are not intended to continue (if already commenced).
		Patients being assessed for the Corticosteroid Domain, Influenza Antiviral Domain, Endothelial Domain, and/ or Influenza Immune Modulation Domain.
		Response options that appear will vary depending on domains being assessed.

Is the patient known to have received treatment with polyclonal antibody therapy with the potential to be active against COVID-19 during this acute illness	• Polyclonal antibody therapy includes convalescent plasma and hyperimmunoglobulin against SARS-CoV-2. • Regular replacement immunoglobulin (intravenous or subcutaneous) does not meet this criteria.	Patients being assessed for the COVID-19 Immunoglobulin Domain

Field / Question	Definition	Applies to
Is the patient receiving any of the following as a pre-hospital usual medication	• Select all medications that the patient was receiving as a usual medication at home prior to this hospitalisation • **Imatinib, or another tyrosine kinase inhibitor targeting the same pathway as imatinib** • Other tyrosine kinase inhibitors targeting the same pathway as imatinib include dasatinib, nilotinib, ponatinib • **Tocilizumab** • **Sarilumab** • **Any other IL-6 receptor antagonist** • **Baricitinib** • **Tofacitinib or another JAK inhibitor** • **None of the above**	Patients being assessed for the Endothelial Domain, and/ or Influenza Immune Modulation Domain Response options that appear will vary depending on domains being assessed.
Has the patient received any of the following during this hospitalisation	• Select all medications that the patient has received during this hospitalisation • **Tocilizumab** • **Sarilumab** • **Any other IL-6 receptor antagonist** • **Baricitinib** • **Tofacitinib or another JAK inhibitor** • **Two or more doses of oseltamivir (or any other neuraminidase inhibitor)** • Other neuraminidase inhibitors include zanamivir or peramivir • **One of more doses of baloxavir** • **None of the above**	Patients being assessed for the Influenza Antiviral Domain, and/ or Influenza Immune Modulation Domain Response options that appear will vary depending on domains being assessed.
Has the patient received more than 24 hours of an antiviral agent intended to be active against SARS-CoV-2 within the past 7 days	• Includes antiviral agents received in the community prior to this hospital admission for this acute illness	Patients being assessed for the COVID-19 Antiviral Domain

Field / Question	Definition	Applies to
Was SARS-CoV-2 infection confirmed by positive rapid antigen test or polymerase chain reaction test within the last 7 days	• Select '**Yes**' if the patient has had a positive rapid antigen test or PCR test for SARS-CoV-2 within the last 7 calendar days. • If the patient has not had a RAT or PCR test for SARS-CoV-2 within the last seven days select '**No**'	Patients being assessed for the COVID-19 Antiviral Domain with confirmed SARS-CoV-2 infection

Is the patient expected to still be receiving invasive mechanical ventilation tomorrow	• Select '**Yes**' if the treating clinician believes that the patient is likely to receive invasive mechanical ventilation until tomorrow.
	  ◦ For example, if the eligibility assessment is being completed on Monday, the treating clinician must expect that the patient will remain invasively ventilated until at least Tuesday.
	  ◦ The patient does not need to be expected to remain ventilated for the entirety of the day following the eligibility assessment.
	• Select '**No**' if the treating clinician expects the patient to be extubated on the same calendar day as this eligibility assessment.
		Patients being assessed for the Mechanical Ventilation Domain who are receiving IMV

Date and time of first intubation for this acute illness	• Enter the date and time that the patient was intubated for the first time for this acute illness during this hospitalisation. • Includes intubation at another hospital, if the patient was transferred to this hospital. • If intubated for a procedure, this should only be counted if the duration of invasive ventilation was longer than 4 hours. • If the patient is receiving long-term invasive mechanical ventilation prior to hospital admission (e.g. chronic invasive ventilation at home), select '**receiving long-term invasive ventilation**'.	Patients being assessed for the Mechanical Ventilation Domain who are receiving IMV

Field / Question	Definition	Applies to
Has the patient received supplemental oxygen on this calendar day	• Select '**Yes**' if the patient has received any form of supplemental oxygen therapy (FiO_2 > 0.21) by any modality after midnight on the calendar day of the eligibility assessment. • For example, if a patient was receiving oxygen via nasal prongs at 2L/min at 03:00, and at 04:30 it was removed, and the eligibility assessment is being completed at 11:45, answer '**Yes**'. • The indication for the supplemental oxygen is not relevant to this question. • Patients on long term domiciliary oxygen who continue on that in hospital will be considered to be receiving supplemental oxygen.	Patients being assessed for the COVID-19 Antiviral (II) Domain who are not currently receiving oxygen support

Does the patient have confirmed invasive fungal or mycobacterial infection	• Select '**Yes**' if, in the patient has microbiologically confirmed invasive fungal or mycobacterial infection; or if these are strongly suspected by the treating clinician.
	• Examples of invasive fungal infections include any fungaemia (growth of a fungus such as
	  ◦ a Candida species from a blood culture),
	  ◦ invasive aspergillosis (e.g. pulmonary aspergillosis),
	  ◦ invasive mould infection (e.g. mucormycosis),
	  ◦ Pneumocystis jirovecii pneumonia, and
	  ◦ cryptococcal infection (e.g. cryptococcal pneumonia or meningitis).
	• Do not select '**yes**' if the patient has a fungal infection that is not invasive - such as oral candidiasis, esophageal candidiasis, or fungal infection of the skin.
	• Examples of mycobacterial infections include tuberculosis, leprosy, and non-tuberculous mycobacterial (NTM) infections such as Mycobacterium avium infection of the lungs.
		Patients being assessed for the Influenza Immune Modulation Domain

Field / Question	Definition	Applies to
Is the patient receiving renal replacement therapy	• At this time • Renal replacement therapy is defined in General Definitions	Patients being assessed for the Influenza Immune Modulation Domain and/ or the COVID-19 Antiviral (II) Domain.
Does the patient have known severe liver disease	• Includes known portal hypertension, for example splenomegaly attributed to portal hypertension; varices demonstrated on endoscopy; or current or past episodes of hepatic encephalopathy severe enough to result in reduced level of consciousness. • Any patient with Child-Pugh class C liver disease will meet this definition • Abnormal liver function tests alone are not sufficient to meet this definition	Patients being assessed for the Endothelial Domain and/ or COVID-19 Antiviral (II) Domain
What is the patient's bilirubin	• Enter bilirubin taken from serum or plasma samples closest to the eligibility assessment, during this hospitalisation and within the last 72 hours. • If bilirubin level was not measured within the last 72 hours during this hospitalisation, select '**not recorded**'.	Patients being assessed for the Endothelial Domain
What is the upper limit of normal for bilirubin for this patient at this location	• Enter the upper limit of normal of bilirubin for this patient at your location	Patients being assessed for the Endothelial Domain

Field / Question	Definition	Applies to
What is the patient's platelet count	• Enter platelet count from laboratory sample obtained closest to randomisation and during this hospitalisation within the last 72 hours. • If platelet count was not measured within the last 72 hours during this hospitalisation, select '**not recorded**'.	Patients being assessed for the Endothelial Domain and/ or Influenza Immune Modulation Domain
What is the patient's neutrophil count	• Enter neutrophil count from laboratory sample obtained closest to randomisation and during this hospitalisation within the last 72 hours. • If neutrophil count was not measured within the last 72 hours during this hospitalisation, select '**not recorded**'.	Patients being assessed for the Endothelial Domain and/ or Influenza Immune Modulation Domain
What is the patient's ALT or AST	• Enter alanine transaminase or aspartate transaminase recorded closest to eligibility assessment, during this hospitalisation and within the last 72 hours. • If no samples were collected within the last 72 hours during this hospitalisation, select '**not measured**'	Patients being assessed for the Endothelial Domain, COVID-19 Antiviral Domain, and/ or Influenza Immune Modulation Domain

Field / Question	Definition	Applies to
What is the upper limit of normal for ALT or AST for this patient at this location	• Enter the upper limit of normal of ALT or AST for this patient at your location	Patients being assessed for the Endothelial Domain, COVID-19 Antiviral Domain, and/ or Influenza Immune Modulation Domain
What is the patient's serum creatinine	• Enter the most recent serum creatinine measured during this hospital admission. • If serum creatinine has not been measured during this hospital admission, select 'not measured' • Serum creatinine is used together with the patient's age and (if aged < 18 years) height to estimate glomerular filtration rate (eGFR) to determine domain eligibility.	Patients being assessed for the Influenza Immune Modulation Domain, Endothelial Domain, and/ or the COVID-19 Antiviral (II) Domain
Patient height	• Record the patient's height and select the unit of measurement (cm or feet and inches). • Height may be measured or estimated if it is not documented in the medical record. • If estimated, estimate height during this hospital admission. Document estimated height in the patient's medical record. • If not measured during this hospitalization, any measurement in the medical record taken whilst the patient was an adult (over the age of 18 years) can be used. • If height is estimated and a measurement becomes available during this hospital admission, update the field.	Paediatric patients being assessed for the Influenza Immune Modulation Domain, and adult patients being assessed for the Mechanical Ventilation Domain

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5.1.7 Intervention Eligibility and Contraindications

Field / Question	Definition	Applies to

Is the patient pregnant or breastfeeding	• Select the response that best describes the pregnancy status of the patient.
	• Select '**pregnant**' if pregnancy has been confirmed by one or more of:
	  • An ultrasound or other imaging
	  • A urine or blood Beta Human Chorionic Gonadotropin (β-hCG test)
	  • A clinical diagnosis
	• Select '**breastfeeding**' if the patient is currently breastfeeding or was breastfeeding prior to this hospitalisation.
	  • If a patient is known to be both pregnant and breastfeeding, select '**pregnant**'
	• If a patient is not known to be pregnant or breastfeeding and they are of childbearing potential select '**unknown**'.
	  • In some regions, an 'unknown' response is not accepted, and the patient's pregnancy status must be confirmed prior to randomisation.
		Female patients aged 12 - 55 years

Does the patient have any contraindications to penicillins	• Select '**Yes**' if any contraindication to penicillins is documented in the patient's medical record, irrespective of the severity.
	• Any history of the following related to penicillin or any beta-lactam:
	  • Anaphylaxis
	  • Penicillin induced autoimmune haemolytic anemia
	  • Penicillin-induced interstitial nephritis
	  • Stevens-Johnson Syndrome
	  • Toxic Epidermal Necrolysis
	  • Other non-life-threatening adverse drug reactions such as rash
		Patients being assessed for the Antibiotic Domain

Field / Question	Definition	Applies to

Does the patient have any contraindications to cephalosporins	• Select '**Yes**' if any contraindication to cephalosporins is documented in the patient's medical record, irrespective of the severity.
	• Any history of the following related to cephalosporins or any beta-lactam:
	  • Anaphylaxis
	  • Penicillin induced autoimmune haemolytic anemia
	  • Penicillin-induced interstitial nephritis
	  • Stevens-Johnson Syndrome
	  • Toxic Epidermal Necrolysis
	  • Other non-life-threatening adverse drug reactions such as rash
		Patients being assessed for the Antibiotic Domain

Does the patient have any contraindications to quinolones	• Select '**Yes**' if any contraindication to quinolones is documented in the patient's medical record, irrespective of the severity.	Patients being assessed for the Antibiotic Domain with the Levofloxacin / Moxifloxacin intervention available
Does the patient have any contraindications to macrolides	• Select '**Yes**' if any contraindication to macrolides is documented in the patient's medical record, irrespective of the severity.	Patients being assessed for the Antibiotic Domain. Also influences eligibility for the Macrolide Domain, where active
Does the patient have any contraindications to any corticosteroid	• Select '**Yes**' if any contraindication to corticosteroids that is documented in the patient's medical record, irrespective of the severity.	Patients being assessed for the Corticosteroid Domain

Field / Question	Definition	Applies to
Does the patient have any contraindications to oseltamivir	• Select '**Yes**' if any contraindication to oseltamivir is documented in the patient's medical record, irrespective of the severity.	Patients being assessed for the Influenza Antiviral Domain, with oseltamivir-containing interventions available
Does the patient have any contraindications to baloxavir	• Select '**Yes**' if any contraindication to baloxavir is documented in the patient's medical record, irrespective of the severity.	Patients being assessed for the Influenza Antiviral Domain, with baloxavir-containing interventions available

Does the patient have any contraindications to tocilizumab	• Select '**Yes**' if any contraindication to tocilizumab is documented in the patient's medical record, irrespective of the severity.
	• Includes:
	  • Known adverse drug reaction
	  • AST / ALT level more than 5 times the upper limit of normal range, or
	  • Platelet count < 50 cells x 10^9 / L
		Patients being assessed for the Influenza Immune Modulation Domain, with the tocilizumab intervention available

Does the patient have any contraindications to baricitinib	• Select '**Yes**' if any contraindication to baricitinib is documented in the patient's medical record, irrespective of the severity. • Includes: • Known adverse drug reaction	Patients being assessed for the Influenza Immune Modulation Domain, with the baricitinib intervention available

Field / Question	Definition	Applies to

Does the patient have any contraindications to imatinib	• Select '**Yes**' if any contraindication to imatinib is documented in the patient's medical record, irrespective of the severity.
	• Includes:
	  • Known hepatitis B or C
	  • Currently receiving strong CYP3A4 inhibitors (e.g. -azoles, erythromycin) or inducers (e.g. rifampicin, phenobarbital, carbamazepine, phenytoin)
	  • Currently receiving a calcineurin inhibitor (e.g. cyclosporine, tacrolimus, everolimus, or sirolimus)
		Patients being assessed for the Endothelial Domain

Does the patient have any contraindications to the transfusion of blood products	• Select '**Yes**' if any contraindication to the transfusion of blood products is documented in the patient's medical record, irrespective of the severity.
	• Includes:
	  • Known history of moderate or severe allergy or transfusion reaction to blood components
	  • Known history of transfusion-related lung injury
	  • Known objection to receiving plasma products
		Patients being assessed for the Immunoglobulin Domain

Does the patient have any contraindications to protocolised invasive mechanical ventilation	• Select '**Yes**' if the patient has any contraindication to protocolized mechanical ventilation strategy in the opinion of the treating clinician. • Consider treated or untreated active air leak through an intercostal catheter, severe airflow limitation (including bronchospasm), and elevated intracranial pressure.	Patients being assessed for the Mechanical Ventilation Domain

Does the patient have any contraindications to enteral nirmatrelvir/ ritonavir (paxlovid)	• Select '**Yes**' if any contraindication to nirmatrelvir or ritonavir, or both, is documented in the patient's medical record, irrespective of the severity.
	• Includes:
	  • Known adverse drug reaction
	  • The patient is unable to take, tolerate or absorb oral or enteral medications, or
	  • Receipt of a concomitant drug with a high-risk interaction with nirmatrelvir / ritonavir which cannot be ceased or substituted
		Patients being assessed for the COVID-19 Antiviral (II) Domain, with a nirmatrelvir / ritonavir-containing intervention available

Field / Question	Definition	Applies to

Does the patient have any contraindications to intravenous remdesivir	• Select '**Yes**' if any contraindication to remdesivir is documented in the patient's medical record, irrespective of the severity.
	• Includes:
	  • Known adverse drug reaction
	  • No venous access is available and none can be created
		Patients being assessed for the COVID-19 Antiviral (II) Domain, with a remdesivir-containing intervention available

In the opinion of the treating clinician, is the patient at very high risk for progression to severe COVID-19	• Patients at high risk include those who have not completed at least a primary course of vaccination OR do not have a history of previous COVID-19 infection OR who may not have responded well to vaccination (e.g., immunocompromised). • "*Very high risk for progression to severe COVID-19*" includes patients who have had previous severe COVID-19 pneumonitis requiring admission to ICU, or other patients for whom the clinician lacks equipoise to randomise to no antiviral treatment	Patients being assessed for the COVID-19 Antiviral (II) Domain, with the 'no antiviral' intervention available
Is nirmatrelvir- ritonavir available for administration to this patient, if they are assigned to this intervention	• Different healthcare providers may have specific criteria to allow access to nirmatrelvir-ritonavir. Select '**Yes**' if this patient satisfies such criteria for access at this time, at your location. • If your patient would satisfy the local access criteria but nirmatrelvir-ritonavir is contraindicated due to drug interactions, please answer '**Yes**' to this question.	Patients being assessed for the COVID-19 Antiviral (II) Domain, with a nirmatrelvir / ritonavir-containing intervention available
Is remdesivir available for administration to this patient, if they are assigned to this intervention	• Different healthcare providers may have specific criteria to allow access to remdesivir. Select '**Yes**' if this patient satisfies such criteria for access at this time, at your location. • If your patient would satisfy the local access criteria but remdesivir is contraindicated (e.g., hepatic or renal failure), please answer '**Yes**' to this question.	Patients being assessed for the COVID-19 Antiviral (II) Domain, with a remdesivir-containing intervention available

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5.1.8 Consent

Field / Question	Definition	Applies to
At this time is the patient sufficiently capable of providing informed consent to participate	• Select '**Yes**' if the patient is competent to make an informed decision about their participation in this trial at this time • If the patient does not have capacity to provide consent for their participation, select '**No**'. • It is important to consider if the patient is competent to provide consent for participation. It is not sufficient that a patient is able to sign a consent form, they must be capable of understanding their participation and making an informed choice regarding a decision to take part in the study. • An individual's capacity to provide consent may fluctuate over time. • If the patient is capable of providing consent, speak to a Research Coordinator or the Principal Investigator at your site before approaching the patient.	All patients
Is a suitable proxy or legal representative available to provide consent to participate	• Select '**Yes**' if a suitable proxy or legal representative is available to make a decision about the patient's participation in this trial. • Select '**No**' if the patient has no suitable proxy or legal representative, or if such a person is unavailable or unable to be contacted at this time. • In some settings, suitable proxies may include independent clinicians who are able to provide agreement to enrol this patient without prospective consent from the patient or a personal legal representative	Patients who are not capable of providing their own consent to participate

Field / Question	Definition	Applies to

Has agreement been obtained for participation in the following domains	• The eligibility system will display all of the domains for which the patient is potentially eligible. Indicate, for each domain, whether:
	  • The patient or a suitable representative has **agreed** to participation in the domain.
	  • The patient or a suitable representative has **declined** to participate in the domain.
	  • The patient or a suitable representative has **not yet** made a decision about participation in the domain.
	  • The treating clinician does not believe that participation in the domain is **not in the patient's best interest**, and therefore consent for participation in the domain will not be sought.
	• In some jurisdictions, for some domains, consent is not required prior to randomisation.
		All patients, where the patient or a suitable proxy or representative were available for a consent discussion

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5.1.9 Best Interest Statement

Field / Question	Definition	Applies to
In the opinion of the treating clinician, is allocation to any of the options listed above appropriate for this patient	• The eligibility system will display all domains and interventions for which the patient is eligible. • For each domain, select whether the treating clinician believes that all of the listed interventions are equally clinically appropriate for this patient and that there is no other treatment option that the treating clinician believes to be superior to any of these options.	All patients

5.2 Domain Reveal

Some domains may permit randomisation with delayed or deferred reveal of allocation. This occurs when additional information is required to confirm a patient's eligibility, such as confirmation of microbiological testing results, or confirmation that requirements for informed consent have been met for that domain.

5.2.1 Antibiotic Domain Reveal

Field / Question	Definition	Applies to
Have requirements for informed consent for this domain at this location, and for this patient been met	• Select '**Yes**' if informed consent for participation in this domain has been obtained in accordance with ethical and regulatory approvals at your site.	All participants who have been randomised to the Antibiotic Domain with Delayed or Deferred reveal of allocation
In the opinion of the treating clinician, is allocation to any of the options listed above appropriate for this patient	• The eligibility system will display all interventions for which the patient is eligible within this domain. • Select '**Yes**' if the treating clinician believes that all of the listed interventions are equally clinically appropriate for this patient and that there is no other treatment option that the treating clinician believes to be superior to any of these options.	All participants who have been randomised to the Antibiotic Domain with Delayed or Deferred reveal of allocation

5.2.2 Macrolide Domain Reveal

Field / Question	Definition	Applies to
Is the patient's pneumonia due to a microbiologically proven or strongly suspected infection with Legionella or another atypical organism	• Select '**Yes**' if the patient's pneumonia is suspected or confirmed to be caused by Legionella or another atypical organism that may require an extended course of Macrolide.	All participants who have been randomised to the Macrolide Domain
Has macrolide been ceased for more than 36 hours	• Select '**Yes**' if the patient has not received a macrolide for any period of 36 hours or more since reveal of allocation in the Antibiotic Domain.	All participants who have been randomised to the Macrolide Domain
In the opinion of the treating clinician, is allocation to any of the options listed above appropriate for this patient	• The eligibility system will display all interventions for which the patient is eligible within this domain. • Select '**Yes**' if the treating clinician believes that all of the listed interventions are equally clinically appropriate for this patient and that there is no other treatment option that the treating clinician believes to be superior to any of these options.	All participants who have been randomised to the Macrolide Domain

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5.2.3 Corticosteroid Domain Reveal

Field / Question	Definition	Applies to

Has SARS-CoV-2 infection been confirmed with microbiological testing	• If SARS-CoV-2 has been reported as isolated or detected on microbiological testing, select '**Yes**'.
	• On pathology reports, SARS-CoV-2 may be documented as:
	  • SARS-CoV-2
	  • COVID-19
	  • Novel Coronavirus
	  • 2019-nCoV
		All participants who have been randomised to the Immunoglobulin Domain with Delayed or Deferred reveal of allocation

Have requirements for informed consent for this domain at this location, and for this patient been met	• Select '**Yes**' if informed consent for participation in this domain has been obtained in accordance with ethical and regulatory approvals at your site.	All participants who have been randomised to the Corticosteroid Domain with Delayed or Deferred reveal of allocation
In the opinion of the treating clinician, is allocation to any of the options listed above appropriate for this patient	• The eligibility system will display all interventions for which the patient is eligible within this domain. • Select '**Yes**' if the treating clinician believes that all of the listed interventions are equally clinically appropriate for this patient and that there is no other treatment option that the treating clinician believes to be superior to any of these options. • Note that pregnant patients who are allocated to the fixed-course dexamethasone intervention will have their dexamethasone replaced by oral prednisolone or IV hydrocortisone.	All participants who have been randomised to the Corticosteroid Domain with Delayed or Deferred reveal of allocation

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5.2.4 Influenza Antiviral Domain Reveal

Field / Question	Definition	Applies to
Does the patient have microbiologically confirmed influenza infection	• If influenza has been reported as isolated or detected on microbiological testing during this acute illness, select '**Yes**'.	All participants who have been randomised to the Influenza Antiviral Domain with Delayed or Deferred reveal of allocation
Since admission to any hospital for this illness, has the patient received two or more doses of oseltamivir (or any other neuraminidase inhibitor)	• Select '**Yes**' if the patient has already received two or more doses of oseltamivir since they were first admitted to hospital for this acute illness. • Other neuraminidase inhibitors include zanamivir or peramivir.	All participants who have been randomised to the Influenza Antiviral Domain with Delayed or Deferred reveal of allocation
Since admission to any hospital for this illness, has the patient received one or more doses of baloxavir	• Select '**Yes**' if the patient has already received one or more doses of baloxavir since they were first admitted to hospital for this acute illness.	All participants who have been randomised to the Influenza Antiviral Domain with Delayed or Deferred reveal of allocation

Field / Question	Definition	Applies to
Will the patient commence or continue (if already commenced) an antiviral that is active against influenza, other than oseltamivir or baloxavir	• Select '**Yes**' if treatment with an antiviral that is active against influenza, other than oseltamivir or baloxavir, is intended to be commenced or will be continued (if already commenced).	All participants who have been randomised to the Influenza Antiviral Domain with Delayed or Deferred reveal of allocation
Have requirements for informed consent for this domain at this location, and for this patient been met	• Select '**Yes**' if informed consent for participation in this domain has been obtained in accordance with ethical and regulatory approvals at your site.	All participants who have been randomised to the Influenza Antiviral Domain with Delayed or Deferred reveal of allocation
In the opinion of the treating clinician, is allocation to any of the options listed above appropriate for this patient	• The eligibility system will display all interventions for which the patient is eligible within this domain. • Select '**Yes**' if the treating clinician believes that all of the listed interventions are equally clinically appropriate for this patient and that there is no other treatment option that the treating clinician believes to be superior to any of these options.	All participants who have been randomised to the Influenza Antiviral Domain with Delayed or Deferred reveal of allocation

5.2.5 Immunoglobulin Domain Reveal

Field / Question	Definition	Applies to

Has SARS-CoV-2 infection been confirmed with microbiological testing	• If SARS-CoV-2 has been reported as isolated or detected on microbiological testing, select '**Yes**'.
	• On pathology reports, SARS-CoV-2 may be documented as:
	  • SARS-CoV-2
	  • COVID-19
	  • Novel Coronavirus
	  • 2019-nCoV
		All participants who have been randomised to the Immunoglobulin Domain with Delayed or Deferred reveal of allocation

is the patient known to have received treatment with monoclonal antibody therapy active against SARS-CoV-2 during this acute illness	• Select YES if the patients is known to have received treatment with monoclonal antibody therapy with the potential to be active against SARS-CoV-2 at any time during this acute illness.
	• Includes prior to hospital admission during this acute illness
	• Examples of monoclonal antibody therapy include:
	  • Bamlanivimab / etesevimab
	  • Casirivimab / imdevimab (also known as REGEN-COV or Ronapreve)
	  • Sotrovimab
		All participants who have been randomised to the Immunoglobulin Domain with Delayed or Deferred reveal of allocation

Can two litres of high-titre convalescent plasma be made available for administration to this participant if they are assigned to this intervention	• Select '**Yes**' only once the availability of two units of high titre convalescent plasma has been confirmed. • Please confirm availability of high titre convalescent plasma with your blood service in your region or hospital blood bank. • If two units of high titre convalescent plasma are not available, the participant's allocation in this domain cannot be revealed.	All participants who have been randomised to the Immunoglobulin Domain with Delayed or Deferred reveal of allocation

Field / Question	Definition	Applies to
Has the clinical team agreed not to administer convalescent plasma if the patient is allocated to the 'no convalescent plasma' intervention	• Select '**Yes**' if the clinical team caring for the participant have agreed not to administered convalescent plasma if the participant is allocated to the 'no convalescent plasma' intervention within this domain. • If the treating clinical team cannot agree to withhold convalescent plasma if the participant is allocated to the 'no convalescent plasma' intervention, select '**No**'. The participant's allocation in this domain will not be revealed.	All participants who have been randomised to the Immunoglobulin Domain with Delayed or Deferred reveal of allocation
Have requirements for informed consent for this domain at this location, and for this patient been met	• Select '**Yes**' if informed consent for participation in this domain has been obtained in accordance with ethical and regulatory approvals at your site.	All participants who have been randomised to the Immunoglobulin Domain with Delayed or Deferred reveal of allocation
In the opinion of the treating clinician, is allocation to any of the options listed above appropriate for this patient	• The eligibility system will display all interventions for which the patient is eligible within this domain. • Select '**Yes**' if the treating clinician believes that all of the listed interventions are equally clinically appropriate for this patient and that there is no other treatment option that the treating clinician believes to be superior to any of these options.	All participants who have been randomised to the Immunoglobulin Domain with Delayed or Deferred reveal of allocation

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5.2.6 Mechanical Ventilation Domain Reveal

Field / Question	Definition	Applies to
Is the patient receiving invasive mechanical ventilation	• At the time of eligibility assessment (now). • Invasive Mechanical ventilation (IMV) is defined in General Definitions. • If the patient has undergone tracheal intubation and is receiving invasive mechanical ventilation check '**Yes**'. • If the patient is receiving long-term invasive ventilation, answer '**Yes**' only if there is a significant increase in intensity of provision or IMV (e.g. a clinically significant increase in FiO_2, PEEP, or inspiratory support).	All participants who have been randomised to the Mechanical Ventilation Domain with Delayed or Deferred reveal of allocation
Has an arterial blood gas been taken while the patient was receiving invasive mechanical ventilation	• This question only applies if the patient is receiving invasive mechanical ventilation at the time of eligibility assessment. • Select '**Yes**' if an arterial blood gas (ABG) has been performed within 6 hours prior to this eligibility assessment and after commencement of invasive mechanical ventilation. • If an ABG has not been performed since mechanical ventilation commenced, check '**No**'.	All participants who have been randomised to the Mechanical Ventilation Domain with Delayed or Deferred reveal of allocation
What is the patient's PaO_2	• This question is only required if an ABG was performed. • The partial pressure of oxygen (PaO_2) measured on the most recent ABG analysis while the patient was invasively mechanically ventilated. • If more than one ABG was drawn, use the most recent sample while the patient was receiving IMV. • Record the result and select the appropriate unit of measurement (mmHg or kPa).	All participants who have been randomised to the Mechanical Ventilation Domain with Delayed or Deferred reveal of allocation

Field / Question	Definition	Applies to
What was the corresponding FiO_2	• The fraction of inspired oxygen (FiO_2) (range 0.21 -1.0) the patient was receiving at the time that the ABG used to record the patient's PaO_2 in the previous question was obtained.	All participants who have been randomised to the Mechanical Ventilation Domain with Delayed or Deferred reveal of allocation
What was the corresponding PEEP	• The PEEP in cmH2O that the patient was receiving at the time that the ABG used to record the patient's PaO_2 and FiO_2 was obtained. • If the patient was receiving invasive ventilation using APRV mode at the time that the ABG was obtained, select '**patient receiving APRV**'.	All participants who have been randomised to the Mechanical Ventilation Domain with Delayed or Deferred reveal of allocation

Is the patient expected to still be receiving invasive ventilation tomorrow	• Select '**Yes**' if the treating clinician believes that the patient is likely to receive invasive mechanical ventilation until tomorrow.
	  • For example, if the eligibility assessment is being completed on Monday, the treating clinician must expect that the patient will remain invasively ventilated until at least Tuesday.
	  • The patient does not need to be expected to remain ventilated for the entirety of the day following the eligibility assessment.
	• Select '**No**' if the treating clinician expects the patient to be extubated on the same calendar day as this eligibility assessment.
		All participants who have been randomised to the Mechanical Ventilation Domain with Delayed or Deferred reveal of allocation

Field / Question	Definition	Applies to
Patient height	• Record the patient's height and select the unit of measurement (cm or feet and inches). • Measured height or length is preferred, however height may be estimated if it is not documented in the medical record. • If estimated, estimate height during this hospital admission. • If not measured during this hospitalization, any measurement in the medical record taken whilst the patient was an adult (over the age of 18 years) can be used. • If estimated, document estimated height in the patient's medical record.	All participants who have been randomised to the Mechanical Ventilation Domain with Delayed or Deferred reveal of allocation
Does the patient have any contraindications to protocolized invasive mechanical ventilation	• Include any contraindication to protocolized mechanical ventilation strategy in the opinion of the treating clinician. • Consider treated or untreated active air leak through an intercostal catheter, severe airflow limitation (including bronchospasm), and elevated intracranial pressure.	All participants who have been randomised to the Mechanical Ventilation Domain with Delayed or Deferred reveal of allocation
Have requirements for informed consent for this domain at this location, and for this patient been met	• Select '**Yes**' if informed consent for participation in this domain has been obtained in accordance with ethical and regulatory approvals at your site.	All participants who have been randomised to the Mechanical Ventilation Domain with Delayed or Deferred reveal of allocation

Field / Question	Definition	Applies to
In the opinion of the treating clinician, is allocation to any of the options listed above appropriate for this patient	• The eligibility system will display all interventions for which the patient is eligible within this domain. • Select '**Yes**' if the treating clinician believes that all of the listed interventions are equally clinically appropriate for this patient and that there is no other treatment option that the treating clinician believes to be superior to any of these options.	All participants who have been randomised to the Mechanical Ventilation Domain with Delayed or Deferred reveal of allocation

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5.2.7 Endothelial Domain Reveal

Field / Question	Definition	Applies to
Does the patient have a bilirubin more than 3 times the upper limit of normal	• Select '**Yes**' if the most recent bilirubin recorded within the past 72 hours was greater than three times the upper limit of normal	All participants who have been randomised to the Endothelial Domain with Delayed or Deferred reveal of allocation
Does the patient have a platelet count of < 50 cells x 10^9 /L	• Select '**Yes**' if the most recent platelet count recorded within the past 72 hours was less than 50 cells x 10^9 / L	All participants who have been randomised to the Endothelial Domain with Delayed or Deferred reveal of allocation

Field / Question	Definition	Applies to
Does the patient have a neutrophil count < 1.0 cells x 10^9 /L	• Select '**Yes**' if the most recent neutrophil count recorded within the past 72 hours was less than 1.0 x 10^9 / L	All participants who have been randomised to the Endothelial Domain with Delayed or Deferred reveal of allocation
Does the patient have an alanine aminotransferase or aspartate aminotransferase more than 5 times the upper limit of normal	• Select '**Yes**' if the most recent alanine aminotransferase or aspartate aminotransferase recorded within the past 72 hours was greater than five times the upper limit of normal	All participants who have been randomised to the Endothelial Domain with Delayed or Deferred reveal of allocation
Have requirements for informed consent for this domain at this location, and for this patient been met	• Select '**Yes**' if informed consent for participation in this domain has been obtained in accordance with ethical and regulatory approvals at your site.	All participants who have been randomised to the Endothelial Domain with Delayed or Deferred reveal of allocation

Field / Question	Definition	Applies to
In the opinion of the treating clinician, is allocation to any of the options listed above appropriate for this patient	• The eligibility system will display all interventions for which the patient is eligible within this domain. • Select '**Yes**' if the treating clinician believes that all of the listed interventions are equally clinically appropriate for this patient and that there is no other treatment option that the treating clinician believes to be superior to any of these options.	All participants who have been randomised to the Endothelial Domain with Delayed or Deferred reveal of allocation

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5.2.8 Influenza Immune Modulation Domain Reveal

Field / Question	Definition	Applies to
Does the patient have microbiologically confirmed influenza infection	• If influenza has been reported as isolated or detected on microbiological testing during this acute illness, select '**Yes**'.	All participants who have been randomised to the Influenza Immune Modulation Domain with Delayed or Deferred reveal of allocation

Field / Question	Definition	Applies to

Has SARS-CoV-2 infection been confirmed by microbiological testing	• If SARS-CoV-2 has been reported as isolated or detected on microbiological testing, select '**Yes**'.
	• On pathology reports, SARS-CoV-2 may be documented as:
	  • SARS-CoV-2
	  • COVID-19
	  • Novel Coronavirus
	  • 2019-nCoV
		All participants who have been randomised to the Influenza Immune Modulation Domain with Delayed or Deferred reveal of allocation

Does the patient have a neutrophil count < 1.0 cells x 10^9 /L	• Select '**Yes**' if the most recent neutrophil count recorded within the past 72 hours was less than 1.0 cells x 10^9 / L	All participants who have been randomised to the Influenza Immune Modulation Domain with Delayed or Deferred reveal of allocation
Does the patient have a platelet count of < 50 cells x 10^9 /L	• Select '**Yes**' if the most recent platelet count recorded within the past 72 hours was less than 50 cells x 10^9 / L	All participants who have been randomised to the Influenza Immune Modulation Domain with Delayed or Deferred reveal of allocation

Field / Question	Definition	Applies to
Does the patient have an alanine aminotransferase or aspartate aminotransferase more than 5 times the upper limit of normal	• Select '**Yes**' if the most recent alanine aminotransferase or aspartate aminotransferase recorded within the past 72 hours was greater than five times the upper limit of normal	All participants who have been randomised to the Influenza Immune Modulation Domain with Delayed or Deferred reveal of allocation
Is the patient receiving renal replacement therapy	• At this time • Renal replacement therapy is defined in General Definitions.	All participants who have been randomised to the Influenza Immune Modulation Domain with Delayed or Deferred reveal of allocation
Serum creatinine	• Enter the most recent serum creatinine measured during this hospital admission • Serum creatinine is used together with the patient's age and height to estimate glomerular filtration rate (eGFR) to determine domain eligibility.	All participants who have been randomised to the Influenza Immune Modulation Domain with Delayed or Deferred reveal of allocation

Field / Question	Definition	Applies to
Patient height	• Record the patient's height and select the unit of measurement (cm or feet and inches). • Measured height or length is preferred, however height may be estimated if a measured height is not documented in the medical record. • For adults, if height has not been measured during this hospitalization, any measurement in the medical record taken whilst the patient was an adult (over the age of 18 years) can be used. ◦ If no height has been documented in the medical record while the patient was an adult, use estimated height. • For paediatric patients, if height has not been measured during this hospitalization, use estimated height. • If estimated, document estimated height in the patient's medical record.	All participants who have been randomised to the Influenza Immune Modulation Domain with Delayed or Deferred reveal of allocation
Have requirements for informed consent for this domain at this location, and for this patient been met	• Select '**Yes**' if informed consent for participation in this domain has been obtained in accordance with ethical and regulatory approvals at your site.	All participants who have been randomised to the Influenza Immune Modulation Domain with Delayed or Deferred reveal of allocation
In the opinion of the treating clinician, is allocation to any of the options listed above appropriate for this patient	• The eligibility system will display all interventions for which the patient is eligible within this domain. • Select '**Yes**' if the treating clinician believes that all of the listed interventions are equally clinically appropriate for this patient and that there is no other treatment option that the treating clinician believes to be superior to any of these options.	All participants who have been randomised to the Influenza Immune Modulation Domain with Delayed or Deferred reveal of allocation

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5.2.9 COVID-19 Antiviral (II) Domain Reveal

Field / Question	Definition	Applies to
Has SARS-CoV-2 infection been confirmed with microbiological testing	• Select '**Yes**' if the patient has had a positive rapid antigen test or PCR test for SARS-CoV-2 within the last 7 calendar days. • If the patient has not had a RAT or PCR test for SARS-CoV-2 within the last seven days, or if all tests within this time period have been negative, select '**No**'.	All participants who have been randomised to the COVID-19 Antiviral (II) Domain with Delayed or Deferred reveal of allocation
Is nirmatrelvir-ritonavir available for administration to this patient, if they are assigned to this intervention	• Different healthcare providers may have specific criteria to allow access to nirmatrelvir-ritonavir. This question confirms whether this patient satisfies such criteria for access. If your patient would satisfy the local access criteria but nirmatrelvir-ritonavir is contraindicated due to drug interactions, please answer '**Yes**' to this question.	All participants who have been randomised to the COVID-19 Antiviral (II) Domain with Delayed or Deferred reveal of allocation
Is remdesivir available for administration to this patient, if they are assigned to this intervention	• Different healthcare providers may have specific criteria to allow access to remdesivir. This question confirms whether this patient satisfies such criteria for access. If your patient would satisfy the local access criteria but remdesivir is contraindicated (e.g., hepatic or renal failure), please answer '**Yes**' to this question.	All participants who have been randomised to the COVID-19 Antiviral (II) Domain with Delayed or Deferred reveal of allocation

Field / Question	Definition	Applies to
Does the patient have an alanine aminotransferase or aspartate aminotransferase more than 5 times the upper limit of normal	• Select '**Yes**' if the most recent alanine aminotransferase or aspartate aminotransferase recorded within the past 72 hours was greater than five times the upper limit of normal	All participants who have been randomised to the COVID-19 Antiviral (II) Domain with Delayed or Deferred reveal of allocation
Is the patient receiving renal replacement therapy	• At this time • Renal replacement therapy is defined in General Definitions	All participants who have been randomised to the COVID-19 Antiviral (II) Domain with Delayed or Deferred reveal of allocation
Serum creatinine	• Enter the most recent serum creatinine measured during this hospital admission • Serum creatinine is used together with the patient's age and height to estimate glomerular filtration rate (eGFR) to determine domain eligibility.	All participants who have been randomised to the COVID-19 Antiviral (II) Domain with Delayed or Deferred reveal of allocation

Field / Question	Definition	Applies to
Patient height	• Record the patient's height and select the unit of measurement (cm or feet and inches). • Measured height or length is preferred, however height may be estimated if it is not documented in the medical record. • If estimated, estimate height during this hospital admission. • If not measured during this hospitalization, any measurement in the medical record taken whilst the patient was an adult (over the age of 18 years) can be used. • If estimated, document estimated height in the patient's medical record.	All participants who have been randomised to the COVID-19 Antiviral (II) Domain with Delayed or Deferred reveal of allocation
Have requirements for informed consent for this domain at this location, and for this patient been met	• Select '**Yes**' if informed consent for participation in this domain has been obtained in accordance with ethical and regulatory approvals at your site.	All participants who have been randomised to the COVID-19 Antiviral (II) Domain with Delayed or Deferred reveal of allocation
In the opinion of the treating clinician, is allocation to any of the options listed above appropriate for this patient	• The eligibility system will display all interventions for which the patient is eligible within this domain. • Select '**Yes**' if the treating clinician believes that all of the listed interventions are equally clinically appropriate for this patient and that there is no other treatment option that the treating clinician believes to be superior to any of these options.	All participants who have been randomised to the COVID-19 Antiviral (II) Domain with Delayed or Deferred reveal of allocation

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6 Baseline Form

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6.1 Baseline Data

The following guidance relates to the Baseline Form. For the Mechanical Ventilation Domain-Specific Baseline Form, click here.

> Participants who have received an allocation to one or more domains in the Moderate State, and later receive further allocations to one or more domains in the Severe State, will have two Baseline forms. The Supplementary (second) Baseline form will only collect data points that may have changed since the first randomisation.

6.1.1 Demographics

Field / Question	Definition	Applies to
Height	• Record the patient's height and select the unit of measurement (cm or feet and inches). • Height may be measured or estimated if it is not documented in the medical record. If estimated, estimate height during this hospital admission. • If estimated, estimate height during this hospital admission. Document estimated height in the patient's medical record. • If not measured during this hospitalization, any measurement in the medical record taken whilst the patient was an adult (over the age of 18 years) can be used. • If height is estimated and a measurement becomes available during this hospital admission, update the field.	All participants
Weight	• Record the participant's weight and select the unit of measurement (kg or lbs). • Weight may be measured or estimated if it is not documented in the medical record. • If weight is estimated, estimate weight at the time of randomization. • If not measured prior to randomization, any measurement in the medical record taken within the last two months can be used. • If estimated, document estimated weight in the participant's medical record	All participants

6.1.2 Pregnancy

Field / Question	Definition	Applies to

Was the patient pregnant at hospital admission	• This question will only appear for female participants aged 12 - 55 years or younger.
	• Defined as pregnancy status at time of first hospital admission for this illness.
	• Pregnancy status at hospital admission may be confirmed by one or more of:
	  • An ultrasound or other imaging
	  • A urine or blood β-hCG test
	  • A clinical diagnosis
	• If there is documented evidence of menopause, hysterectomy, or surgical sterilization, select '**No**'.
	• If pregnancy status was not confirmed at the time of hospital admission, select '**No**'.
		Female participants aged 12 - 55 years

Gestation in weeks	• Enter the approximate gestation in weeks at the time of hospital admission.	Participants who were pregnant at hospital admission
Postpartum at hospital admission	• Select '**Yes**' if the patient has given birth to a foetus (live born or still born) of gestational age of more than 24 weeks within the past 40 days	Female participants aged 12 - 55 years who were not pregnant at hospital admission

Field / Question	Definition	Applies to

Was the patient pregnant at the time of randomisation	• This question is pre-filled on the basis of information entered during the eligibility assessment. Update the response if new information has become available, or the initial question was answered incorrectly.
	• Select '**pregnant**' if pregnancy has been confirmed by one or more of:
	  • An ultrasound or other imaging
	  • A urine or blood Beta Human Chorionic Gonadotropin (β-hCG test)
	  • A clinical diagnosis
	• Select '**breastfeeding**' if the participant is currently breastfeeding or was breastfeeding prior to this hospitalisation.
	  • If a participant is known to be both pregnant and breastfeeding, select '**pregnant**'
	• If a participant is not known to be pregnant or breastfeeding and they are of childbearing potential select '**unknown**'.
	  • In some regions, an 'unknown' response is not accepted, and the participant's pregnancy status must be confirmed prior to randomisation.
		Female participants aged 12 - 55 years

Estimated date of delivery	• Enter the date that the infant(s) are estimated to be delivered (i.e. the "due date"). • If the anticipated date of delivery was prior to randomisation, but the participant has not delivered at the time of randomisation, enter the date that the infant(s) are now expected to be delivered.	Participants who were pregnant at time of randomisation
Gravidity	• The number of times the participant has been pregnant, regardless of the outcome of the pregnancy. • Include the current pregnancy in this count.	Participants who were pregnant at time of randomisation
Parity	• The number of times the participant has given birth (including live births and stillbirths) to a foetus with a gestational age of 24 weeks or more. • A multiple pregnancy (e.g. twins) that are carried to more than 24 weeks are counted as one (1).	Participants who were pregnant at time of randomisation

Field / Question	Definition	Applies to
Is this a multiple pregnancy	• Select '**Yes**' if the participant was pregnant with more than one foetus at time of randomisation. • If the pregnancy was a multiple pregnancy, but the participant was only carrying on foetus at the time of randomisation, select '**No**'	Participants who were pregnant at time of randomisation
Number of foetuses	• Enter the number of foetuses that the participant was pregnant with at the time of randomisation.	Participants who were pregnant with multiple foetuses at time of randomisation

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6.1.3 Medical history

Field / Question	Definition	Applies to

Chronic respiratory or pharyngeal neuromuscular weakness	• Select '**Yes**' if the participant has weakness sufficient to have resulted in documented or implied functional impairment of one or both of respiratory muscle strength or laryngeal protective mechanisms.
	• Associated conditions include:
	  ◦ Stroke with swallowing difficulty
	  ◦ Cerebral palsy
	  ◦ Motor Neuron Disease, including Lou Gehrig's disease (aka Amyotrophic lateral sclerosis, Progressive Muscular Atrophy, Progressive Bulbar Palsy and Primary Lateral Sclerosis)
	  ◦ Muscular dystrophy
	  ◦ Myotonic dystrophy
	  ◦ Chronic demyelinating polyneuropathy
	  ◦ Current (not recovered) Guillain–Barré syndrome
	  ◦ Bulbar neuromuscular weakness (including stroke).
	• If unknown, select '**No**'.
		Participants who have received an allocation in the Antibiotic Domain

Field / Question	Definition	Applies to
Diabetes	• Select one option. • Select '**Type 1**' or '**Type 2**' if the participant has documented clinical diagnosis of either type of diabetes mellitus prior to randomization. • Select '**gestational diabetes**' if the participant has been diagnosed with gestational diabetes - that is, hyperglycaemia that was first diagnosed or developed during pregnancy ◦ A participant with documented Type 1 or Type 2 diabetes (diagnosed prior to pregnancy) who is also pregnant does not have gestational diabetes. • Select '**Not diagnosed with diabetes**' if there is no history of diabetes in the medical record. • Select '**Not diagnosed with diabetes**' for participants who have an elevated blood glucose level due to critical illness but do not have a diagnosis of diabetes prior to this hospital admission.	All participants

Field / Question	Definition	Applies to

Chronic kidney disease	• Select one option.
	• Chronic kidney disease status is determined from the most recent stable serum creatinine in the year prior to this hospital admission, except for participants who were receiving chronic dialysis prior to this hospital admission.
	  ◦ If only one serum creatinine measurement is available, assume that this value has remained stable since it was measured.
	• If no stable creatinine measurement available in the year prior to hospital admission:
	  ◦ If creatinine measurement at admission is within normal ranges (see below), select '**normal renal function**'
	  ◦ If creatinine measurement at admission is abnormal / outside of normal ranges, select '**not recorded**'
	• **Normal renal function** is defined as a creatinine level of < 130 umol/L (1.5 mg/dL) for males, or <100 umol/L (1.1 mg/dL) for females.
	• **Abnormal renal function not normally receiving dialysis** refers to a creatine level outside of these normal ranges in participants who are not receiving chronic dialysis prior to this hospital admission.
	  ◦ If an arteriovenous fistula or shunt has been placed in readiness for chronic dialysis but dialysis has not commenced, select '**Abnormal renal function not normally receiving dialysis**'.
	• Select '**normally receiving dialysis**' if the participant was receiving chronic dialysis prior to this hospital admission.
		All participants

Field / Question	Definition	Applies to

Respiratory comorbidities	• Select '**Yes**' if the patient has respiratory comorbidities that are documented in the participant's medical records as being present and diagnosed prior to this hospital admission
	• If '**Yes**' is selected, you will be asked to specify the comorbidities:
	• **Asthma**
	• **Bronchiectasis**
	• **Chronic Obstructive Pulmonary Disease (COPD)**
	• **Interstitial lung disease:** defined as a group of disorders that cause progressive scarring of the lung tissue, including:
	  • Idiopathic pulmonary fibrosis
	  • Other idiopathic interstitial pneumonias
	  • Interstitial lung disease associated with systemic diseases or connective tissue diseases (e.g., rheumatoid arthritis, scleroderma, sarcoidosis)
	• Current diagnosis of **Primary lung cancer**
	  • Does not include resection of primary lung cancer without recurrence, or secondary (metastatic) cancer of the lung
	• **Chronic lung disease of prematurity (not asthma)**
	• **Other:** any other respiratory comorbidity that can be associated with severe functional respiratory impairment, including (but not limited to):
	  • Primary pulmonary hypertension
	  • Severe restrictive lung disease, including kyphoscoliosis or morbid obesity with documented severe respiratory impairment
	  • Cystic fibrosis
	  • Severe respiratory neuromuscular weakness
	• If none of the above recorded in the participant's medical record as being present and diagnosed prior to this hospital admission, select '**No**'.
		All participants

Field / Question	Definition	Applies to

Severe respiratory comorbidity	• This question will only appear if a respiratory co-morbidity was indicated in the previous question.
	• Select '**Yes**' if any of the respiratory comorbidities indicated in the previous question are considered to be severe.
	• A severe respiratory co-morbidity is defined as:
	  • Chronic respiratory disease resulting in severe exercise restriction (unable to climb stairs or perform household duties) OR
	  • Documented chronic hypoxia, hypercapnia, secondary polycythaemia, severe pulmonary hypertension (mean > 40 mmHg).
		Participants with a respiratory comorbidity

Immunosuppressive treatment	• Select '**Yes**' if the participant has received therapy that has suppressed resistance to infection prior to this hospital admission. • Immunosuppressive treatments are defined in the following row.	All participants
Specify immunosuppressive treatment	• Select all therapies that the participant has received prior to this hospitalisation. • **Chemotherapy** within 4 weeks prior to this hospitalisation. • **High dose steroid treatment:** >15mg/kg methyl prednisolone or equivalent for ≥5 days. • **Long-term steroid treatment:** for example, > 20mg/day of a systemic steroid. • **High dose radiotherapy** including myeloablative radiotherapy (e.g. prior to a stem cell transplant) or high-dose radiotherapy for lung cancer. • **Anti-CD20 antibodies** such as rituximab, obinutuzumab, ocrelizumab • **Bruton's Tyrosine Kinase Inhibitors** such as ibrutinib, acalabrutinib, zanubrutinib • **Allogeneic stem cell transplant** in the last 12 months or anytime if on-going treatment for chronic GVHD • **Autologous stem cell transplant** in the last 6 months • **Solid organ transplant** • **Chimeric antigen receptor T-cell (CAR-T) therapy** within the last 12 months • **Other immunosuppressive biological therapies**	Participants who have received an allocation in the COVID-19 Immunoglobulin Domain who are receiving an immunosuppressive treatment

Field / Question	Definition	Applies to
Immune suppressive disease	• Select '**Yes**' if the participant had one or more of the following diseases that are sufficiently advanced to suppress resistance to infection at the time of this hospitalisation. • Excludes malignancy which has been in remission for five years or more.	All participants

Field / Question	Definition	Applies to

Specify immune suppressive disease	• Select all of the immunosuppressive diseases that were diagnosed and present prior to this hospitalisation.
	• **Acquired Immunodeficiency syndrome (AIDS)**:
	  • Includes any clinical syndrome of AIDS-HIV positive with AIDS defining complications (e.g. pneumocystitis carinii pneumonia, Kaposi's sarcoma, lymphoma, tuberculosis, or toxoplasma infection).
	• **Acute leukaemia (including high-risk MDS):**
	  • Any type of active leukaemia, including acute myeloid leukaemia (AML) and acute lymphoblastic leukaemia (ALL).
	• **Lymphoma**
	• **Metastatic cancer:**
	  • Proven distant metastases (not regional lymph nodes or contiguous spread) by surgery, CT scan, or other method.
	• **Myeloma**
	• **Aplastic anemia** of any severity
	• **Severe chronic neutropenia**:
	  • Any type of severe chronic neutropenia, including congenital, autoimune, or idiopathic.
	• **Myelodysplastic syndrome:**
	  • Includes chronic myelomonocytic leukemia (CMML), atypical chronic myeloid leukemia (aCML), or unclassifiable myelodysplastic/ myeloproliferative neoplasms (MDS/MPN).
	• **Primary or inherited immune deficiency syndromes**
	  • including B cell deficiencies (such as Bruton agammaglobulinemia), T cell deficiencies (such as Wiskott Aldrich disease), or combined deficiencies (such as Common variable immunodeficiency).
	• **Secondary immune deficiency syndromes** requiring treatment with regular IV immunoglobulin.
	• Any **other** disease that is sufficiently advanced to suppress resistance to infection.
		Participants who have an immunosuppressive disease

Field / Question	Definition	Applies to

Chronic cardiovascular disease	• New York Heart Association Class IV Heart Failure, defined as:
	  • Angina or other symptoms at rest or on minimal exertion (whilst getting dressed or during self-care)
	  • Unable to carry out any physical activity without discomfort.
	  • If physical activity is undertaken, discomfort increases.
		All adult participants

Cirrhosis	• Includes documented:
	  • Biopsy or imaging proven cirrhosis and documented portal hypertension, or
	  • Episodes of past upper gastrointestinal bleeding attributed to portal hypertension.
	• Select '**No**' if the participant has a functioning liver transplant.
		All adult participants

Hepatic failure	• Includes documented episodes of hepatic failure, encephalopathy, or coma	All adult participants

Field / Question	Definition	Applies to

Clinical frailty score	• Select the option that best describes the participant's level of function in the two months prior to this hospitalisation
	• Clinical frailty status may be obtained from the medical record or the participant directly, or other sources, if easily accessible.
	• Other information including employment, recreational activities, and performance of activities of daily living can be used to determine frailty.
	• If no information is available with which to determine the participant's frailty status, select '**unable to be determined**'.
	• For assistance refer to the Clinical Frailty Score guidance here
	• For participants with dementia:
	  • The degree of frailty corresponds to the severity of dementia. Common symptoms of *mild* dementia include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.
	  • In *moderate* dementia, recent memory is very impaired, even though they seemingly can remember their past life events well. They can perform personal care with prompting.
	  • In *severe* dementia, they cannot perform personal care without help.
	Descriptions of each category are as follows:
	1. **Very fit**: People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.
	2. **Well**: People who have no active disease symptoms but exercise less regularly than those who are *very fit*. They often exercise or are very active occasionally (e.g. seasonally).
	3. **Managing well:** People whose medical problems are well controlled, but are not regularly active beyond routine walking.
	4. **Vulnerable**: While not dependent on others for daily help, often their symptoms limit activities. A common complaint of vulnerable people is being 'slowed up', and/or being tired during the day.
		All adult participants

Field / Question	Definition	Applies to
	5. **Mildly frail**: People who often have more evident slowing, and need help in higher order instrumental activities of daily living (IADLs) (e.g. finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping, walking outside alone, meal preparation and house work. 6. **Moderately frail**: People who need help with all outside activities and with keeping house. Inside, they often have problems with stairs, need help with bathing and might need minimal assistance (e.g., cuing, standby) with dressing. 7. **Severely frail**: People who are completely dependent for personal care, from whatever cause (physical or cognitive), but seem stable and not at high risk of dying (within the next 6 months). 8. **Very severely frail**: People who are completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness. 9. **Terminally ill**: Approaching the end of life. This category applies to people with a life expectancy < 6 months who are not otherwise evidently frail.	
COVID-19 vaccination	• Select '**Yes**' if the patient is known to have ever received at least one dose of an approved COVID-19 vaccine prior to this acute illness • Select '**No**' if it is known that the patient has not received any dose of an approved COVID-19 vaccine prior to this acute illness • Select '**Unknown**' if the participant's vaccination status is unknown or unavailable	Participants who have received an allocation in the Immunoglobulin Domain, Endothelial Domain, Mechanical Ventilation Domain, or COVID-19 Antiviral Domain

Field / Question	Definition	Applies to
Influenza vaccination within the last 12 months	• Select '**Yes**' if the patient is known to have received at least one dose of an approved influenza vaccine within the 12 months prior to this acute illness • Select '**No**' if it is known that the patient has not received any dose of an approved influenza vaccine within the 12 months prior to this acute illness • Select '**Unknown**' if this patient's vaccination status is unknown or unavailable	Participants who have received an allocation in the Influenza Antiviral or Influenza Immune Modulation Domain
Have SARS-CoV-2 anti-spike antibodies been detected	• Select '**not tested**' if only nucleocapsid protein antibodies have been tested for	Participants who have received an allocation in the COVID-19 Immunoglobulin Domain
Was etomidate administered between hospital admission and randomisation	• Select 'Yes' if etomidate was administered (for example, for induction of anesthesia or emergency intubation) between hospital admission and randomisation to the Corticosteroid Domain.	Participants who have received an allocation in the Corticosteroid Domain

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6.1.4 Vital Signs

Field / Question	Definition	Applies to
Respiratory rate	• Enter respiratory rate recorded closest to and prior to randomization • Only use respiratory rate measurements recorded during this hospital admission	All participants
Heart rate	• Enter heart rate recorded closest to and prior to randomization • Only use heart rate measurements recorded during this hospital admission	All participants

Field / Question	Definition	Applies to
Systolic blood pressure	• Enter systolic blood pressure recorded closest to and prior to randomization • Only use systolic blood pressure measurements recorded during this hospital admission • Invasive measurements are preferred. If no invasive blood pressure has been recorded, use non-invasive measurements.	All participants
Diastolic blood pressure	• Enter diastolic blood pressure recorded closest to and prior to randomization • Only use diastolic blood pressure measurements recorded during this hospital admission • Invasive measurements are preferred. If no invasive blood pressure has been recorded, use non-invasive measurements.	All participants
Glasgow Coma Scale Score	• Enter the GCS recorded closest to randomisation when the participant was free of the effects of sedative, paralyzing or neuromuscular blocking agents. • Total GCS score is the sum of the three components of the GCS (eye opening, verbal, and motor), and is scored out of 15. • If not clearly documented in medical record, ancillary information should be used to provide the best estimate of pre-sedation GCS. • If no information is available with which to determine the participant's GCS score prior to sedation, enter a score of **15** (i.e. normal).	All participants
Body temperature	• Enter temperature recorded closest to and prior to randomization • Only use temperatures recorded during this hospital admission. • Core temperature measurement (such as rectal, tympanic, esophageal or via pulmonary artery catheter) is preferred. ◦ If an oral or axillary temperature is available add 0.5°C to the oral or axillary temperature. • Do not include temperatures measured while the patient is being actively cooled.	All participants

6.1.5 Respiratory

Field / Question	Definition	Applies to
pH	• Enter pH recorded closest to randomization. • Only use pH measurements recorded during this hospital admission. • Enter values obtained from ABG or laboratory sample.	All participants in the Severe State, and all participants in the Moderate State who are admitted to an ICU.
Lactate	• Enter lactate in mmol/L measured closest to randomisation • If a laboratory measured serum value is not available, a venous or arterial measurement from an ABG machine or laboratory is acceptable. • Only use samples collected during this hospital admission prior to randomization. • If lactate was not measured, select '**not recorded**'.	All participants in the Severe State, and all participants in the Moderate State who are admitted to an ICU.
Has a blood gas been taken during this admission, prior to randomisation	• Select '**arterial blood gas**' (ABG) if at least one arterial blood gas was measured during this hospital admission, prior to randomisation. • Select '**capillary blood gas**' (CBG) if no arterial blood gas measurements were obtained, and at least one capillary blood gas was measured during this hospital admission, prior to randomisation. • Select '**none**' if no arterial or capillary blood gas measurements have been obtained during this hospital admission and prior to randomisation.	All participants in the Severe State, and all participants in the Moderate State who are admitted to an ICU.
Date and time of arterial or capillary blood gas	• Enter the date and time of the blood gas measurement obtained closest to randomisation and during this hospital admission. • If multiple ABGs or CBGs were taken between hospital admission and randomisation, use the sample collected closest to randomization.	All participants who have had an ABG or CBG measurement

Field / Question	Definition	Applies to
FiO_2 at time of blood gas	• Record the FiO_2 (range 0.21 - 1.0) the participant was receiving at the time the ABG or CBG was taken. • If no ABG or CBG was taken, enter the FiO_2 that corresponds to the SpO_2 recorded closest to randomisation.	All participants who have had an ABG or CBG measurement
Corresponding SpO_2	• If no ABG or CBG has been obtained, enter the participant's SpO_2 closest to randomisation.	All participants
Corresponding PaO_2	• Enter the PaO_2 on the ABG or CBG. • Select the unit of measurement and enter the value in the appropriate field.	All participants who have had an ABG or CBG measurement
Corresponding $PaCO_2$	• Enter the $PaCO_2$ on the ABG or CBG. • Select the unit of measurement and enter the value in the appropriate field.	All participants who have had an ABG or CBG measurement
Corresponding PEEP	• The PEEP or CPAP the participant was receiving at the time the ABG or CBG used above was collected. • If no ABG or CBG was collected enter PEEP at the time of randomization. • If the participant is receiving invasive mechanical ventilation or NIV and the PEEP/CPAP is set to 0, enter 0. • If the participant was receiving High-Flow oxygen at the time of the ABG or CBG, enter the PEEP as zero (i.e. 0). • If the participant is not receiving invasive mechanical ventilation, NIV, or HFNP, select '**Not recorded**'. • If the participant was receiving invasive mechanical ventilation using APRV mode at the time that the ABG or CBG was obtained, select '**patient receiving APRV**'.	All participants who have had an ABG or CBG measurement

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6.1.6 Laboratory

Field / Question	Definition	Applies to
Sodium	• Enter sodium recorded closest to randomization, up to 24 hours prior to randomization. • An ABG machine measured sodium may be used but only if a laboratory measured serum value is not available. • Only use samples collected during this hospital admission prior to randomisation. • Select the unit of measurement and record the result in the appropriate field. • If sodium was not measured, select '**not recorded**'.	All participants in the Severe State, and all participants in the Moderate State who are admitted to an ICU.
Potassium	• Enter potassium recorded closest to randomization, up to 24 hours prior to randomization. • An ABG machine measured potassium may be used but only if a laboratory measured serum value is not available. • Only use samples collected during this hospital admission prior to randomisation. • Select the unit of measurement and record the result in the appropriate field. • If potassium was not measured, select '**not recorded**'.	All participants in the Severe State, and all participants in the Moderate State who are admitted to an ICU.
Bicarbonate	• Enter serum bicarbonate recorded closest to randomization, up to 24 hours prior to randomisation • Enter values obtained from ABG or laboratory sample • Only use bicarbonate measurements recorded during this hospital admission • Select the unit of measurement and record the result in the appropriate field. • If potassium was not measured, select '**not recorded**'.	All participants in the Severe State, and all participants in the Moderate State who are admitted to an ICU.

Field / Question	Definition	Applies to
Creatinine	• Enter creatinine measured closest to randomisation, up to 24 hours prior to randomization. • Taken from serum or plasma samples. • If a laboratory measured serum or plasma value is not available, an ABG machine measured creatinine may be used. • Only use samples collected during this hospital admission prior to randomisation. • Select the unit of measurement and record the result in the appropriate field. • If creatinine was not measured, select '**not recorded**'.	All participants in the Severe State, and all participants in the Moderate State who are admitted to an ICU.
Urea	• Enter urea measured closest to randomisation up to 24 hours prior to randomization. • Taken from serum or plasma samples. • If a laboratory measured serum or plasma value is not available, an ABG machine measured urea may be used. • Only use samples collected during this hospital admission prior to randomisation. • Select the unit of measurement and record the result in the appropriate field. • If urea was not measured, select '**not recorded**'.	All participants in regions that report urea rather than BUN
Blood urea nitrogen (BUN)	• Enter BUN measured closest to randomisation. • Taken from serum or plasma samples. • If a laboratory measured serum or plasma value is not available, an ABG machine measured BUN may be used. • Only use samples collected during this hospital admission prior to randomization. • Select the unit of measurement and record the result in the appropriate field. • If BUN was not measured, select '**not recorded**'.	All participants in regions that report BUN rather than urea

Field / Question	Definition	Applies to
Bilirubin	• Enter bilirubin measured closest to randomisation. • Taken from serum or plasma samples. • Only use results from samples collected during this hospital admission prior to randomization. • Select the unit of measurement and record the result in the appropriate field. • If bilirubin level was not measured, select '**not recorded**'.	All participants in the Severe State, and all participants in the Moderate State who are admitted to an ICU.
White cell count	• Enter White Cell Count (WCC) count in cells x 10^9 /L measured closest to randomisation. • Taken from laboratory sample. • Only use results from samples collected during this hospital admission prior to randomization (closest to randomization). • If WCC was not measured, select '**not recorded**'.	All participants in the Severe State, and all participants in the Moderate State who are admitted to an ICU.
Haematocrit	• Enter haematocrit recorded closest to randomization. • Only use haematocrit measurements recorded during this hospital admission. • Enter values obtained from ABG or laboratory sample. • Enter as percentage (%).	All participants in the Severe State, and all participants in the Moderate State who are admitted to an ICU.
Platelet count	• Enter platelet count in cells x 10^9/L measured closest to randomisation. • Taken from laboratory sample. • Only use results from samples collected during this hospital admission prior to randomization (closest to randomization). • If platelet count was not measured, select '**not recorded**'.	All participants in the Severe State, and all participants in the Moderate State who are admitted to an ICU.

6.1.7 Organ Support

Field / Question	Definition	Applies to

Vasoactive medication	• Select the option that best represents what vasopressors or inotropes the participant was receiving as a continuous infusion for at least one hour at the indicated dose, at the time of randomisation.
	  • None
	  • Dopamine ≤ 5 mcg/kg/min; any dobutamine, levosimendan, or milrinone
	  • Dopamine > 5 mcg/kg/min; norepinephrine/ noradrenaline ≤ 0.1 mcg/kg/min; epinephrine/ adrenaline ≤ 0.1 mcg/kg/min; any metaraminol, phenylephrine, or vasopressin
	  • Dopamine > 15 mcg/kg/min; norepinephrine/ noradrenaline > 0.1 mcg/kg/min; epinephrine/ adrenaline > 0.1 mcg/kg/min
	  • Norepinephrine/noradrenaline > 0.3 mcg/kg/ min; epinephrine/adrenaline > 0.3 mcg/kg/min
		All participants

Renal replacement therapy	• Select '**Yes**' if the participant received renal replacement therapy (RRT) at any time during this hospital admission prior to randomisation. • The participant does not have to be receiving RRT at the time of randomization. • RRT is defined in General Definitions. • Select '**No**' if the participant usually receives chronic RRT but did not receive RRT during this hospital admission prior to randomization.	All participants
Extracorporeal gas exchange	• Extracorporeal gas exchange is defined as extracorporeal provision of oxygen and/or removal of carbon dioxide. • Select '**Yes**' if the participant received extracorporeal gas exchange at any time during this hospital admission prior to randomization. • The participant does not have to be receiving extracorporeal gas exchange at the time of randomization.	All participants

Field / Question	Definition	Applies to

Type of extracorporeal gas exchange received	• Select all modes of extracorporeal gas exchange the the participant received during this hospital admission prior to randomisation
	• **Extracorporeal Membrane Oxygenation (ECMO)**:
	  • Includes all forms of ECMO (e.g. veno-venous, veno-arterial and other combinations), irrespective of site of cannulation or location where the ECMO was instituted.
	• **Extracorporeal Carbon Dioxide Removal ($ECCO_2R$)**:
	  • Includes all forms of $ECCO_2R$, irrespective of site of cannulation or location where the $ECCO_2R$ was instituted.
		Participants who have received extracorporeal gas exchange

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6.1.8 Ethnicity

Field / Question	Definition	Applies to

Australian ethnicity	• Select the option that best describes the participant's ethnicity.
	• An ethnic group is made up of people who have some or all of the following:
	  • A shared culture, such as traditions, customs, beliefs, or language.
	  • A common ancestry or history.
	  • A similar geographic, tribal, or clan origin.
	• Select the appropriate box from the list provided, based on the information obtained from the medical record, the participant directly, or other sources, if easily accessible.
		Participants enrolled at Australian sites

Field / Question	Definition	Applies to

New Zealand ethnicity	• Select up to two options that best describe the participant's ethnicity.
	• Never guess or decide ethnicity for the participant.
	• An ethnic group is made up of people who have some or all of the following:
	  • A shared culture, such as traditions, customs, beliefs, or language
	  • A common ancestry or history
	  • A similar geographic, tribal, or clan origin.
	• Select the appropriate box from the list provided, based on the information obtained from the medical record, the participant directly, family, or other sources, if easily accessible.
	• If the participant identifies with more than one ethnic group select up to two ethnicities from the list provided.
		Participants enrolled at sites in New Zealand

Canadian ethnicity	• Select the option that best describes the participant's ethnicity.
	• An ethnic group is made up of people who have some or all of the following:
	  • A shared culture, such as traditions, customs, beliefs, or language.
	  • A common ancestry or history.
	  • A similar geographic, tribal, or clan origin.
	• Select the appropriate box from the list provided, based on the information obtained from the medical record, the participant directly, or other sources, if easily accessible.
		Participants enrolled at Canadian sites

6.2 Mechanical Ventilation Domain Baseline

Additional baseline data are collected for participants who have received an allocation in the Mechanical Ventilation Domain.

6.2.1 Acute Respiratory Distress Syndrome (ARDS)

Field / Question	Definition	Applies to
Was chest imaging performed within the last 24 hours	• Chest x-ray or chest computerized tomography (CT) scan. • Performed within 24 hours prior to reveal of allocation in the Ventilation Domain. • If multiple chest x-rays or CTs have been performed within the 24 hours prior to reveal of allocation to the Mechanical Ventilation Domain, use the interpretable image obtained closest to but prior to reveal of allocation within this domain.	Participants who have received an allocation in the Mechanical Ventilation Domain
Select all lung quadrants with lung infiltrates	• Select all lung quadrants with lung infiltrates on chest x-ray or CT performed closest to and before reveal of allocation in the Mechanical Ventilation Domain. • Pleural effusions, lobar collapse, lung collapse (atelectasis) and nodules or solid masses are not lung infiltrates and do not meet this definition.	Participants who have received an allocation in the Mechanical Ventilation Domain

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6.2.2 Baseline Arterial Blood Gas

Field / Question	Definition	Applies to
What was the PaO2 on the most recent ABG	• Enter the PaO2 on the ABG collected closest to and within 6 hours prior to reveal of allocation in the Mechanical Ventilation Domain • Select the unit of measurement and enter the result in the appropriate box.	Participants who have received an allocation in the Mechanical Ventilation Domain

Field / Question	Definition	Applies to
What was the corresponding FiO2	• Record the FiO2 (range 0.21 - 1.0) the participant was receiving at the time the ABG was taken. The most recent ABG within 6 hours prior to reveal of allocation should be used. • If necessary, convert FiO2 percentage to value between 0.21 and 1.00, i.e. 40% = 0.40 • Only use a sample collected during this hospital admission prior to reveal of allocation. • If multiple ABGs were taken between hospital admission and reveal of allocation use the sample collected closest to reveal of allocation.	Participants who have received an allocation in the Mechanical Ventilation Domain
What was the corresponding PEEP	• The PEEP the participant received at the time the ABG used above was collected. • If the participant was receiving invasive ventilation using APRV mode at the time that the ABG was obtained, select '**patient receiving APRV**'.	Participants who have received an allocation in the Mechanical Ventilation Domain
pH	• Record the pH from the participant's ABG collected closest to and within 6 hours prior to reveal of allocation in the Mechanical Ventilation Domain	Participants who have received an allocation in the Mechanical Ventilation Domain
$PaCO_2$	• Enter the partial pressure of carbon dioxide ($PaCO_2$) on the ABG collected closest to and within 6 hours prior to reveal of allocation in the Mechanical Ventilation Domain. • Select the unit of measurement and enter the result in the appropriate field.	Participants who have received an allocation in the Mechanical Ventilation Domain

Field / Question	Definition	Applies to
Bicarbonate	• Enter the actual bicarbonate on the ABG collected closest to and within 6 hours prior to reveal of allocation to the Mechanical Ventilation Domain.	Participants who have received an allocation in the Mechanical Ventilation Domain
SaO_2	• Record the arterial oxygen saturation from the ABG collected closest to and within 6 hours prior to reveal of allocation to the Mechanical Ventilation Domain. • Note that this is oxygen saturation (SaO_2) from the ABG, not pulse oximetry (SpO_2).	Participants who have received an allocation in the Mechanical Ventilation Domain
Lactate	• Enter the lactate value recorded closest to and within 6 hours prior to reveal of allocation in the Mechanical Ventilation Domain. • If a laboratory measured serum value is not available, a venous or arterial measurement from an ABG machine or laboratory is acceptable. • Select the unit of measurement and enter the result in the appropriate field.	Participants who have received an allocation in the Mechanical Ventilation Domain
Base Excess	• Enter the calculated base excess on the ABG collected closest to and within 6 hours prior to reveal of allocation to the Mechanical Ventilation Domain. • Select “+” to indicate that the Base Excess is a positive value, or “-“ if Base Excess is a negative value	Participants who have received an allocation in the Mechanical Ventilation Domain

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6.2.3 Therapies At Randomisation

Field / Question	Definition	Applies to
Is the patient receiving continuous or intermittent neuromuscular blockade	• Select '**Yes**' if the participant was receiving ongoing continuous neuromuscular blockade by infusion or intermittent bolus administration at the time of reveal of allocation to the Mechanical Ventilation Domain. • When considering if boluses are included in this definition, consider whether the aim is to keep the participant paralyzed. If that is the case, select '**Yes**'. However, ongoing neuromuscular blockade will usually be in the form of an infusion or ongoing intermittent doses. If the participant receives a "one-off" bolus, with no intention to keep the participant paralyzed, then select '**No**'. • Neuromuscular blockade for the sole purpose of intubation or other procedures does not meet this definition	Participants who have received an allocation in the Mechanical Ventilation Domain
Is the patient receiving continuous vasopressor and/or inotrope infusion	• If a participant was receiving a continuous infusion at the time of reveal of allocation to the Mechanical Ventilation Domain select '**Yes**'. • The infusion must have been administered for at least one continuous hour. If the ICU Chart only records hourly interventions the treatment must have been recorded for at least two consecutive hours. • If the participant received intermittent doses of a vasopressor or inotrope, even if given frequently, select '**No**'. • Vasopressors and inotropes are defined in General Definitions.	Participants who have received an allocation in the Mechanical Ventilation Domain
Renal replacement therapy	• Select '**Yes**' if at the time of reveal of allocation in the Mechanical Ventilation Domain the participant was receiving and will continue to receive intermittent or continuous RRT • RRT is defined in General Definitions.	Participants who have received an allocation in the Mechanical Ventilation Domain

Field / Question	Definition	Applies to
Extracorporeal gas exchange	• Extracorporeal gas exchange is defined as extracorporeal provision of oxygen and/or removal of carbon dioxide. • Select '**Yes**' if the participant was receiving extracorporeal gas exchange at time of reveal of allocation in the Mechanical Ventilation Domain.	Participants who have received an allocation in the Mechanical Ventilation Domain
Extracorporeal Membrane Oxygenation (ECMO)	• Includes all forms of ECMO (e.g. veno-venous, veno-arterial and other combinations), irrespective of site of cannulation or location where the ECMO was instituted. • Includes participants already on ECMO at admission to ICU.	Participants who have received an allocation in the Mechanical Ventilation Domain who were receiving extracorporeal gas exchange at baseline
$ECCO_2R$	• Includes all forms of $ECCO_2R$, irrespective of site of cannulation or location where the $ECCO_2R$ was instituted. • Includes participants already on $ECCO_2R$ at admission to ICU.	Participants who have received an allocation in the Mechanical Ventilation Domain who were receiving extracorporeal gas exchange at baseline

Field / Question	Definition	Applies to
Recruitment maneuver	• Select '**Yes**' if the participant underwent a recruitment maneuver within the 24 hours prior to reveal of allocation in the Mechanical Ventilation Domain. • A recruitment maneuver is defined as any transient, sustained increases in transpulmonary pressure designed to open collapsed airless alveoli. These increases in transpulmonary pressure can be achieved through increases in PEEP and/or tidal volume.	Participants who have received an allocation in the Mechanical Ventilation Domain
Nitric oxide	• Select '**Yes**' if the participant was receiving inhaled nitric oxide at the time of reveal of allocation in the Mechanical Ventilation Domain.	Participants who have received an allocation in the Mechanical Ventilation Domain
Prone positioning	• Select '**Yes**' if the participant has had any period of invasive mechanical ventilation while in the prone position within the 24 hours prior to reveal of allocation in the Mechanical Ventilation Domain.	Participants who have received an allocation in the Mechanical Ventilation Domain
Inhaled prostacyclin	• Select '**Yes**' if the participant was receiving inhaled prostacyclin at the time of reveal of allocation in the Mechanical Ventilation Domain. • Includes continuous or intermittent administration.	Participants who have received an allocation in the Mechanical Ventilation Domain

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6.2.4 Baseline Ventilation Parameters

Field / Question	Definition	Applies to
Mode of invasive ventilation	• Select the mode of invasive ventilation the patient was receiving at the time of reveal of allocation in the Mechanical Ventilation Domain. • Ventilator Modes are listed here.	Participants who have received an allocation in the Mechanical Ventilation Domain
SpO_2	• Enter oxygen saturation using pulse oximetry recorded closest to and prior to reveal of allocation in the Mechanical Ventilation Domain. • Note that this is not arterial oxygen saturation measured on ABG.	Participants who have received an allocation in the Mechanical Ventilation Domain
$EtCO_2$	• Enter end-tidal carbon dioxide recorded closest to and prior to reveal of allocation in the Mechanical Ventilation Domain. • Note that this is not $PaCO_2$ measured on ABG.	Participants who have received an allocation in the Mechanical Ventilation Domain
Set respiratory rate	• Enter the last set respiratory rate (in breaths per minute) that is set on the ventilator prior to reveal of allocation in the Mechanical Ventilation Domain. • The set respiratory rate is the number of mandatory breaths delivered by the ventilator per minute. • If the participant is on a mode of ventilation in which all breaths are triggered or spontaneous, enter zero ('**0**').	Participants who have received an allocation in the Mechanical Ventilation Domain

Field / Question	Definition	Applies to
Recorded total respiratory rate	• Enter the last total respiratory rate (bpm) recorded prior to reveal of allocation in the Mechanical Ventilation Domain. • Total respiratory rate is the sum of breaths delivered by the ventilator (mandatory breaths) plus any breaths initiated by the patient (spontaneous breaths).	Participants who have received an allocation in the Mechanical Ventilation Domain
Are the mandatory breaths that the patient is receiving pressure-cycled or volume-cycled	• Select pressure-cycled if the ventilator is set to deliver a specified amount of pressure during inspiration for the mandatory breaths. • Select volume-cycled if the ventilatory is set to deliver a specified tidal volume during inspiration for the mandatory breaths.	Participants who have received an allocation in the Mechanical Ventilation Domain, who are receiving mandatory breaths
Expired Tidal Volume	• Enter the last mandatory tidal volume (in mL) recorded prior to reveal of allocation in the Mechanical Ventilation Domain. • If the participant is on a fully spontaneous mode of ventilation, enter the last recorded tidal volume prior to reveal of allocation in the Mechanical Ventilation Domain.	Participants who have received an allocation in the Mechanical Ventilation Domain
Recorded Peak Inspiratory Pressure	• Enter the last peak inspiratory pressure (in cmH_2O) recorded prior to reveal of allocation in the Mechanical Ventilation Domain.	Participants who have received an allocation in the Mechanical Ventilation Domain

Field / Question	Definition	Applies to
Set pressure support	• If the participant is receiving inspiratory pressure support for spontaneous breaths enter the last pressure support (in cmH_2O) that was set on the ventilator prior to reveal of allocation in the Mechanical Ventilation Domain. • Record the amount of pressure support as the set pressure applied above PEEP • Enter "**0**" if the participant is taking spontaneous breaths without inspiratory pressure support. • Select "**Not applicable**" if participant is receiving only mandatory breaths. • If the ventilator is providing tube compensation, ignore tube compensation.	Participants who have received an allocation in the Mechanical Ventilation Domain
Recorded Plateau pressure	• If performed and recorded, enter the last plateau pressure (in cmH_2O) recorded prior to reveal of allocation in the Mechanical Ventilation Domain. • Plateau pressure is measured by setting a 0.5 second inspiratory pause and recording the pressure at the end of the hold. • Select "**not recorded**" if plateau pressure has not been performed or is not recorded.	Participants who have received an allocation in the Mechanical Ventilation Domain, who are receiving mandatory breaths
Set PEEP	• Enter the last PEEP (in cmH_2O) recorded prior to reveal of allocation in the Mechanical Ventilation Domain. • If the participant was receiving invasive ventilation using APRV mode at the time that the ABG was obtained, select '**patient receiving APRV**'.	Participants who have received an allocation in the Mechanical Ventilation Domain

Field / Question	Definition	Applies to
I:E ratio	• Enter the last inspiratory to expiratory (I:E) ratio recorded prior to reveal of allocation in the Mechanical Ventilation Domain.	Participants who have received an allocation in the Mechanical Ventilation Domain, who are receiving mandatory breaths
Set P_{LOW}	• Enter the last P_{LOW} (cmH_20) set on the ventilator prior to reveal of allocation. • P_{LOW} is the pressure set for the short period of airway release during APRV ventilation.	Participants who have received an allocation in the Mechanical Ventilation Domain, on APRV ventilator mode
Set P_{HIGH}	• Enter the last P_{HIGH} (cmH_20) set on the ventilator prior to reveal of allocation. • P_{HIGH} is the pressure used to determine the inspiratory plateau during APRV ventilation.	Participants who have received an allocation in the Mechanical Ventilation Domain, on APRV ventilator mode
T_{LOW}	• Enter the last T_{LOW} (in seconds) recorded prior to reveal of allocation. • T_{LOW} is the time spent in P_{LOW} during APRV ventilation.	Participants who have received an allocation in the Mechanical Ventilation Domain, on APRV ventilator mode

Field / Question	Definition	Applies to
T_{HIGH}	• Enter the last T_{HIGH} (in seconds) recorded prior to reveal of allocation. • T_{HIGH} is the time spent in P_{HIGH} during APRV ventilation. • If T_{LOW} is recorded it is not necessary to also enter T_{HIGH}.	Participants who have received an allocation in the Mechanical Ventilation Domain, on APRV ventilator mode

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6.2.5 Oxygenation Target

Field / Question	Definition	Applies to
Did the patient have a specified target for oxygenation or carbon dioxide	• Select '**Yes**' if the participant had a documented oxygenation target prior to reveal of allocation in the Mechanical Ventilation Domain.	Participants who have received an allocation in the Mechanical Ventilation Domain
Oxygenation target range upper value	• Select whether oxygenation target was specified in SpO_2 or PaO_2 and enter the upper limit of the oxygenation target. • If oxygenation target has been set in both SpO_2 and PaO_2, select the oxygenation target that is most frequently applied. • If no upper limit for oxygenation target has been documented, select "**no upper limit documented**".	Participants who have received an allocation in the Mechanical Ventilation Domain, where an oxygenation target was documented

Field / Question	Definition	Applies to
Oxygenation target range lower value	• Select whether oxygenation target was specified in SpO_2 or PaO_2 and enter the lower limit of the oxygenation target. • If oxygenation target has been set in both SpO_2 and PaO_2, select the oxygenation target that is most frequently applied. • If no lower limit for oxygenation target has been documented, select "**no lower limit documented**".	Participants who have received an allocation in the Mechanical Ventilation Domain, where an oxygenation target was documented
$PaCO_2$ target range upper value	• Enter the upper limit of target $PaCO_2$ range. • If no upper limit for $PaCO_2$ has been documented, select "**no upper limit documented**".	Participants who have received an allocation in the Mechanical Ventilation Domain, where an oxygenation target was documented
$PaCO_2$ target range lower value	• Enter the lower limit of target $PaCO_2$ range. • If no lower limit for $PaCO_2$ has been documented, select "**no lower limit documented**".	Participants who have received an allocation in the Mechanical Ventilation Domain, where an oxygenation target was documented

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7 Microbiology Form

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- Causative Organism
- Positive Blood Culture
- Late Positive Blood Culture
- Pleural Aspirate
- Positive Lower Respiratory Tract Specimen Culture
- Immunocompromised Patients

7.1 Causative Organism

Field / Question	Definition	Applies to

Upper or lower respiratory tract PCR test result	• For each of the organisms listed, select:
	  • **Positive**, if isolated or detected on PCR test of upper or lower respiratory tract specimens collected within 72 hours of hospital admission.
	  • **Negative**, if not reported as isolated or detected on any PCR tests of upper or lower respiratory tract specimens collected within 72 hours of hospital admission.
	  • **Not tested**, if no PCR test on an upper or lower respiratory tract specimen was collected within 72 hours of hospital admission.
	• Polymerase Chain Reaction (PCR) tests may also be known as a nucleic acid test (NAT) or GeneXpert test.
	• Upper respiratory tract specimens include:
	  • Oropharyngeal swab
	  • Nasopharyngeal swab, wash or aspirate
	  • Nasal swab or wash
	• Lower respiratory tract specimens include:
	  • Sputum specimens
	  • ETT aspirate
	  • Bronchial alveolar lavage (BAL) samples, or any specimen collected by bronchoscopy
	• If Influenza A has been isolated on upper or lower respiratory tract specimen, you will be asked to specify the strain of Influenza A that was detected.
		All participants

Field / Question	Definition	Applies to

Other upper or lower respiratory tract PCR detected organisms	• Select any of the listed organisms that were detected on PCR testing of upper or lower respiratory tract samples.
	• Only include samples isolated or detected on PCR test of upper or lower respiratory tract specimens collected within 72 hours of hospital admission.
	• **Chlamydophila pneumoniae**
	  • May be documented as *C. pneumoniae* or *Chlamydophila pneumoniae*.
	  • Do not select if other species of chlamydia (e.g. Chlamydia trachomatis and Chlamydia psittaci) are reported.
	• **Legionella spp.**
	• **Mycoplasma pneumoniae**
	• **Other (non-SARS-CoV-2) coronavirus**
	  • May be documented as: coronavirus, Alpha coronavirus (229E and NL63), Beta Coronavirus (OC43, HKU1, SARS-CoV and MERS-CoV), Severe Acute Respiratory Syndrome related coronavirus (SARS-CoV), Middle East Respiratory Syndrome Coronavirus (MERS-CoV).
	  • Do not select this option if the participant has tested positive for SARS-CoV-2 (COVID-19).
	  • Do not select this option if rhinoviruses or picornaviruses are reported.
	• **Adenovirus**
	• Select '**not tested or none of the above are positive**' if none of the listed organisms were isolated from upper or lower respiratory tract specimen samples collected within 72 hours of hospital admission.
		All participants

Field / Question	Definition	Applies to

Was mycobacterium tuberculosis detected on PCR or cultured	• Select '**Yes**' if mycobacterium tuberculosis was detected by PCR or culture from specimens collected at any time during this hospital admission.
	• Only include samples taken from the lower respiratory tract or pleural aspirate/biopsy.
	• On pathology reports tuberculosis can be documented as:
	  • Mycobacterium tuberculosis
	  • TB
	  • MTB
	  • Mycobacterium tuberculosis
	  • M tuberculosis complex.
	• If there is a report stating "positive acid-fast bacilli suggestive of tuberculosis" in the absence of the above criteria, select '**No**'.
	• Note that blood tests for TB, including Interferon gamma release assay (IGRA) also known as Quantiferon Gold or EliSpot tests do not confirm TB. In the absence of the above criteria, select '**No**'.
		All participants

Was a urinary antigen test performed	• Select '**Yes**' if urinary antigen testing was performed at any time during this hospital admission.
	• These tests may be referred to as:
	  • Urinary legionella antigen
	  • Urinary pneumococcal antigen
	  • Streptococcus pneumoniae antigen card
	• If a urinary antigen test was performed, you will be asked to indicate which organisms were detected:
	  • Any species of **Legionella**
	  • **Streptococcus pneumoniae**, also known as *S. pneumoniae* or Pneumococcus
	  • **None of the above**
		All participants

Was aspergillus isolated from the lower respiratory tract	• Select '**Yes**' if Aspergillus was isolated from the lower respiratory tract from specimens collected at any time during this hospital admission. • If aspergillus was isolated from the lower respiratory tract from specimens collected at any time during this hospital admission, you will be asked to enter the date and time of collection of the first sample in which aspergillus was isolated	All participants

Field / Question	Definition	Applies to
Was invasive pulmonary aspergillosis diagnosed and treated with one or more systemic antifungal agents	• If the patient was treated with antifungal agents for pulmonary Aspergillus during this hospital admission, select '**Yes**' • Select '**Yes**' only if invasive pulmonary Aspergillus infection was diagnosed and treated by the treating clinician.	All participants

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7.2 Positive Blood Culture

The following section relates to specimens collected within 72 hours of hospital admission.

Field / Question	Definition	Applies to
Positive blood culture result	• If no blood cultures were taken within 72 hours, select '**Not tested**'. • If any of the blood culture sets collected in the first 72 hours of hospital admission were positive, select '**Yes**'. • If all blood culture sets collected in the first 72 hours of hospital admission were negative, select '**No**'.	All participants
Which organisms were detected	• This question is only required if a positive blood culture was collected in the first 72 hours of hospital admission. • Select all organisms detected from specimens collected within 72 hours of hospital admission. • Note that different organisms may be detected on different blood cultures. Review the results of all blood culture specimens collected within 72 hours of hospital admission. • If an organism was detected and is not listed, select '**Other**'. ◦ You will be asked to then enter the full organism name, as it appears on the pathology report. • Alternate or abbreviated names may be reported for some organisms. See Appendix for common alternative ways that organisms may be reported.	All participants with a positive blood culture result

Field / Question	Definition	Applies to

Is the organism reported as being resistant to a specified antibiotic	• For selected organisms, you will be asked to indicate whether the organism was reported as being resistant to specific antimicrobial agents.
	• Select '**Yes**' if the organism's resistance to the agent is reported as 'intermediate' or 'resistant'.
	• Organisms are considered resistant to ceftriaxone and/or ceftazidime if the organism is noted to be an Extended Spectrum Beta-Lactamases (ESBL).
	• Organisms are considered resistant to meropenem and/or imipenem if the organism is noted to be a Carbapenemase-producing Enterobacteriaceae (CPE) or a Carbapenem-resistant Enterobacteriaceae (CRE).
	• *Staphylococcus aureus* is considered resistant to methicillin if it is reported as intermediate or resistant to any of the following:
	  • Methicillin
	  • Oxacillin
	  • Dicloxacillin
	  • Flucloxacillin
	  • Nafcillin
	• *Staphylococcus aureus* that is reported as resistant to methicillin may also be reported as:
	  • MRSA
	  • ca-MRSA
	  • ha-MRSA
	  • nm-MRSA
	  • m-MRSA (multi-resistant MRSA)
		All participants with an allocation in the Antibiotic Domain and a positive blood culture

7.3 Late Positive Blood Culture

The following section relates to specimens collected between 72 hours after hospital admission, and discharge from the index hospitalisation. It is only required for participants who have received an allocation in the Influenza Immune Modulation Domain.

Field / Question	Definition	Applies to
Positive blood culture result	• If no blood cultures were taken between 72 hours after hospital admission and index hospital discharge, select '**Not tested**'. • If any of the blood culture sets collected between 72 hours after hospital admission and index hospital discharge were positive, select '**Yes**'. • If all blood culture sets collected between 72 hours after hospital admission and index hospital discharge were negative, select '**No**'.	All participants with an allocation in the Influenza Immune Modulation Domain
Which organisms were detected	• This question is only required if a positive blood culture was collected between 72 hours after hospital admission and index hospital discharge. • Select all organisms detected from specimens collected between 72 hours after hospital admission and index hospital discharge. • Note that different organisms may be detected on different blood cultures. Review the results of all blood culture specimens collected between 72 hours after hospital admission and index hospital discharge. • If an organism was detected and is not listed, select '**Other**'. • You will be asked to then enter the full organism name, as it appears on the pathology report. • Alternate or abbreviated names may be reported for some organisms. See Appendix for common alternative ways that organisms may be reported.	All participants with an allocation in the Influenza Immune Modulation Domain with a positive late blood culture result

Field / Question	Definition	Applies to

Is the organism reported as being resistant to a specified antibiotic	• For selected organisms, you will be asked to indicate whether the organism was reported as being resistant to specific antimicrobial agents.
	• Select '**Yes**' if the organism's resistance to the agent is reported as 'intermediate' or 'resistant'.
	• Organisms are considered resistant to ceftriaxone and/or ceftazidime if the organism is noted to be an Extended Spectrum Beta-Lactamases (ESBL).
	• Organisms are considered resistant to meropenem and/or imipenem if the organism is noted to be a Carbapenemase-producing Enterobacteriaceae (CPE) or a Carbapenem-resistant Enterobacteriaceae (CRE).
	• *Staphylococcus aureus* is considered resistant to methicillin if it is reported as intermediate or resistant to any of the following:
	  • Methicillin
	  • Oxacillin
	  • Dicloxacillin
	  • Flucloxacillin
	  • Nafcillin
	• *Staphylococcus aureus* that is reported as resistant to methicillin may also be reported as:
	  • MRSA
	  • ca-MRSA
	  • ha-MRSA
	  • nm-MRSA
	  • m-MRSA (multi-resistant MRSA)
		All participants with an allocation in the Influenza Immune Modulation Domain with a positive late blood culture

Date and time first positive sample collected	• For any organism that was identified between 72 hours after hospital admission and index hospital discharge, enter the date and time that the first positive sample was collected.	All participants with an allocation in the Influenza Immune Modulation Domain with a positive late blood culture

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7.4 Pleural Aspirate

Field / Question	Definition	Applies to
Microbiological tests performed on pleural fluid	• Select '**Yes**' if specimens were collected within the first 7 calendar days of this hospital admission. • Pleural fluid can be collected by needle aspiration, from a drain or intercostal drain tubes or at the time of surgery (thoracotomy, video-assisted thoroscopy (VATS) or decortication). • If a culture or PCR was performed on pleural fluid select '**Yes**'.	All participants
Positive pleural aspirate culture result	• If no pleural fluid cultures were taken within the first 7 calendars days of hospital admission, select '**No**'. • If any of the pleural fluid cultures were taken within the first 7 calendars days of hospital admission were positive, select '**Yes**'. • If all pleural fluid cultures were taken within the first 7 calendars days of hospital admission were negative, select '**No**'.	All participants with microbiological tests performed on pleural fluid
Which organisms were detected	• This question is only required if a positive pleural fluid specimen was collected in the first 7 calendar days of hospital admission. • Select all organisms detected from specimens collected within the first 7 days of hospital admission. • Note that different organisms may be detected on different cultures. Review the results of all specimens collected within the first 7 days of hospital admission. • If an organism was detected and is not listed, select '**Other**'. ◦ You will be asked to then enter the full organism name, as it appears on the pathology report. • Alternate or abbreviated names may be reported for some organisms. See Appendix for common alternative ways that organisms may be reported.	All participants with a positive pleural aspirate culture result

Field / Question	Definition	Applies to

Is the organism reported as being resistant to a specified antibiotic	• For selected organisms, you will be asked to indicate whether the organism was reported as being resistant to specific antimicrobial agents.
	• Select '**Yes**' if the organism's resistance to the agent is reported as 'intermediate' or 'resistant'.
	• Organisms are considered resistant to ceftriaxone and/or ceftazidime if the organism is noted to be an Extended Spectrum Beta-Lactamases (ESBL).
	• Organisms are considered resistant to meropenem and/or imipenem if the organism is noted to be a Carbapenemase-producing Enterobacteriaceae (CPE) or a Carbapenem-resistant Enterobacteriaceae (CRE).
	• *Staphylococcus aureus* is considered resistant to methicillin if it is reported as intermediate or resistant to any of the following:
	  • Methicillin
	  • Oxacillin
	  • Dicloxacillin
	  • Flucloxacillin
	  • Nafcillin
	• *Staphylococcus aureus* that is reported as resistant to methicillin may also be reported as:
	  • MRSA
	  • ca-MRSA
	  • ha-MRSA
	  • nm-MRSA
	  • m-MRSA (multi-resistant MRSA)
		All participants with an allocation in the Antibiotic Domain and a positive pleural aspirate culture result

PCR performed on pleural fluid	• Select '**Yes**' if a PCR test was performed on pleural fluid within 7 days of hospital admission. • A PCR test is also known as a NAT or GeneXpert. • Pleural fluid can be collected by needle aspiration, from a drain or intercostal drain tubes or at the time of surgery (thoracotomy, video-assisted thoroscopy (VATS) or decortication).	All participants
Was the PCR positive for *Streptococcus pneumoniae*	• Select '**Yes**' if any PCR test performed on pleural fluid was positive for *Streptococcus pneumoniae*. • Select '**No**' if none of the PCR tests performed on pleural fluid within the first 7 days of this hospital admission were positive for *Streptococcus pneumoniae*.	All participants with a PCR performed on pleural fluid

7.5 Positive Lower Respiratory Tract Specimen Culture

The following section is only required if no positive microbiological tests were reported from blood cultures obtained within 72 hours after hospital admission, or pleural fluid within 7 days of hospital admission.

Field / Question	Definition	Applies to

Positive lower respiratory tract specimen culture	• Only include specimens collected within 72 hours after hospital admission.
	• Select '**Not tested**' if no lower respiratory tract culture was collected.
	• A lower respiratory tract specimen is defined as:
	  • Sputum
	  • ETT aspirate
	  • BAL samples or any specimen collected by bronchoscopy.
		Participants without a positive blood culture and no microbiological testing of pleural aspirate

Which organisms were detected	• This question is only required if a positive lower respiratory tract culture was collected within 72 hours after hospital admission. • Select all organisms detected from lower respiratory tract specimens collected within the first 72 hours after hospital admission. • Note that different organisms may be detected in different lower respiratory tract cultures, and multiple organisms may be detected in the same lower respiratory tract culture. • If an organism was detected and is not listed, select '**Other**'. • You will be asked to then enter the full organism name, as it appears on the pathology report. • Alternate or abbreviated names may be reported for some organisms. See Appendix for common alternative ways that organisms may be reported.	Participants with a positive lower respiratory tract culture

Field / Question	Definition	Applies to

Is the organism reported as being resistant to a specified antibiotic	• For selected organisms, you will be asked to indicate whether the organism was reported as being resistant to specific antimicrobial agents.
	• Select '**Yes**' if the organism's resistance to the agent is reported as 'intermediate' or 'resistant'.
	• Organisms are considered resistant to ceftriaxone and/or ceftazidime if the organism is noted to be an Extended Spectrum Beta-Lactamases (ESBL).
	• Organisms are considered resistant to meropenem and/or imipenem if the organism is noted to be a Carbapenemase-producing Enterobacteriaceae (CPE) or a Carbapenem-resistant Enterobacteriaceae (CRE).
	• *Staphylococcus aureus* is considered resistant to methicillin if it is reported as intermediate or resistant to any of the following:
	  • Methicillin
	  • Oxacillin
	  • Dicloxacillin
	  • Flucloxacillin
	  • Nafcillin
	• *Staphylococcus aureus* that is reported as resistant to methicillin may also be reported as:
	  • MRSA
	  • ca-MRSA
	  • ha-MRSA
	  • nm-MRSA
	  • m-MRSA (multi-resistant MRSA)
		Participants with a positive lower respiratory tract culture

7.6 Immunocompromised Patients

This section is only required for participants who are immunosuppressed at baseline.

Field / Question	Definition	Applies to

Positive lower respiratory tract or lung tissue specimen	• If no lower respiratory tract or lung tissue specimens were taken within the first 7 calendars days of hospital admission, select '**Not tested**'.
	• If any of the lower respiratory tract or lung tissue specimens taken within the first 7 calendars days of hospital admission were positive, select '**Yes**'.
	• If all lower respiratory tract or lung tissue specimens taken within the first 7 calendars days of hospital admission were negative, select '**No**'.
	• The lung tissue specimen must have been collected by bronchoscopy or other type of lung biopsy (e.g. open, VATS, bronchoscopy, transbronchial).
	• A lower respiratory tract specimen is defined as:
	  • Sputum
	  • ETT aspirate
	  • BAL samples or any specimen collected by bronchoscopy.
		Participants with immuno-suppressive disease or receiving immune- suppressive treatment

Field / Question	Definition	Applies to
Which organisms were detected	• This question is only required if a positive lower respiratory tract or lung tissue specimen was collected in the first 7 calendar days of hospital admission. • Select all organisms detected from specimens collected within the first 7 days of hospital admission. • Note that different organisms may be detected on different specimens. Review the results of all blood culture specimens collected within the first 7 days of hospital admission. • If an organism was detected and is not listed, select '**Other**'. • You will be asked to then enter the full organism name, as it appears on the pathology report. • Alternate or abbreviated names may be reported for some organisms. See Appendix for common alternative ways that organisms may be reported. • Only select an organism if it was identified by the microbiological tests indicated in the Appendix.	Participants with immuno-suppressive disease or receiving immune- suppressive treatment, with a positive lower respiratory tract or lung tissue specimen

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8 Daily Data

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    - Daily Ventilatory Parameters
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8.1 Daily Organ Support

The following guidance relates to completion of the Daily Organ Support Form. These data are required until 28 days after last randomisation, or until index hospital discharge, whichever occurs first.

Field / Question	Definition	Applies to
Study Day	• This field is auto-populated by the database, based on the date and time of randomisation • See Study Day Definition. Note that Study Day 1 is a short day, commencing at the time of randomisation and ending at midnight on the same day	All participants
Date	• This field is auto-populated by the database, based on the date and time of randomisation.	All participants
Location	• Select the participant's location at the start of the study day. • A definition of ICU is included in General Definitions.	All participants

Field / Question	Definition	Applies to
Highest level of oxygen therapy received	• Select the highest level of oxygen therapy that the participant received on the study day. • Respiratory support received for less than one hour, or solely for the purposes of a procedure are not included. • The hierarchy of ventilatory support is as follows (from highest level of support to lowest level of support): 1. Extracorporeal gas exchange (ECMO or ECCOR) 2. Invasive mechanical ventilation 3. Non-invasive mechanical ventilation 4. High-flow oxygen therapy 5. Low-intensity oxygen therapy 6. No oxygen therapy • Definitions of these oxygen therapies are provided in General Definitions. • If there is no information available to determine the highest level of oxygen therapy on a study day, select '**unknown**'.	All participants
Vasopressors and/or inotropes	• Select '**Yes**' if the participant received vasopressors, inotropes, or both as a continuous infusion for at least one hour. • If the participant is receiving only intermittent doses of a vasopressor or inotrope, even if administered frequently, select '**No**'. • A definition of vasopressors and inotropes is provided in General Definitions. • If there is no information available to determine whether or not the participant received vasopressors or inotropes on a study day, select '**unknown**'.	All participants

Field / Question	Definition	Applies to
Renal replacement therapy	• Select '**Yes**' if the participant received renal replacement therapy for at least one hour on the study day. • Select '**No**' if the participant did not receive renal replacement therapy for at least one hour on the study day, even if the participant is receiving intermittent haemodialysis. • Renal replacement therapy is defined in General Definitions • If there is no information available to determine whether or not the participant received renal replacement therapy on a study day, select '**unknown**'.	All participants

8.2 Mechanical Ventilation Domain Daily Data

As the Mechanical Ventilation Domain permits allocation to be revealed up to 96 hours after randomisation, the following guidance refers to 'Mechanical Ventilation Domain Study Days', which represent the number of study days after reveal of allocation in the Mechanical Ventilation Domain.

Mechanical Ventilation Domain Study Day 1 represents the study day on which allocation in the Mechanical Ventilation was revealed, and the data collected on Mechanical Ventilation Study Day 1 relates to the time between reveal of allocation in the Mechanical Ventilation Domain and midnight on that Study Day.

The following daily data is required for participants who have received an allocation in the Mechanical Ventilation Domain. The following data is collected on Mechanical Ventilation Domain Study Days 1, 2, 3, 5, 7, 10, 14, 21, 28 while the participant is receiving invasive mechanical ventilation in a participating ICU.

On the first three study days after randomization to the Mechanical Ventilation Domain, ABGs and corresponding ventilatory parameters will be recorded twice per day (once per half study day), or once per day if the duration of the study day is less than 16 hours. For all study days after Mechanical Ventilation Study Day 3 (i.e. Mechanical Ventilation Study Days 5, 7, 10, 14, 21, and 28), these data will only be required once per day.

8.2.1 Arterial Blood Gas Measurements

Field / Question	Definition	Applies to

Was an arterial blood gas taken during the specified period	• While the participant was receiving invasive mechanical ventilation (see definition above).
	• On the first, second and third study days following randomization to the Mechanical Ventilation Domain, ABGs and corresponding ventilatory parameters are to be recorded twice per day.
	  • On these study days, the specified period relates separately to the first and second 12-hour period during the study day.
	  • Where the duration of mechanical ventilation on a study day is less than 16 hours (e.g. the day of randomization, day of extubation) there is only one specified period and only one set of observations and corresponding ABG will be required.
	• For study days more than three days after randomization to the Mechanical Ventilation Domain, ABGs and corresponding ventilatory parameters will be recorded once per day.
	  • On these study days, the specified period relates to the period
		All participants who have received an allocation in the Mechanical Ventilation Domain

FiO_2	• If the participant has had one or more ABGs during the specified period, record the FiO_2 associated with the lowest P:F ratio while the participant is receiving IMV. • If a PaO_2 is not available or no ABG was taken, enter the highest FiO_2 recorded during the specified period while the participant received IMV. • Short periods of higher FiO_2 for suctioning or a transient desaturation should not be entered.	All participants who have received an allocation in the Mechanical Ventilation Domain
PaO_2	• This question is only required if an ABG was collected. • Enter the PaO_2 from the ABG associated with the lowest P:F ratio during the specified period. • Select the unit of measurement and enter the result in the appropriate field.	All participants who have received an allocation in the Mechanical Ventilation Domain

Field / Question	Definition	Applies to
$PaCO_2$	• This question is only required if an ABG was collected. • Enter the $PaCO_2$ from the ABG associated with the lowest P:F ratio during the specified period. • Select the unit of measurement and enter the result in the appropriate field.	All participants who have received an allocation in the Mechanical Ventilation Domain
pH	• This question is only required if an ABG was collected. • Enter the pH from the ABG associated with the lowest P:F ratio during the specified period.	All participants who have received an allocation in the Mechanical Ventilation Domain
Bicarbonate	• This question is only required if an ABG was collected. • Enter the actual bicarbonate from the ABG associated with the lowest P:F ratio during the specified period.	All participants who have received an allocation in the Mechanical Ventilation Domain
SaO_2	• This question is only required if an ABG was collected. • Enter the arterial oxygen saturation from the ABG associated with the lowest P:F ratio during the specified period. • Note that this is oxygen saturation from the ABG, not pulse oximetry.	All participants who have received an allocation in the Mechanical Ventilation Domain

Field / Question	Definition	Applies to
Lactate	• This question is only required if an ABG was collected. • Enter the lactate from the ABG associated with the lowest P:F ratio during the specified period. • If a laboratory measured serum value is not available, a venous or arterial measurement from an ABG machine or laboratory is acceptable. • Select the unit of measurement and enter the result in the appropriate box.	All participants who have received an allocation in the Mechanical Ventilation Domain
Base excess	• This question is only required if an ABG was collected. • Enter the base excess from the ABG associated with the lowest P:F ratio during the specified period.	All participants who have received an allocation in the Mechanical Ventilation Domain
SpO_2	• Enter oxygen saturation using pulse oximetry documented closest to the FiO_2 entered above. • Note that this is not arterial oxygen saturation measured on ABG.	All participants who have received an allocation in the Mechanical Ventilation Domain
End-tidal CO_2	• Record end-tidal carbon dioxide ($EtCO_2$) documented closest to the FiO_2 entered above. • Note that this is not $PaCO_2$ measured on ABG.	All participants who have received an allocation in the Mechanical Ventilation Domain

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8.2.2 Daily Ventilatory Parameters

Field / Question	Definition	Applies to
Mode of invasive ventilation	• Select the mode of invasive ventilation the participant was receiving at the time of the ABG entered above. • If no ABG was recorded, enter the mode of invasive ventilation that the participant was receiving at the time that the FiO_2 entered above was documented. • Ventilator Modes are listed here.	All participants who have received an allocation in the Mechanical Ventilation Domain
Set respiratory rate	• Enter the set respiratory rate (in breaths/minute) that is set on the ventilator closest to the time of the ABG entered above. • If no ABG was recorded, enter the set respiratory rate that the participant was receiving at the time that the FiO_2 entered above was documented. • The set respiratory rate is the number of mandatory breaths delivered by the ventilator per minute. • If the participant is on a mode of ventilation in which all breaths are triggered or spontaneous, enter zero (“0”).	All participants who have received an allocation in the Mechanical Ventilation Domain
Recorded total respiratory rate	• Enter the total respiratory rate (bpm) recorded closest to the time of the ABG entered above. • If no ABG was recorded, enter the total respiratory rate documented at the time that the highest FiO_2 entered above was documented. • Total respiratory rate is the sum of breaths delivered by the ventilator (mandatory breaths) plus any breaths initiated by the participant (spontaneous breaths).	All participants who have received an allocation in the Mechanical Ventilation Domain
Are the mandatory breaths that the patient is receiving pressure-cycled or volume-cycled	• This question is only required if the participant is receiving mandatory breaths. • Select ‘**pressure-cycled**’ if the ventilator is set to deliver a specified amount of pressure during inspiration for the mandatory breaths. • Select ‘**volume-cycled**’ if the ventilatory is set to deliver a specified tidal volume during inspiration for the mandatory breaths.	All participants who have received an allocation in the Mechanical Ventilation Domain

Field / Question	Definition	Applies to
Expired tidal volume	• Enter the mandatory tidal volume (in mL) recorded closest to the time of the ABG entered above. • If the participant is on a fully spontaneous mode of ventilation, enter the tidal volume recorded closest to the time of the ABG entered above. • If no ABG was recorded, enter the expired tidal volume that the participant was receiving at the time that the FiO_2 entered above was documented.	All participants who have received an allocation in the Mechanical Ventilation Domain
Recorded peak inspiratory pressure	• Enter the peak inspiratory pressure (in cmH_2O) recorded closest to the time of the ABG entered above. • If no ABG was recorded, enter the peak inspiratory pressure that the participant was receiving at the time that the FiO_2 entered above was documented.	All participants who have received an allocation in the Mechanical Ventilation Domain
Set pressure support	• If the participant is receiving inspiratory pressure support for spontaneous breaths enter the last pressure support (in cmH2O) that was set on the ventilator recorded closest to the time of the ABG entered above. • Record the amount of pressure support as the set pressure applied above PEEP. • Enter “0” if the participant is taking spontaneous breaths without inspiratory pressure support. • Select “**not applicable**” if participant is receiving only mandatory breaths. • If the ventilator is providing tube compensation, ignore tube compensation. • If no ABG was recorded, enter the pressure support that was set on the ventilator at the time that the FiO_2 entered above was documented.	All participants who have received an allocation in the Mechanical Ventilation Domain

Field / Question	Definition	Applies to
Recorded plateau pressure	• This question is only required for participants who are receiving mandatory breaths. • If performed and recorded, enter the last plateau pressure (in cmH_2O) recorded closest to the time of the ABG entered above. • If no ABG was recorded, enter the plateau pressure that the participant was receiving at the time that the FiO_2 entered above was documented. • Plateau pressure is measured by setting a 0.5 second inspiratory pause and recording the pressure at the end of the hold. This is only possible in participants who are not breathing spontaneously. • Select "**not recorded**" if plateau pressure has not been performed or is not recorded.	All participants who have received an allocation in the Mechanical Ventilation Domain
Set PEEP	• Enter the PEEP (in cmH_2O) recorded closest to the time of the ABG entered above. • If no ABG was recorded, enter the PEEP that the participant was receiving at the time that the FiO_2 entered above was documented. • If the participant was receiving invasive ventilation using APRV mode at the time that the ABG was obtained, select '**patient receiving APRV**'.	All participants who have received an allocation in the Mechanical Ventilation Domain
I:E ratio	• Enter the Inspiratory : Expiratory (I:E) ratio recorded closest to the time of the ABG entered above. • If no ABG was recorded, enter the I:E ratio that the participant was receiving at the time that the FiO_2 entered above was documented. • If the participant was receiving a spontaneous mode of ventilation at the time of the ABG select "**patient receiving spontaneous ventilation mode**".	All participants who have received an allocation in the Mechanical Ventilation Domain

Field / Question	Definition	Applies to
Set P_{LOW}	• Enter the last P_{LOW} (cmH_20) set on the ventilator closest to the time of the ABG entered above. • If no ABG was recorded, enter the PLOW that the participant was receiving at the time that the FiO_2 entered above was documented. • P_{LOW} is the pressure set for the short period of airway release during APRV ventilation.	All participants who have received an allocation in the Mechanical Ventilation Domain, who are on APRV ventilator mode
Set P_{HIGH}	• Enter the last P_{HIGH} (cmH_20) set on the ventilator closest to the time of the ABG entered above. • If no ABG was recorded, enter the P_{HIGH} that the participant was receiving at the time that the FiO_2 entered above was documented. • P_{HIGH} is the pressure used to determine the inspiratory plateau during APRV ventilation	All participants who have received an allocation in the Mechanical Ventilation Domain, who are on APRV or BiLEVEL ventilator modes
T_{LOW}	• Enter the last T_{LOW} (in seconds) recorded closest to the time of the ABG entered above. • If no ABG was recorded, enter the T_{LOW} that the participant was receiving at the time that the FiO_2 entered above was documented. • T_{LOW} is the time spent in P_{LOW} during APRV or BiLEVEL ventilation.	All participants who have received an allocation in the Mechanical Ventilation Domain, who are on APRV or BiLEVEL ventilator modes

Field / Question	Definition	Applies to
T_{HIGH}	• Enter the last T_{HIGH} (in seconds) recorded closest to the time of the ABG entered above. • If no ABG was recorded, enter the T_{HIGH} that the participant was receiving at the time that the FiO_2 entered above was documented. • T_{HIGH} is the time spent in P_{HIGH} during APRV ventilation.	All participants who have received an allocation in the Mechanical Ventilation Domain, who are on APRV or BiLEVEL ventilator modes

8.2.3 Daily Therapies

Field / Question	Definition	Applies to

Did the patient receive any of the following	• **Neuromuscular blockade:**
	  • Select if the participant received continuous neuromuscular blockade by infusion or intermittent bolus administration on this study day.
	  • When considering if boluses are included in this definition, consider whether the aim is to keep the participant paralyzed. If that is the case, select '**neuromuscular blockade**'. However, ongoing neuromuscular blockade will usually be in the form of an infusion or ongoing intermittent doses. If the participant receives a "one-off" bolus, with no intention to keep the participant paralyzed, then do not select this option.
	  • Neuromuscular blockade for the sole purpose of intubation or other procedures does not meet this definition.
	• **Recruitment maneuver**:
	  • A recruitment maneuver is defined as any transient, sustained increases in transpulmonary pressure designed to open collapsed airless alveoli. These increases in transpulmonary pressure can be achieved through increases in PEEP and/or tidal volume.
	• **Nitric oxide:**
	  • At any time on the study day.
	• **Inhaled prostacyclin:**
	  • At any time on the study day.
	• **Other hypoxemic rescue therapy:**
	  • Select if the participant received any other therapy aiming to rescue from hypoxemia on this study day.
	  • If this option is selected, specify what the other rescue therapy was.
		All participants who have received an allocation in the Mechanical Ventilation Domain

Field / Question	Definition	Applies to
Did the patient undergo a formal or informal unassisted breathing trial	• Select '**formal unassisted breathing trial**' if the participant underwent one or more unassisted breathing trial by: • T-tube circuit • Tracheostomy mask, hood, or shield • Mechanical ventilator circuit using CPAP of 5 cmH_2O with minimum support (i.e. PSV ≤ 10 cmH_2O) and FiO_2 ≤ 0.5 • Select '**informal unassisted breathing trial**' if the participant was breathing spontaneously and there has been a successful or unsuccessful attempt to progressively wean the participant to a level of PEEP or pressure support that the treating clinician regards as sufficient to permit extubation • If both formal and informal unassisted breathing trials occurred on the study day, select '**formal unassisted breathing trial**'	All participants who have received an allocation in the Mechanical Ventilation Domain

Did the patient pass any unassisted breathing trial	• This question is only required if the participant underwent one or more formal or informal unassisted breathing trials on this study day
	• Select '**Yes**' if the participant successfully passed one or more formal or informal unassisted breathing trial on this study day
	• To have successfully passed an unassisted breathing trial the participant must have met the following criteria after 30 minutes of unassisted breathing:
	  • Respiratory rate < 35 breaths per minute; and
	  • SaO_2 > 90% whilst receiving FiO_2 ≤ 0.5; and
	  • Systolic blood pressure > 90 mmHg and < 180 mmHg; and
	  • Heart rate either < 140 bpm or not increased by more than 20% since the beginning of the unassisted breathing trial; and
	  • Clinically stable
	• If a formal or informal unassisted breathing trial has not been documented in the medical notes, answer '**Yes**' if the participant met the above criteria based on observations recorded in the hour prior to extubation.
		All participants who have received an allocation in the Mechanical Ventilation Domain

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9 Medication Administration Form

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9.1 Pre-Hospital Medications of Interest

Field / Question	Definition	Applies to
Did the patient receive any of the following medications for the treatment of this acute illness, prior to this hospitalisation	• Select any of the listed medications that the participant received for the treatment of this acute illness, prior to this hospital admission. • It is not necessary to contact clinicians involved in the care of the patient prior to hospital admission or while admitted to a hospital prior to admission to the randomizing hospital to obtain this information.	Participants who have received an allocation in the Influenza Antiviral Domain or Immunoglobulin Domain

9.2 Antibiotics and Macrolides

The following sections record the administration of all antibiotics and macrolides. This section is required for all participants who receive an allocation in the Antibiotic or Macrolide Domains.

9.2.1 Assigned Intervention Daily Administration

Daily dose of each allocated medication will be recorded for 14 days post-randomisation or hospital discharge, whichever occurs first. Where an allocated intervention includes more than one medication (e.g., a beta-lactam and a macrolide), administration of each medication will be collected separately.

Study Days are defined in General Definitions.

9.2.1.1 Antibiotics

Field / Question	Definition	Applies to
Total daily dose - IV bolus	• For each study day, enter the total dose of the allocated intervention that was administered intravenously or intramuscularly as a bolus. • A bolus or short infusion is defined as an infusion prescribed to be administered over a period of less than 3 hours. • Enter the value and select the appropriate units. • If the allocated intervention was not administered via this route on a study day, enter a dose of '**0**' (zero).	Participants who have received an allocation in the Antibiotic Domain

Field / Question	Definition	Applies to
Total daily dose - IV extended infusion	• For each study day, enter the total dose of the allocated intervention that was administered intravenously as an extended infusion. • An extended infusion is defined as an infusion prescribed to be administered over a period of at least 3 hours, but given intermittently. • Enter the value and select the appropriate units . • If the allocated intervention was not administered via this route on a study day, enter a dose of '**0**' (zero).	Participants who have received an allocation to ceftriaxone, piperacillin-tazobactam, or amoxicillin-clavulanate in the Antibiotic Domain
Total daily dose - continuous infusion	• For each study day, enter the total dose of the allocated intervention that was administered intravenously as a continuous infusion. • A continuous infusion is defined as an infusion that is prescribed to be administered as an infusion over 24 hours per day. Administration is not intermittent, with planned interruptions only for bag / syringe resupply. • Enter the value and select the appropriate units. • If the allocated intervention was not administered via this route on a study day, enter a dose of '**0**' (zero).	Participants who have received an allocation to ceftriaxone, piperacillin-tazobactam, or amoxicillin-clavulanate in the Antibiotic Domain

Total daily dose - oral / enteral	• For each study day, enter the total dose of the allocated intervention that was administered intravenously.
	• Enter the value and select the appropriate units.
	• If the allocated intervention was not administered on a study day, enter a dose of '**0**' (zero).
	• Includes administration of the medication via the following routes:
	  ◦ Oral or oro-gastric (OG)
	  ◦ Nasogastric (NG) or nasojejunal (NJ)
	  ◦ Percutaneous endoscopic gastrostomy (PEG) or percutaneous endoscopic jejunostomy (PEJ)
		Participants who have received an allocation in the Antibiotic Domain

9.2.1.2 Macrolides

Field / Question	Definition	Applies to
Agent	• Select the macrolide that was administered as the macrolide component of a beta-lactam + macrolide intervention within the Antibiotic Domain. • If more than one macrolide was administered on a Study Day (e.g. if the macrolide was changed), enter the daily dose administered for each medication separately on each study day.	Participants who have received an allocation to a beta-lactam + macrolide intervention in the Antibiotic Domain, with or without an allocation in the Macrolide Domain
Total daily dose - IV	• For each study day, enter the total dose of the allocated intervention that was administered intravenously or intramuscularly as a bolus. • Enter the value and select the appropriate units. • If the allocated intervention was not administered via this route on a study day, enter a dose of '**0**' (zero).	Participants who have received an allocation to a beta-lactam + macrolide intervention in the Antibiotic Domain, with or without an allocation in the Macrolide Domain

Total daily dose - oral / enteral	• For each study day, enter the total dose of the allocated intervention that was administered intravenously.
	• Enter the value and select the appropriate units.
	• If the allocated intervention was not administered on a study day, enter a dose of '**0**' (zero).
	• Includes administration of the medication via the following routes:
	  ◦ Oral or oro-gastric (OG)
	  ◦ Nasogastric (NG) or nasojejunal (NJ)
	  ◦ Percutaneous endoscopic gastrostomy (PEG) or percutaneous endoscopic jejunostomy (PEJ)
		Participants who have received an allocation to a beta-lactam + macrolide intervention in the Antibiotic Domain, with or without an allocation in the Macrolide Domain

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9.2.2 Non-Assigned Medication Administration

Field / Question	Definition	Applies to
Did the patient receive any of the following medications during the treatment period	• The treatment period for the Antibiotic and Macrolide Domains is from randomisation to the end of Study Day 14 or hospital discharge, whichever occurs first. • Select any of the medications listed that were administered during the intervention period, that were not interventions allocated within the Platform as part of the Antibiotic or Macrolide Domains.	Participants who have received an allocation in the Antibiotic Domain or Macrolide Domain

9.3 Corticosteroids

The following sections record the administration of all systemic corticosteroids. This section is required for all participants who receive an allocation in the Corticosteroid Domain.

9.3.1 Assigned Intervention Daily Administration

Daily dose of each allocated medication will be recorded for 14 days post-randomisation or hospital discharge, whichever occurs first.

Study Days are defined in General Definitions.

Field / Question	Definition	Applies to
Agent	• For participants who were pregnant at the time of randomisation and were allocated to the fixed-dose dexamethasone intervention, dexamethasone should be substituted for prednisolone or hydrocortisone. • Select '**prednisolone**' or '**hydrocortisone**' to indicate which systemic corticosteroid was used as an alternative to dexamethasone. • For all other participants, only the name of the allocated systemic corticosteroid will be shown in the eCRF.	Participants who have received an allocation in the Corticosteroid Domain

Field / Question	Definition	Applies to
Total daily dose - IV	• For each study day, enter the total dose of the allocated intervention that was administered intravenously or intramuscularly. • Enter the value and select the appropriate units. • If the allocated intervention was not administered via this route on a study day, enter a dose of '**0**' (zero).	Participants who have received an allocation in the Corticosteroid Domain

Total daily dose - oral / enteral	• For each study day, enter the total dose of the allocated intervention that was administered intravenously.
	• Enter the value and select the appropriate units.
	• If the allocated intervention was not administered on a study day, enter a dose of '**0**' (zero).
	• Includes administration of the medication via the following routes:
	  ◦ Oral or oro-gastric (OG)
	  ◦ Nasogastric (NG) or nasojejunal (NJ)
	  ◦ Percutaneous endoscopic gastrostomy (PEG) or percutaneous endoscopic jejunostomy (PEJ)
		Participants who have received an allocation in the Corticosteroid Domain

9.3.2 Non-Assigned Medication Administration

Field / Question	Definition	Applies to
Did the patient receive any of the following medications during the treatment period	• The treatment period for the Corticosteroid Domain is from randomisation to the end of Study Day 14 or hospital discharge, whichever occurs first. • Select any of the medications listed that were administered during the intervention period, that were not interventions allocated within the Platform as part of the Corticosteroid Domain.	Participants who have received an allocation in the Corticosteroid Domain, Endothelial Domain, or Influenza Immune Modulation Domain

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9.4 Influenza Antivirals

The following sections record the administration of all antiviral medications active against influenza. This section is required for all participants who receive an allocation in the Influenza Antiviral Domain.

9.4.1 Pre-Randomisation Medications of Interest

Field / Question	Definition	Applies to
Did the patient receive any of the following medications between admission to hospital for this acute illness and randomisation	• Select any of the listed medications that the participant received for the treatment of this acute illness, after admission to hospital and before randomisation.	Participants who have received an allocation in the Immunoglobulin Domain

9.4.2 Assigned Intervention Daily Administration

Daily dose of each allocated medication will be recorded for 14 days post-randomisation or hospital discharge, whichever occurs first.

Study Days are defined in General Definitions.

Field / Question	Definition	Applies to
Agent	• Select the agent that was administered from the list of assigned medications. • The eCRF will only display the name of the medication(s) included in the interventions the participant has been allocated to. • For participants allocated to an intervention that contains more than one active intervention, enter the total daily dose of each medication separately for each study day.	Participants who have received an allocation in the Influenza Antiviral Domain

Field / Question	Definition	Applies to

Total daily dose - oral / enteral	• For each study day, enter the total dose of the allocated intervention that was administered intravenously.
	• Enter the value and select the appropriate units.
	• If the allocated intervention was not administered on a study day, enter a dose of '**0**' (zero).
	• Includes administration of the medication via the following routes:
	  • Oral or oro-gastric (OG)
	  • Nasogastric (NG) or nasojejunal (NJ)
	  • Percutaneous endoscopic gastrostomy (PEG) or percutaneous endoscopic jejunostomy (PEJ)
		Participants who have received an allocation in the Influenza Antiviral Domain

9.4.3 Non-Assigned Medication Administration

Field / Question	Definition	Applies to
Did the patient receive any of the following medications during the treatment period	• The treatment period for the Influenza Antiviral Domain is from randomisation to the end of Study Day 14 or hospital discharge, whichever occurs first. • Select any of the medications listed that were administered during the intervention period, that were not interventions allocated within the Platform as part of the Influenza Antiviral Domain.	Participants who have received an allocation in the Influenza Antiviral Domain

9.5 Immunomodulatory Therapy and Antibodies

The following sections record the administration of all immunomodulatory therapy administered for COVID-19. This section is required for all participants who receive an allocation in the Immunoglobulin Domain.

9.5.1 Assigned Intervention Administration

Volume of each unit of high-titre convalescent plasma will be recorded.

Field / Question	Definition	Applies to
Volume transfused	• Enter the volume of the antibody therapy that was transfused from the unit. • If one or both of the allocated units of immunoglobulin were not transfused, enter a dose of '**0**' for that unit.	Participants who have received an allocation to the high-titre convalescent plasma intervention in the Immunoglobulin Domain
Donation number	• Enter the donation number of the unit of intravenous immunoglobulin or convalescent plasma administered.	Participants who have received an allocation to the high-titre convalescent plasma intervention in the Immunoglobulin Domain

9.5.2 Non-Assigned Medication Administration

Field / Question	Definition	Applies to
Did the patient receive any of the following medications during the treatment period	• The treatment period for the Immunoglobulin Domain is from randomisation to the end of Study Day 14 or hospital discharge, whichever occurs first. • Select any of the medications listed that were administered during the intervention period, that were not interventions allocated within the Platform as part of the Influenza Antiviral Domain.	Participants who have received an allocation in the Influenza Antiviral Domain

9.6 Endothelial Modulators

The following sections record the administration of all endothelial modulators. This section is required for all participants who receive an allocation in the Endothelial Domain.

9.6.1 Assigned Intervention Daily Administration

Daily dose of each allocated medication will be recorded for 14 days post-randomisation or hospital discharge, whichever occurs first.

Study Days are defined in General Definitions.

Field / Question	Definition	Applies to
Total daily dose - IV	• For each study day, enter the total dose of the allocated intervention that was administered intravenously or intramuscularly. • Enter the value and select the appropriate units. • If the allocated intervention was not administered via this route on a study day, enter a dose of '**0**' (zero).	Participants who have received an allocation in the Endothelial Domain

Total daily dose - oral / enteral	• For each study day, enter the total dose of the allocated intervention that was administered intravenously.
	• Enter the value and select the appropriate units.
	• If the allocated intervention was not administered on a study day, enter a dose of '**0**' (zero).
	• Includes administration of the medication via the following routes:
	  ◦ Oral or oro-gastric (OG)
	  ◦ Nasogastric (NG) or nasojejunal (NJ)
	  ◦ Percutaneous endoscopic gastrostomy (PEG) or percutaneous endoscopic jejunostomy (PEJ)
		Participants who have received an allocation in the Endothelial Domain

9.6.2 Non-Assigned Medication Administration

Field / Question	Definition	Applies to
Did the patient receive any of the following medications during the treatment period	• The treatment period for the Influenza Antiviral Domain is from randomisation to the end of Study Day 14 or hospital discharge, whichever occurs first. • Select any of the medications listed that were administered during the intervention period, that were not interventions allocated within the Platform as part of the Endothelial Domain.	Participants who have received an allocation in the Endothelial Domain

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9.7 Immune Modulators

The following sections record the administration of all immune modulating medications. This section is required for all participants who receive an allocation in the Influenza Immune Modulation Domain.

9.7.1 Assigned Intervention Daily Administration

Daily dose of each allocated medication will be recorded for 14 days post-randomisation or hospital discharge, whichever occurs first.

Study Days are defined in General Definitions.

Field / Question	Definition	Applies to
Total daily dose - IV	• For each study day, enter the total dose of the allocated intervention that was administered intravenously or intramuscularly. • Enter the value and select the appropriate units. • If the allocated intervention was not administered via this route on a study day, enter a dose of '**0**' (zero).	Participants who have received an allocation to the tocilizumab intervention in the Influenza Immune Modulation Domain

Total daily dose - oral / enteral	• For each study day, enter the total dose of the allocated intervention that was administered intravenously.
	• Enter the value and select the appropriate units.
	• If the allocated intervention was not administered on a study day, enter a dose of '**0**' (zero).
	• Includes administration of the medication via the following routes:
	  ◦ Oral or oro-gastric (OG)
	  ◦ Nasogastric (NG) or nasojejunal (NJ)
	  ◦ Percutaneous endoscopic gastrostomy (PEG) or percutaneous endoscopic jejunostomy (PEJ)
		Participants who have received an allocation to the baricitinib intervention in the Influenza Immune Modulation Domain

9.7.2 Non-Assigned Medication Administration

Field / Question	Definition	Applies to
Did the patient receive any of the following medications during the treatment period	• The treatment period for the Influenza Antiviral Domain is from randomisation to the end of Study Day 14 or hospital discharge, whichever occurs first. • Select any of the medications listed that were administered during the intervention period, that were not interventions allocated within the Platform as part of the Influenza Immune Modulation Domain.	Participants who have received an allocation in the Influenza Immune Modulation Domain or Endothelial Domain

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9.8 COVID-19 Antivirals

The following sections record the administration of all antivirals intended to be active against SARS-CoV-2 infection. This section is required for all participants who receive an allocation in the COVID-19 Antiviral (II) Domain.

9.8.1 Assigned Intervention Daily Administration

Daily dose of each allocated medication will be recorded for 14 days post-randomisation or hospital discharge, whichever occurs first.

Study Days are defined in General Definitions.

Field / Question	Definition	Applies to
Agent	• Select the agent that was administered from the list of assigned medications. • The eCRF will only display the name of the medication(s) included in the interventions the participant has been allocated to. • For participants allocated to an intervention that contains more than one active intervention, enter the total daily dose of each medication separately for each study day.	Participants who have received an allocation to the COVID-19 Antiviral (II) Domain

Field / Question	Definition	Applies to
Total daily dose - IV	• For each study day, enter the total dose of the allocated intervention that was administered intravenously or intramuscularly. • Enter the value and select the appropriate units. • If the allocated intervention was not administered via this route on a study day, enter a dose of '**0**' (zero).	Participants who have received an allocation to the remdesivir intervention in the COVID-19 Antiviral (II) Domain

Total daily dose - oral / enteral	• For each study day, enter the total dose of the allocated intervention that was administered intravenously.
	• Enter the value and select the appropriate units.
	• If the allocated intervention was not administered on a study day, enter a dose of '**0**' (zero).
	• Includes administration of the medication via the following routes:
	  ◦ Oral or oro-gastric (OG)
	  ◦ Nasogastric (NG) or nasojejunal (NJ)
	  ◦ Percutaneous endoscopic gastrostomy (PEG) or percutaneous endoscopic jejunostomy (PEJ)
		Participants who have received an allocation to the COVID-19 Antiviral (II) Domain

9.8.2 Non-Assigned Medication Administration

Field / Question	Definition	Applies to
Did the patient receive any of the following medications during the treatment period	• The treatment period for the Influenza Antiviral Domain is from randomisation to the end of Study Day 14 or hospital discharge, whichever occurs first. • Select any of the medications listed that were administered during the intervention period, that were not interventions allocated within the Platform as part of the COVID-19 Antiviral (II) Domain.	Participants who have received an allocation in the COVID-19 Antiviral (II) Domain

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10 Consent

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10.1 General Guidance

The following guidance relates to the documentation of consent discussions for participation in this trial. Enter all consent discussions that occur, even where the discussion does not result in a decision regarding participation, or a written outcome. Each discussion that has occurred should be entered as a separate event.

For example, if there is a consent discussion with the participant that results in no decision being made (e.g., they would like more time to consider their participation), enter that discussion as a single event. If the participant then later decides to consent to participation, enter that as a separate event.

10.2 Consent Discussion Details

Field / Question	Definition	Applies to
Randomisation that the discussion event is related to	• Some participants may be randomised in the Moderate Illness Severity State, and later be randomised again to receive additional allocations if they have progressed to the Severe Illness Severity State. • For such participants, enter all consent discussions as separate events, indicating which of these randomisation events the discussion related to. • If both randomisation events were discussed at the same time, both may be selected.	Consent discussions for participants who have received allocations in both the Moderate State and the Severe State
Date and time of discussion	• Enter the date and time of the discussion.	All consent discussions

Field / Question	Definition	Applies to

Discussion with	• Select whether the discussion event was with:
	  • the **patient** (i.e., the participant),
	  • a **personal legal representative** (e.g. a family member, next-of-kin, or carer), or
	  • In some regions, discussions may involve a **professional legal representative** (e.g. an independent clinician)
	• If the discussion involved both the patient and their family, select '**patient**'.
	• If the discussion was with an individual who does not fall into one of the above categories, select '**other**' and specify their relationship to the participant.
	  • Do not enter the individual's name into this field. Only enter their relationship to the participant using a succinct description.
		All consent discussions

Outcome	• If the discussion resulted in the patient, their personal legal representative, or a professional legal representative (where applicable) agreeing to participation in at least one domain, select "**agreed to participation in one or more domain**". • If the discussion resulted in the patient, their personal legal representative, or a professional legal representative (where applicable) declining or withdrawing consent for participation in all domains, select "**declined / withdrew consent for participation in all domains**". • If no decision was made about participation at the time of the discussion (e.g. the participant or their legal representative wanted more time to consider participation), select "**Information provided, no decision made**". • Any subsequent discussions should be entered as separate events • In some jurisdictions, an opt-out consent model may be utilised. In these regions, you may select "**opt-out information sheet provided**".	All consent discussions

Field / Question	Definition	Applies to

Was the outcome provided in writing, or verbal only	• If there was a decision to agree to participation or to decline/withdraw participation, please indicate whether this was provided in writing.
	• A decision in writing means that the decision is documented in writing using an approved informed consent form.
	• If the outcome was communicated verbally, the following questions will be asked in some jurisdictions, where applicable:
	  • Did an impartial witness observe the verbal consent process
	  • If yes, did the impartial witness sign and informed consent form
	  • Was verbal consent recorded through appropriate alternative means, such as audio or video recording
		All consent discussions

Which domains did they agree to participation in	• If the outcome of the discussion was agreement to participate in one or more domains, select all domains that the patient or their representative agreed to participation in. • The eCRF will display a list of all domains in which the participant has received an allocation.	Consent discussions resulting in agreement to participate in one or more domain

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10.2.1 Consent for use of data

If the participant or their authorised representative decline participation in all domains, you will be asked to specify data use conditions.

Field / Question	Definition	Applies to
Can data collected to the point of withdrawal be used	• Indicate whether the participant or authorised representative has agreed to allow any data collected up to the point of withdrawal to be stored and used. • The default in this trial is to use data collected to the point of withdrawal, unless otherwise specified. Select '**no**' only where the participant or their representative has clearly expressed that they do not want any of their data to be used.	Consent discussions resulting in consent for all domains being withdrawn or declined

Field / Question	Definition	Applies to
Can data available from medical records be used to continue to collect data, where available	• Indicate whether the participant or their authorised representative agreed to the continued collection of data using routinely-collected hospital records available to research staff (e.g. medical records created as part of the patient's routine care).	Consent discussions resulting in consent for all domains being withdrawn or declined
Can the participant be contacted to collect follow-up information at Day 90 and Day 180	• Indicate whether the participant of their authorised representative agree to be contacted to participate in follow-up interviews conducted after hospital discharge at day 90 and day 180.	Consent discussions resulting in consent for all domains being withdrawn or declined
Was the agreement for the storage and use of data for other research studies that are closely related to this research project, or any future research	• Indicate whether the participant or their authorised representative agree to the storage and use of data for other future research. • These questions will only appear in regions where IRBs have approved the potential storage and use of participant data for future research.	Consent discussions in regions or countries where retention of data for future research is permitted

10.3 No Written Consent Obtained From Participant

This following questions will appear where all consent discussions have been entered and there is no entry indicating that consent for participation has been obtained in writing from the participant. While it is expected that every attempt will be made to obtain consent in writing from the participant, it is acknowledged that this may not be possible or necessary in every instance.

Field / Question	Definition	Applies to

Indicate why written consent was not obtained from the participant	• Select the reason that best describes why written consent could not be obtained from the participant. This includes situations where:
	  • the **participant was deceased** before consent could be obtained
	  • the **participant did not have capacity to provide consent** for participation, and is not anticipated to regain capacity to do so
	  • **Verbal agreement was obtained but written consent could not be obtained**, for example due to isolation requirements during a pandemic
	  • **Patient lost to follow up**, for example patients who leave hospital against medical advice before consent can be obtained
	  • In some regions, an **opt-out** consent model may have been used
	  • **Another reason** not specified above
		Situations where no written consent could be obtained from the participant

Can patient data be used without written consent from the participant, according to local regulations and approvals	• Select '**no**' only where applicable regulations and approvals exclude the use of patient data in this context. • If you are unsure of the answer to this question, contact your regional coordinating center for assistance	Situations where no written consent could be obtained from the participant
Date of ethics committee / regulatory approval to use data in the absence of written consent	• Enter the date of approval from the appropriate ethics committee or regulator in your jurisdiction to use patient data in the absence of written consent from the participant. • If such approval is not required, select '**not applicable**'. • If you are unsure about how to answer this question, contact your regional coordinating center for assistance.	Situations where no written consent could be obtained from the participant

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11 Discharge Form

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- Index Hospital Discharge
- Pregnancy Status At Index Hospital Discharge
- Domain-Specific Outcomes
- Domain-Specific SAEs

11.1 Change Of Location During Index Hospitalisation

This section documents the movement of the participant between randomisation and discharge from the index acute hospitalisation. This includes transfers to other acute hospitals during the index hospitalisation.

Field / Question	Definition	Applies to
Transfer to	• Select the option that best describes where the participant was transferred to. • Only include transfers occurring between randomisation and index hospital discharge.	All participants
Hospital	• Select the hospital location that the participant was transferred to. • By default, the eCRF will show the name of the current location. If the transfer was to another acute hospital, select the name of that hospital from the list of participating hospitals • If the hospital is not participating in this trial, select '**non-participating hospital**'	All participants

Date and time of transfer	• Enter the date and time that the participant physically arrived in the transferred location.
	• If that date and time is unknown, enter the date and time that the participant physically left the transferring location.
	  • If the date of both is unknown, select '**unknown**'
	  • If the date of transfer is known, but the time of transfer is unknown, and cannot be approximated from available information, enter '**12:00**' on the date of transfer.
		All participants

11.2 Index Hospital Discharge

Field / Question	Definition	Applies to
Date and time of discharge from index hospitalisation	• Index hospitalisation is defined in General Definitions. • If the patient died in hospital, enter the date and time of death. ◦ If the participant was deemed to be brain dead, enter the date and time of the second confirmation of this diagnosis as the date and time of discharge (death). • If the date of discharge is known, but the time of index hospital discharge is unknown and cannot be approximated from available information, enter '**12:00**' on the date of discharge. • If date of index hospital discharge is unknown select '**unable to ascertain**'	All participants
Status at hospital discharge	• Select the option that describes the participant's vital status at index hospital discharge. • Select '**Alive**' if the participant was alive at the time of index hospital discharge. ◦ Includes participants discharged alive from the index hospitalisation for palliation who are not expected to survive. • Select '**Deceased**' if the participant died during the index hospitalisation. • Select '**Unknown**' if it is not possible to ascertain the participant's vital status at index hospital discharge.	All participants
Discharge destination	• Select the option that best describes the place or facility that the participant was discharged from hospital to, at the time of index hospital discharge. • **Home**: as defined in General Definitions • **Nursing home or long-term care facility**: as defined in General Definitions • **Rehabilitation hospital**: as defined in General Definitions • **Palliative care:** select this option if the participant was discharged to a sub-acute facility or a mode of care (including at home) for the explicit and imminent purpose of provision of care at the end-of-life	Participants who were alive at index hospital discharge

Field / Question	Definition	Applies to
Did the patient have a tracheostomy between randomisation and index hospital discharge	• Select '**Yes**' if the participant underwent a tracheostomy at any time between randomisation and index hospital discharge. • If the participant has an end stoma, with no tracheostomy tube (for example after laryngectomy) select '**No**'.	All participants
Date and time of first cannulation	• Enter the date and time of first placement of a tracheostomy tube at time of procedure to perform the tracheostomy • Select '**cannulated at randomisation**' if the participant had a tracheostomy or long-term end stoma (for example, after laryngectomy) prior to randomisation	All participants who had a tracheostomy during this index hospitalisation

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11.3 Pregnancy Status At Index Hospital Discharge

Field / Question	Definition	Applies to
Is the patient pregnant at hospital discharge	• Select '**Yes**' if the patient remained pregnant at the time of index hospital discharge. • Select '**No**' if the patient was no longer pregnant at time of index hospital discharge. • This may be due to miscarriage, termination, or delivery (live- or still-born) occurring between randomisation and index hospital discharge.	Participants who were pregnant at time of randomisation to the Influenza Immune Modulation Domain

11.4 Domain-Specific Outcomes

Field / Question	Definition	Applies to
Clostridium difficile toxin detected on a fecal specimen	• Select '**Yes**' if Clostridium difficile toxin was detected on a fecal specimen collected at any time during this hospital admission. • See Appendix for alternative names for Clostridium difficile • If Clostridium difficile is isolated in the absence of toxin positive select '**No**'. • Faecal specimens include the PCR (NAT or GeneXpert) tests for toxin genes and EIA for toxin A and/or toxin B.	Participants who have received an allocation in the Antibiotic Domain

Methicillin-resistant Staphylococcus aureus isolated or detected:	• Select '**Yes**' if Methicillin-resistant Staphylococcus aureus (MRSA) was detected on any sample collected at any time during this hospital admission.
	• See Appendix for alternative names for MRSA.
	• Select '**Yes**' if Staphylococcus aureus is reported as intermediate or resistant to any of the following:
	  ◦ Methicillin
	  ◦ Oxacillin
	  ◦ Dicloxacillin
	  ◦ Flucloxacillin
	  ◦ Nafcillin
		Participants who have received an allocation in the Antibiotic Domain

Vancomycin-resistant Enterococci isolated or detected	• Select '**Yes**' if Vancomycin-resistant Enterococci (VRE) was isolated or detected on any sample collected at any time during this hospital admission. • See Appendix for alternative names for VRE. • Vancomycin-resistant Enterococci is defined as an Enterococcus faecalis or E faecium that is resistant to vancomycin and/or teicoplanin, or has vanA or vanB or vanD, genes detected.	Participants who have received an allocation in the Antibiotic Domain

Field / Question	Definition	Applies to
Extended-Spectrum Beta-Lactamases producing Escherichia coli and/ or Klebsiella spp isolated or detected	• Select '**Yes**' if Extended-Spectrum Beta-Lactamases (ESBL) producing Escherichia coli and / or Klebsiella spp were isolated or detected on any sample collected at any time during this hospital admission. • See Appendix for alternative names for Escherichia coli and Klebsiella spp. • Select '**Yes**' if Escherichia coli or Klebsiella spp are reported as being resistant to ceftriaxone or ceftazidime.	Participants who have received an allocation in the Antibiotic Domain

Carbapenem-resistant gram-negative organism isolated or detected	• Select '**Yes**' if Carbapenem-resistant gram-negative organism (CRE or CPE) was isolated or detected on any sample collected at any time during this hospital admission.
	• See Appendix for alternative names for CRE.
	• CRE are defined as gram-negative organisms that are resistant to carbapenem antibiotics (e.g., meropenem or imipenem).
	• Carbapenem resistance can be defined by:
	  • Demonstration of resistance on antibiotic susceptibility testing (see Appendix for details), or
	  • Detection of carbapemenase genes (including NDM, IMP, KPC, VIM)
		Participants who have received an allocation in the Antibiotic Domain

Date first positive specimen was collected	• For each multi-drug resistant organism (MRO) that is isolated or detected, you will be asked to enter the date that the first positive specimen was collected during this hospital admission. • If multiple specimen types report an organism, enter the date that the first positive specimen was collected.	Participants who have received an allocation in the Antibiotic Domain, with one or more MRO detected

Field / Question	Definition	Applies to
History of this organism during previous hospital admissions	• If a multi-drug resistant organism (MRO) has been detected during this hospital admission, you will be asked whether the patient has a history of this organism being detected during a previous hospital admission. • Select '**Yes**' if the patient's medical record has a history of this MRO being detected during a previous hospital admission. • This may include alerts placed at other hospitals prior to this hospital admissions (if known). • It is not necessary to examine microbiology results prior to this hospital admission. • For many MROs, alerts or flags are placed in the patient notes for infection control purposes, indicating that the patient has had a history of infection or colonization in a prior admission. • If the alert has been placed because of the detection of an MRO in the current admission (without the alert being present previously), select '**No**'.	Participants who have received an allocation in the Antibiotic Domain, with one or more MRO detected

Documented serious ventricular arrhythmia	• Select '**Yes**' if the participant experienced documented ventricular arrhythmia between randomisation to the Macrolide Duration Domain and index hospital discharge.
	• A serious ventricular arrhythmia is defined as a suspected or proven sustained ventricular tachycardia requiring intervention and includes:
	  • Torsades de pointes (TdP)
	  • Ventricular fibrillation
	• Only include ventricular arrhythmia that required one or more of the following interventions:
	  • Cardioversion (electrical or pacing cardioversion) OR
	  • Infusion of an antiarrhythmic agent
	• If the ventricular arrhythmia does not require intervention (e.g. 10 beats of self-limiting VT) select '**No**'.
		Participants who have received an allocation in the Macrolide Duration Domain

Field / Question	Definition	Applies to
Date and time of first documented serious ventricular arrhythmia	• Enter the date and time that serious ventricular arrhythmia is documented in the patient's clinical record, between randomization to the Macrolide Duration Domain and hospital discharge.	Participants who have received an allocation in the Macrolide Duration Domain who experienced serious ventricular arrhythmia
Patient died while not receiving continuous cardiac monitoring	• Continuous cardiac monitoring records the electrical activity of the heart as an electrocardiogram (ECG). • If the patient did not have continuous cardiac monitoring at the time of death check YES.	Participants who have received an allocation in the Macrolide Duration Domain who did not experience serious ventricular arrhythmia

Death was unexpected and sudden	• Death is sudden and unexpected if:
	  • Cardiac arrest triggered activation of a medical emergency team, or
	  • If the patient was found dead without a treatment limitation being in place
	• A treatment limitation is defined as documentation within the medical record that the patient is not to receive:
	  • Cardiopulmonary resuscitation
	  • Readmission to an ICU or higher dependency area or both that was active at the time of death.
	  • In many hospitals a treatment limitation is documented on a separate form. This form should be considered the definitive source. In hospitals that do not have such a form, a treatment limitation must be identified in the medical record.
		Participants who have received an allocation in the Macrolide Duration Domain who died while not receiving continuous cardiac monitoring

Field / Question	Definition	Applies to
Was Etomidate administered between randomization in the Corticosteroid Domain and the end of Study Day 8	• Select '**Yes**' if the participant was administered Etomidate at any time between the time of randomization to the Corticosteroid Domain and the end of study day 8.	Patients who have received an allocation in the Corticosteroid Domain, in regions where etomidate is used
Date and time of first unassisted breathing	• Successful unassisted breathing is defined as a patient breathing without invasive mechanical ventilation for at least 48 hours. • Enter the date and time that the patient was first successfully breathing without invasive mechanical ventilation after randomization in the Mechanical Ventilation Domain. • Invasive mechanical ventilation includes any form of positive pressure ventilation applied during inspiration that is higher than the expiratory pressure given during inspiration, delivered via an orotracheal, nasotracheal tube or tracheostomy tube (TT), with or without positive end expiratory pressure (PEEP). • Do not include the 48-hour period without invasive mechanical ventilation. Enter the date and time the 48-hour period without invasive mechanical ventilation commenced.	Patients who have received an allocation in the Mechanical Ventilation Domain
Was one or more intercostal catheter inserted for barotrauma	• Select '**Yes**' if one or more ICC was inserted between randomization to the Mechanical Ventilation Domain and end of invasive mechanical ventilation for barotrauma or air leak.	Patients who have received an allocation in the Mechanical Ventilation Domain

Field / Question	Definition	Applies to

Major bleeding	• Select '**Yes**' if the participant experienced one or more episodes of major bleeding between randomisation and and 14 calendar days (i.e. 336 hours) after randomization.
	• Major bleeding is defined as any of the following:
	  • fatal bleeding, symptomatic or clinically manifest bleeding in a critical area or organ (such as intracranial, intraspinal, intraocular, retroperitoneal, intraarticular, pericardial, or intramuscular with compartment syndrome),
	  • Bleeding causing a fall in hemoglobin of ≥2 g/dL, or leading to the transfusion of 2 or more whole blood or red cell units within a 24 hour period.
		Participants who have received an allocation to the Endothelial Domain

Which major bleeding criteria were met	• Select all of the major bleeding criteria that were met.
	  • **Fatal bleeding**: the major bleeding event directly contributed to the patient's death
	  • **Symptomatic or clinically manifest bleeding in a critical area or organ** (such as intracranial, intraspinal, intraocular, retroperitoneal, intraarticular, or pericardial bleeding, or intramuscular bleeding with compartment syndrome)
	  • **Blood loss causing a fall in hemoglobin of 2g/dL or more** within a 24-hour period
	  • **Blood loss leading to a transfusion of two or more units of red cells or whole blood** within a single transfusion episode within a 24-hours period
		Participants who have received an allocation to the Endothelial Domain who experienced a major bleeding event

Field / Question	Definition	Applies to

Clinically diagnosed acute myocardial infarction	• Select YES if the patient was diagnosed with an Acute Myocardial Infarction (AMI) between randomisation and and 14 calendar days (i.e. 336 hours) after randomization.
	• It is not necessary to evaluate all ECGs, echocardiograms, or recorded symptoms, this question should be answered on the basis of whether there was consideration of a clinical diagnosis of AMI.
	• Select '**No**' if the diagnosis of AMI was considered but the definition of AMI was not met.
	• Among patients in whom a diagnosis of AMI was considered, the definition of an AMI requires detection of rise and fall or just a fall of cardiac biomarkers, such as any form of troponin assay, with at least one value above the upper reference limit (URL) PLUS evidence of myocardial ischemia with <u>at least one of the following</u>:
	  • Symptoms of cardiac ischemia
	  • ECG changes indicative of new ischemia (new ST-T changes or new LBBB)*
	  • Development of pathological Q waves in the ECG**
	  • Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality
	
	*ECG manifestation of acute myocardial ischemia (in the absence of LVH and LBBB):
	• ST Elevation: New ST elevation at the J-point in two contiguous leads with the cut-off points of ≥ 0.2 mV in men or ≥ 0.15 mV in women in leads V2-V3 and/or ≥ 0.1 mV in other leads.
	• ST depression and T-wave changes: New horizontal or down-sloping ST depression ≥ 0.05 mV in two contiguous leads; and/or T inversion ≥ 0.1 mV in two contiguous leads with prominent R waves or R/S ratio >1.
	**Pathological Q waves:
	• Any Q-wave in leads V2-V3 ≥ 0.02 seconds or QS complex in leads V2 and V3.
	• Q-wave ≥ 0.03 seconds and ≥ 0.1 mV deep or QS complex in leads I, II, aVL, aVF, or V4-V6 an any two leads of a contiguous lead grouping (I, aVL, V6; V4-V6; II, III, aVF; V7-V9).
		Participants who have received an allocation to the Endothelial Domain

Field / Question	Definition	Applies to
	• R-wave ≥ 0.04 s in V1–V2 and R/S ≥ 1 with a concordant positive T-wave in the absence of a conduction defect.	
Confirmed deep vein thrombosis	• Select '**Yes**' if the patient has a proximal deep vein thrombosis confirmed on ultrasound or CT between first randomization and 14 calendar days (i.e. 336 hours) after randomization. • Proximal is a thrombus located in axillary vein or more proximal, including the internal jugular vein, and a thrombus located in popliteal vein or more proximal. Confirmation requires imaging with techniques that include ultrasound or CT scan.	Participants who have received an allocation to the Endothelial Domain
Confirmed pulmonary emboli	• Select '**Yes**' if the patient has segmental or multi-sub-segmental pulmonary emboli between randomisation and and 14 calendar days (i.e. 336 hours) after randomization.	Participants who have received an allocation to the Endothelial Domain

Confirmed ischemic stroke	• Select '**Yes**' if the patient was diagnosed with an acute ischemic stroke between randomisation and 14 calendar days (i.e. 336 hours) after randomization.
	• Ischaemic stroke is defined as central nervous system infarction resulting in brain, spinal cord, or retinal cell death, based on any of the following:
	  • Pathological, imaging, or other objective evidence of cerebral, spinal cord, or retinal focal ischemic injury in a defined vascular distribution
	  • Clinical evidence of cerebral, spinal cord, or retinal focal ischemic injury based on symptoms persisting ≥24 hours or until death, and other etiologies excluded (Note: CNS infarction includes types I and II hemorrhagic infarctions).
	  • Infarction or hemorrhage in the brain, spinal cord, or retina because of thrombosis of a cerebral venous structure. Symptoms or signs caused by reversible edema without infarction or hemorrhage do not qualify as stroke.
		Participants who have received an allocation to the Endothelial Domain

Field / Question	Definition	Applies to

Other confirmed thrombotic event	• Select any of the following that occurred between randomisation and index hospitalisation:
	  • **Mesenteric Ischemia:** arterial or venous mesenteric ischemia diagnosed on contrast imaging by CT or angiography or diagnosed at laparotomy or via laparoscopy.
	  • **Limb ischemia:** evidence of acute limb ischemia sufficient to require surgical revascularization including bypass procedure, intraarterial thrombolysis, or embolectomy; amputation of a limb due to acute ischemia; or decision to withdraw of limit treatment because of acute limb ischemia. It is not sufficient for there to be evidence of limb ischemia that does not result in surgical intervention or determine a decision to institute palliative care. Ischemia attributed to vasopressor medication is insufficient unless also meets the above definition.
	  • **Other** thrombotic event, other than ischemic stroke, acute myocardial infarction, mesenteric ischemia, and critical limb ischemia. If this option is selected, you will be asked to describe the event.
		Participants who have received an allocation to the Endothelial Domain

Peak AST / ALT in first 14 days after randomisation	• Enter the highest alanine transaminase (ALT) or aspartate transaminase (AST) measured between randomization and 14 calendar days (i.e. 336 hours) after randomization. • ALT is also known as alanine aminotransferase, or (serum) glutamate-pyruvate transaminase (GTP or SGPT) • AST is also known as aspartate aminotransferase or (serum) or (serum) glutamin-oxaloacetic transaminase (GOT or SGOT)	Participants who have received an allocation in the Endothelial Domain or Influenza Immune Modulation Domain

Field / Question	Definition	Applies to
What is the upper limit of normal for ALT/AST for this patient at this location	• Enter the upper limit of normal of ALT or AST for this patient at your location	Participants who have received an allocation in the Endothelial Domain or Influenza Immune Modulation Domain
Peak bilirubin in the first 14 days after randomisation	• Enter the highest bilirubin measured between randomization and 14 calendar days (i.e. 336 hours) after randomization.	Participants who have received an allocation in the Endothelial Domain or Influenza Immune Modulation Domain
What is the upper limit of normal for bilirubin for this patient at this location	• Enter the upper limit of normal of bilirubin for this patient at your location	Participants who have received an allocation in the Endothelial Domain or Influenza Immune Modulation Domain
Lowest platelet count in first 14 days after randomization	• Enter the lowest platelet count measured between randomization and 14 calendar days (i.e. 336 hours) after randomization.	Participants who have received an allocation in the Endothelial Domain or Influenza Immune Modulation Domain

Field / Question	Definition	Applies to
Lowest neutrophil count in first 14 days after randomization	• Enter the lowest neutrophil count measured between randomization to the Endothelial Domain and 14 calendar days (i.e. 336 hours) after randomization.	Participants who have received an allocation in the Endothelial Domain or Influenza Immune Modulation Domain

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11.5 Domain-Specific SAEs

Indicate whether the participant experienced any of the specified domain-specific SAEs between randomisation and index hospital discharge.

Field / Question	Definition	Applies to
Gastrointestinal intolerance	• Select '**Yes**' if the participant experienced new onset evidence of inability to tolerate feeds, necessitating intervention such as stopping of feeds, or inability to progress feeds within expected timeframe.	Participants who have received an allocation in the Macrolide Duration Domain
Unexpected respiratory depression	• Select '**Yes**' if the participant (not receiving mechanical ventilation in a mandatory mode) experienced new-onset respiratory depression requiring urgent medical intervention such as new or increased respiratory support or administration of naloxone. • Includes respiratory depression resulting from a suspected drug interaction between imatinib and fentanyl.	Participants who have received an allocation in the Endothelial Domain

Field / Question	Definition	Applies to
Cardiac arrhythmia	• Select '**Yes**' if the participant experienced new onset cardiac arrhythmia that requires one or more of CPR, results in major haemodynamic deterioration, or leads to emergency medical intervention such as pacing, urgent cardioversion, or administration of resuscitation medications.	Participants who have received an allocation in the Endothelial Domain

Acute kidney injury	• Select '**Yes**' if the participant experienced an acute loss of kidney function with either:
	  • a serum creatinine increase ≥2 times from baseline measurements (KDIGO Acute Kidney Injury Stage 2 or above)
	  • new renal replacement therapy
		Participants who have received an allocation in the COVID-19 Antiviral (II) Domain

Acute liver injury	• Select '**Yes**' if the participant experienced any of the following:
	  • acute ALT or AST > 5 times the upper limit of normal, or
	  • bilirubin >3 times the upper limit of normal and reflecting an acute change from baseline
		Participants who have received an allocation in the Macrolide Duration Domain or COVID-19 Antiviral (II) Domain

Any adverse event attributable to an interaction between the allocated COVID-19 antiviral and any concurrent non-assigned medication	• Select '**yes**' if, in the opinion of the treating clinician, the participant experienced any adverse event that is possibly, probably, or definitely related to an interaction between an antiviral allocated as an intervention within the COVID-19 Antiviral Domain and another medication that was not assigned as part of this domain.	Participants who have received an allocation in the COVID-19 Antiviral (II) Domain
Gastrointestinal perforation	• Select 'Yes' if the participant experienced gastrointestinal perforation during the intervention period. • Gastrointestinal perforation describes the development of a full-thickness defect in the wall of the gastrointestinal tract (e.g. in the stomach or the bowel), typically resulting in air and gastric/bowel contents leaking into the peritoneal space, and often requiring emergency surgery.	Participants who have received an allocation in the Influenza Immune Modulation Domain

Field / Question	Definition	Applies to
Transfusion-associated acute lung injury	• Select '**Yes**' if the participant experienced transfusion-associated acute lung injury (TRALI) during the intervention period. • The definition of TRALI is based on the definitions used by and reported to local, regional or national hemovigilance systems in your location. If you are unsure of your local definitions, contact your regional coordinating centre.	Participants who have received an allocation in the Immunoglobulin Domain
Transfusion-associated circulatory overload	• Select '**Yes**' if the participant experienced transfusion-associated circulatory overload (TACO) during the intervention period. • The definition of TACO is based on the definitions used by and reported to local, regional or national hemovigilance systems in your location. If you are unsure of your local definitions, contact your regional coordinating centre.	Participants who have received an allocation in the Immunoglobulin Domain
Transfusion-associated dyspnoea	• Select '**Yes**' if the participant experienced transfusion-associated dyspnoea (TAD) during the intervention period. • The definition of TAD is based on the definitions used by and reported to local, regional or national hemovigilance systems in your location. If you are unsure of your local definitions, contact your regional coordinating centre.	Participants who have received an allocation in the Immunoglobulin Domain

Acute Serious haemodynamic reaction	• Select '**Yes**' if the participant experienced an acute serious haemodynamic reaction within 24 hours of transfusion.
	• Defined as a fall in haemoglobin and one or more of the following:
	  ◦ Rise in lactate dehydrogenase (LDH)
	  ◦ Rise in bilirubin
	  ◦ Positive direct antiglobulin test
	  ◦ Positive crossmatch
		Participants who have received an allocation in the Immunoglobulin Domain

Field / Question	Definition	Applies to
Severe allergic reaction or anaphylaxis	• Select '**Yes**' if the participant experienced a severe allergic reaction or anaphylaxis that required emergency treatment during the treatment period. • Severe allergic reactions include severe delayed drug hypersensitivity reaction such as Steven-Johnson syndrome. • Anaphylaxis refers to a severe, potentially life-threatening, allergic reaction characterised b a rapid onset of symptoms affecting multiple organ systems, often including respiratory or cardiovascular compromise. • If the reaction is believed to be possibly, probably, or definitely related to administration of a medication that is an allocated intervention, please enter an SAE report.	Participants who have received an allocation in any domain containing interventions that are medications

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12 Adverse Events and Serious Adverse Events

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12.1 Serious Adverse Events

The following guidance relates to completion of a Serious Adverse Event (SAE) report for participants enrolled in this trial. SAEs are defined as

Field / Question	Definition	Applies to
SAE Diagnosis	• Select the most appropriate diagnostic term to describe the SAE from the list. • You will be asked to select a high-level diagnostic category, which will then reveal a list of sub-categories. • A full list of diagnostic categories is provided here	All Serious Adverse Event reports
SAE severity	• Select the appropriate grading from the Common Terminology Criteria for Adverse Events (CTCAE) categories, in the opinion of the investigator. • **Grade 1:** Mild, asymptomatic or mild symptoms, clinical or diagnostic observations only; intervention not indicated. • **Grade 2:** Moderate, minimal, local or non-invasive intervention indicated; limiting age-appropriate instrumental Activities of Daily Living (ADL). • **Grade 3:** Severe or medically-significant but not immediately life-threatening; hospitalization or prolongation or hospitalization indicated; disabling; limiting self-care ADL. • **Grade 4:** Life-threatening consequences; urgent intervention indicated. • **Grade 5:** Death related to the AE. • Note that an AE with a severity of Grade 1 or 2 is considered an Adverse Event (AE), and should be reported using the AE form.	All Serious Adverse Event reports

Field / Question	Definition	Applies to
SAE description	• Describe the event as succinctly as possible. • Include any results of relevant supportive laboratory data and other investigations, if applicable. • Use standard medical terminology, but avoid unnecessary abbreviations.	All Serious Adverse Event reports
SAE onset date	• Enter the date that the SAE first developed or occurred.	All Serious Adverse Event reports
Which domain is the event related to, or reportable for	• Select all that apply. • Select the domain(s) for which the investigator believes participation may be related to the SAE. • Select '**not related to participation in any domain**' if the SAE is not suspected as being linked to a specific domain intervention / participation.	All Serious Adverse Event reports
Suspected relationship to domain	• Select one option for each domains that are suspected to be related to the SAE • **Unlikely**: it is possible but unlikely that the allocated intervention or participation made some contribution to the event. There is another far more likely cause. • **Possibly**: The investigator determines that the allocated intervention or participation contributed to the event, but may not be the prime cause. There is another contributing factor such as a co-morbid condition which has more likely caused the event. • **Probably**: The investigator determines that the allocated intervention or participation has more likely caused the event than another factor. • **Definitely**: The investigator determines that the allocated intervention or participation caused the event and there are no other factors which could have contributed. This would ordinarily include a strong temporal relationship.	All Serious Adverse Event reports

Field / Question	Definition	Applies to
Is the event expected in the context of available reference safety information for the allocated intervention in the domain	• Select '**Yes**' if the nature and severity of the event is consistent with the current approved version of the reference safety information for the intervention (e.g., summary of product characteristics / investigator brochure / protocol documents). • The event should be assessed as expected or unexpected "*from the perspective of previously observed, not on the basis of what might be anticipated from the pharmacological properties of a medicinal product*" (ICH E2A, 1994). • If you are unsure about whether the event is consistent with current reference safety information, contact your regional coordinating center. • If the event is deemed to be *unexpected* (i.e., if you answer '**No**') then the event may meet the definition of a SUSAR. Please contact your regional coordinating center immediately.	All Serious Adverse Event reports
Date and time intervention started	• Enter the date and time that the allocated intervention was commenced.	All Serious Adverse Event reports
Date and time intervention last administered prior to SAE onset	• Enter the date and time that the intervention was last administered prior to the onset of the SAE. • For interventions administered continuously, enter the date and time that the intervention was ceased prior to SAE onset. If the intervention was being administered at the time on SAE onset, enter the date and time of SAE onset.	All Serious Adverse Event reports

Field / Question	Definition	Applies to
Action taken	• Select one option. • **No action taken**: This may include scenarios where the participant continues to receive the allocated intervention; where the intervention had been completed at the time of the event; or where the AE was not related to an intervention. • **Temporarily discontinued**: the allocated intervention was ceased temporarily, or is currently ceased temporarily with the expectation of recommencing. • **Modification to intervention**: the allocated intervention was modified in some way, for example by reducing the dose or adjusting the intensity or frequency of administration. • **Permanently discontinued**: the allocated intervention has been permanently ceased.	All Serious Adverse Event reports

Outcome	• Select the option that best describes the outcome of the SAE at the time of the report, in the investigator's opinion.
	• **Unknown / lost to follow-up**: The event could not be followed up and it is not known if the event resolved.
	• **Unresolved**: the outcome of the event has not resolved and is still occurring, or it is unclear whether the event is resolved at the time of this report.
	  • Follow up the SAE at regular intervals until resolved or death and report any changes with a follow up SAE report.
	  • If the status of the SAE is unknown at hospital discharge select '**Unknown / lost to follow up**'.
	  • If the SAE is not resolved at hospital discharge or death select '**Unresolved**'.
	• **Resolved**: the outcome of the event has resolved, and the participant does not have sequelae from the event.
	• **Resolved with sequelae**: the event has resolved but the participant continues to have sequelae from the event.
	• **Death**: Date of death if the outcome from the SAE was death. If the cause of death was not related to the SAE do not check this option.
		All Serious Adverse Event reports

Field / Question	Definition	Applies to
Resolution date	• Enter the date that the event resolved in the opinion of the investigator.	All SAEs that are now resolved (with or without sequelae)
Specify sequalae	• Enter a succinct description of the nature of the sequelae that developed and remain as a result of the event.	All SAEs that are now resolved with sequelae
Date of death	• Enter the participant's date of death, if known.	All SAEs where the outcome was death
Cause of death	• Enter the participant's cause of death, as listed on their death certificate.	All SAEs where the outcome was death

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12.2 Adverse Events

The following guidance relates to completion of an Adverse Event (AE) report for participants enrolled in this trial. AEs include any unexpected or untoward medical events experienced by the participant which are not anticipated and, in the opinion of the investigator, are possibly, probably or definitely related to participation in this trial.

The REMAP-CAP Core Protocol does not mandate reporting of AEs, however in some regions, reporting of all AEs is mandated by regulators. Please contact your Regional Coordinating Centre if you are unsure about reporting requirements in your region.

Field / Question	Definition	Applies to
Adverse event diagnosis	• Select the most appropriate diagnostic term to describe the AE from the list. • You will be asked to select a high-level diagnostic category, which will then reveal a list of sub-categories. • A full list of diagnostic categories can be found here.	All Adverse Event reports

Field / Question	Definition	Applies to
Adverse event description	• Describe the event as succinctly as possible. • Include any results of relevant supportive laboratory data and other investigations, if applicable. • Use standard medical terminology, but avoid unnecessary abbreviations.	All Adverse Event reports
Adverse event severity	• Select the appropriate grading from the Common Terminology Criteria for Adverse Events (CTCAE) categories, in the opinion of the investigator. • **Grade 1:** Mild, asymptomatic or mild symptoms, clinical or diagnostic observations only; intervention not indicated. • **Grade 2:** Moderate, minimal, local or non-invasive intervention indicated; limiting age-appropriate instrumental Activities of Daily Living (ADL). • **Grade 3:** Severe or medically-significant but not immediately life-threatening; hospitalization or prolongation or hospitalization indicated; disabling; limiting self-care ADL. • **Grade 4:** Life-threatening consequences; urgent intervention indicated. • **Grade 5:** Death related to the AE. • Note that an AE with a severity of Grade 3 or above is considered a Severe Adverse Event (SAE), and should be reported using the SAE form.	All Adverse Event reports
Adverse event onset date	• Enter the date that the AE first developed or occurred.	All Adverse Event reports
Which domain is the event related to, or reportable for	• Select all that apply. • Select the domain(s) for which the investigator believes participation may be related to the AE. • Select '**not related to participation in any domain**' if the AE is not suspected as being linked to a specific domain intervention / participation.	All Adverse Event reports

Field / Question	Definition	Applies to
Suspected relationship to domain	• Select one option for each domains that are suspected to be related to the AE • **Unlikely**: it is possible but unlikely that the allocated intervention / participation made some contribution to the event. There is another far more likely cause. • **Possibly**: The investigator determines that the allocated intervention / participation contributed to the event, but may not be the prime cause. There is another contributing factor such as a co-morbid condition which has more likely caused the event. • **Probably**: The investigator determines that the allocated intervention / participation has more likely caused the event than another factor. • **Definitely**: The investigator determines that the allocated intervention / participation caused the event and there are no other factors which could have contributed. This would ordinarily include a strong temporal relationship.	All Adverse Event reports
Action taken	• Select one option. • **No action taken**: This may include scenarios where the participant continues to receive the allocated intervention; where the intervention had been completed at the time of the event; or where the AE was not related to an intervention. • **Temporarily discontinued**: the allocated intervention was ceased temporarily, or is currently ceased temporarily with the expectation of recommencing. • **Modification to intervention**: the allocated intervention was modified in some way, for example by reducing the dose, or adjusting the intensity or frequency of administration. • **Permanently discontinued**: the allocated intervention has been permanently ceased.	All Adverse Event reports

Field / Question	Definition	Applies to

Outcome	• Select the option that best describes the outcome of the AE at the time of the report, in the investigator's opinion.
	• **Unknown / lost to follow-up:** the event could not be followed up and it is not known if the event resolved.
	• **Unresolved:** the event is not resolved and is still occurring, or it is unclear whether the event is resolved at the time of this report.
	  ◦ If the status of the AE is unknown at hospital discharge select '**Unknown / lost to follow up**'.
	  ◦ If the AE is not resolved at hospital discharge or death select '**Unresolved**'.
	• **Resolved:** the event is resolved, and the participant does not have sequelae from the event.
	• **Resolved with sequelae:** the event is resolved but the participant continues to have sequelae from the event.
	• **Death:** the participant died as a direct result of the AE. Do not select this option if the cause of death was not the AE.
		All Adverse Event reports

Resolution date	• Enter the date that the event resolved in the opinion of the investigator.	All AEs that are now resolved (with or without sequelae)
Specify sequalae	• Enter a succinct description of the nature of the sequelae that developed and remain as a result of the event.	All AEs that are now resolved with sequelae

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13 Protocol Deviations

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- Protocol Deviation Details
    - Platform Eligibility Protocol Deviation
    - Trial Process Protocol Deviation
    - Domain Protocol Deviation
- Protocol Deviation Description

13.1 General Guidance

Complete a report for each protocol deviation that occurs. For the purposes of this study the term ‘protocol deviation’ is used consistently throughout the protocol and study materials to refer to events that may otherwise be termed protocol deviations or protocol violations. We have elected to use one consistent term to refer to deliberate or accidental deviations from the protocol.

It is acknowledged that there are circumstances in which a deviation from the trial protocol is permitted, for example, premature cessation of an allocated intervention due to a decision of the treating clinician. Such events should be reported for the purposes of documentation, but are considered ‘permitted variations’ to protocolised interventions.

13.2 Protocol Deviation Details

Field / Question	Definition	Applies to
Deviation date	• Enter the date that the protocol deviation occurred. • If the deviation is ongoing or was intermittent, enter the date of the first deviation from the protocol	All protocol deviations that have occurred

Field / Question	Definition	Applies to
Is this report for a permitted variation	• Select '**Yes**' if this report relates to a deviation from an allocated intervention that is permitted by the study protocol(s). • Examples may include the premature cessation of an allocated intervention, or administration of a non-allocated prohibited agent, where these actions were taken because they were believed to be in the best interests of the participant in the opinion of the treating clinician. • Such events are reported for the purposes of documentation, but are considered 'permitted variations' to protocolised interventions.	All protocol deviations that have occurred
Which domain is the protocol deviation related to	• Select which domain the protocol deviation relates to. • Only one may be selected. If more than one protocol deviation has occurred, these should be reported separately. • '**Platform eligibility**' deviations relate to situations where a participant was enrolled in error, being ineligible for inclusion in the Platform.	All protocol deviations that have occurred

13.2.1 Platform Eligibility Protocol Deviation

Field / Question	Definition	Applies to

Select type of Platform eligibility protocol deviation	• Select the option that best describes the Platform eligibility protocol deviation.
	• Such protocol deviations should only be reported where the patient was known to be ineligible for the Platform at the time of enrollment.
	  • This includes where information relating to the patient's eligibility was documented or available at the time of enrollment, but not known to the person completing the eligibility assessment.
	  • It is *not* considered a protocol deviation if aspects of eligibility assessment that are dependent on clinical judgement are found to be incorrect after enrollment, so long as the information entered during the eligibility assessment accurately reflects the clinical assessment made at the time of enrollment.
		All protocol deviations relating to Platform eligibility

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13.2.2 Trial Process Protocol Deviation

Field / Question	Definition	Applies to
Select type of trial process protocol deviation	• Select the option that best describes the trial process protocol deviation. • **Consent process deviations** refer to intentional or unintentional deviations from approved consent processes or requirements. • **Safety reporting deviations** refer to intentional or unintentional deviations from safety reporting requirements in your region. • Select '**other**' to report a protocol deviation that is related to another trial process. ◦ This does not include failure to comply with protocolised interventions, which are reported as domain-specific protocol deviations.	All protocol deviations relating to trial processes

13.2.3 Domain Protocol Deviation

Field / Question	Definition	Applies to
Protocol deviation type	• Select the option and relevant sub-option that best describes the protocol deviation. • If no option appropriately describes the event, select '**other**' and enter a succinct description of the event.	All protocol deviations relating to a specific domain

13.3 Protocol Deviation Description

Field / Question	Definition	Applies to
Reason for deviation	• Describe the reason for the deviation as succinctly as possible. • Do not leave this field blank.	All protocol deviations that have occurred

Field / Question	Definition	Applies to
What actions were taken in response to the protocol deviation	• Briefly describe the consequences and actions taken as a result of the deviation. • There may be no consequences or actions taken due to the protocol deviation. Please state this if it applies. • Do not leave this field blank.	All protocol deviations that have occurred

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14 Follow-up Forms

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        - Baseline Functional Status
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14.1 Day 7 Follow up

This form is only required for participants who have received an allocation in the COVID-19 Antiviral (II) Domain, who were experiencing signs and symptoms of an acute respiratory tract infection at randomisation.

If the participant is still admitted to hospital on Study Day 7, use available medical records to complete this form. If the participant has been discharged from hospital before Study Day 7 after randomisation to this domain, please contact them to ascertain whether the participant is still experiencing respiratory symptoms.

Field / Question	Definition	Applies to
Did the patient still have acute respiratory symptoms on day 7 post-randomisation to the COVID-19 Antiviral (II) Domain	• Respiratory symptoms are defined as one or more of: cough, sore throat, runny nose sneezing, shortness of breath or chest pain. • "Acute" means the symptom in question is not usually present in that individual, or during the current COVID-19 episode was substantially worse or more frequent than usual. • Resolution of all acute respiratory symptoms means return to baseline state, not necessarily the absence of all respiratory symptoms. • Ongoing non-respiratory symptoms (such as fatigue, anorexia, delirium, diarrhea) are not counted as part of this endpoint.	Participants who have received an allocation in the COVID-19 Antiviral (II) Domain, and were experiencing respiratory symptoms at baseline

Information obtained by	• Select the source of information used to complete this form:
	  • **Medical records**
	  • **Follow up interview with patient**
	  • **Follow up interview with proxy**
		Participants who have received an allocation in the COVID-19 Antiviral (II) Domain, and were experiencing respiratory symptoms at baseline

Date information ascertained	• Enter the date that the information was obtained, either by follow-up contact or medical records.	Participants who have received an allocation in the COVID-19 Antiviral (II) Domain, and were experiencing respiratory symptoms at baseline

14.2 Day 90 Follow up

Day 90 follow-up is required for all participants who were alive at index hospital discharge, unless the participant or proxy has requested that they are not contacted.

Vital status at Day 90 is a key component of the primary outcome, and therefore this information is of the utmost importance. All available sources of information should be used to complete this form, including (where available and permitted) medical records, the participant's general practitioner, death records, or patient registries.

This form is to be completed no earlier than Study Day 91, and no later than the end of Study day 104. If vital status cannot be determined during this time, complete the form and update it if and when new information becomes available.

Field / Question	Definition	Applies to
Assessment date	• Enter the date the follow up was conducted. • This is the date that the participant's status was determined, not the date that the follow-up was due	All participants

Status	• Select the option that reflects the participant's status at the end of Study Day 90:
	  • **Alive**: the participant is known to have been alive at midnight at the end of Study Day 90 (including if they are known to have died after this time).
	  • **Deceased**: the participant is known to have died prior to midnight at the end of Study Day 90
	  • **Unable to ascertain**: the participant's vital status at the end of Study Day 90 could not be ascertained by Study Day 104.
		All participants

Date of death	• Enter the participant's date of death. • If the participant is known to be deceased prior to midnight at the end of Study Day 90, but the precise date of death is unknown, select '**unable to ascertain**'.	Participants who were deceased at Day 90
Date last known to be alive	• Enter the date that the participant was last documented or known to be alive.	Participants whose vital status at Day 90 is unable to be ascertained

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14.3 Day 180 Follow up

Day 180 follow-up is required for all participants who were alive at index hospital discharge and Day 90 follow-up, unless the participant or proxy has requested that they are not contacted.

This follow up should be conducted on or after Study Day 181, but not before. Before attempting to contact the participant, check all available sources of information to ascertain whether the participant has died since Day 90 follow up.

14.3.1 Vital Status

Field / Question	Definition	Applies to
Date of follow up	• Enter the date the follow up was conducted. • This is the date that the participant's status was determined, not the date that the follow-up was due	All participants

Status	• Select the option that reflects the participant's status at the end of Study Day 180:
	  • **Alive**: the participant is known to have been alive at midnight at the end of Study Day 180 (including if they are known to have died after this time).
	  • **Deceased**: the participant is known to have died prior to midnight at the end of Study Day 180
	  • **Unable to ascertain**: the participant's vital status at the end of Study Day 180 could not be ascertained after 3-4 attempts have been made to contact the participant or a suitable proxy.
		All participants

Location on study day 180	• Select the option that best describes the participant's location at midnight at the end of Study Day 180:
	  • **Home:** see General Definitions
	  • **Nursing home or long-term care facility:** see General Definitions
	  • **Rehabilitation hospital:** see General Definitions
	  • **Acute care hospital ward:** participant was admitted as an in-patient of a non-ICU ward in an acute hospital
	  • **Admitted to ICU:** see General Definitions
	  • **Other** location not listed
		Participants who were alive at Day 180

Date of death	• Enter the participant's date of death. • If the participant is known to be deceased prior to midnight at the end of Study Day 180, but the precise date of death is unknown, select '**unable to ascertain**'.	Participants who were deceased prior to Day 180

Field / Question	Definition	Applies to
Date last known alive	• Enter the date that the participant was last documented or known to be alive.	Participants whose vital status at Day 180 is unable to be ascertained

14.3.2 Questionnaire Administration

Field / Question	Definition	Applies to
Were any of the survey tools completed	• Select '**Yes**'if one or more of the questionnaires were completed. • Select '**No**' if none of the questionnaires were able to be completed.	All participants

Reason why survey instruments were unable to be administered	• Select the option that best describes why the questionnaires could not be administered:
	  • **Unable to contact participant or a suitable proxy**
	  • **Language or cognitive barrier**
	  • **The participant declined to answer**
	  • **Other**
		All participants, where the Day 180 questionnaires could not be administered

Date completed	• Enter the date that the participant or proxy completed the questionnaires	All participants, where the Day 180 questionnaires were able to be administered

Field / Question	Definition	Applies to

Person interviewed	• Select the option that best describes who completed the follow-up questionnaires
	  • It is preferable that the **participant** completes the questionnaires, where they are able to.
	  • A **proxy** (e.g. family member, person responsible, carer, etc.) may complete the questionnaires if the participant is unable to be interviewed
	• If the interview is being conducted with a proxy:
	  • use the proxy version of the questionnaire instruments (where available).
	  • The proxy must answer the questions (to the best of their ability) about how the participant would feel, not how they view the patient's life. Therefore, it is important to find the best person to answer the questions for the participant and that may take some investigation to establish this.
		All participants, where the Day 180 questionnaires were able to be administered

Do they live with the participant	• Select '**Yes**' if the proxy is living in the same residence as the participant.	Where the Day 180 questionnaires were completed by a proxy

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14.3.3 Adult Participants

14.3.3.1 EQ-5D-5L

The EuroQol EQ5D-5L 5 Level (EQ-5D-5L) is a validated instrument, developed by EuroQol. This quality of life questionnaire may be conducted over the phone or via post (depending on local HREC/IRB approvals) and is available in multiple languages.

There is no right or wrong answer to the quality of life questions. The data should reflect how the participant views their life even if it seems implausible to others.

For more information and tools to help you administer the questionnaire, refer to the EuroQol website.

Field / Question	Definition	Applies to
Was the EQ-5D-5L completed	• Select '**Yes**' if the patient or proxy completed all or some of the EQ-5D-5L questionnaire.	All adult participants
EQ-5D-5L questionnaire	• The appropriate country-specific instrument(s) will be provided by your regional coordinating centre. • Do not use the CRF or eCRF to administer the EQ-5D-5L interview. Please use the appropriate follow-up instruments provided by your regional coordinating centre. • It is recommended that you read the EuroQol User Guide before using the survey for the first time. This guide will be provided by your regional coordinating centre.	All participants, where the EQ-5D-5L has been completed

14.3.3.2 WHODAS

The World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0) is a 12 item questionnaire that is available in multiple languages. This quality of life questionnaire may be conducted over the phone or via post (depending on local HREC/IRB approvals).

It is recommended that interviewers read and are familiar with the instrument manual, particularly the sections including the interview guide and training material. The manual is provided by your regional coordinating centre.

A number of the questions have been removed from the beginning of the questionnaire, as these data have already been collected elsewhere in the CRF (e.g. participant age and sex).

Field / Question	Definition	Applies to
Was the WHODAS completed	• Select '**Yes**' if the patient or proxy completed all or some of the WHODAS questionnaire.	All adult participants
WHODAS 2.0 questionnaire	• The appropriate country-specific instrument(s) will be provided by your regional coordinating centre. • Do not use the CRF or eCRF to administer the WHODAS questionnaire interview. Please use the appropriate follow-up instruments provided by your regional coordinating centre. • Everyone administering the WHODAS is expected to complete pre-interview training provided in the WHODAS 2.0 manual. This manual will be provided by your regional coordinating centre.	All adult participants completing the WHODAS

14.3.3.3 Baseline Functional Status

The following questions aim to better understand the participant's functional status prior to their acute hospitalisation during which they were enrolled in this trial.

Field / Question	Definition	Applies to
Were the baseline questions completed	• Select '**Yes**' if the participant or proxy completed all or some of the baseline questions.	All adult participants, in select regions
Before your hospital admission, which of the following best describes your main work status	• Select the option that best describes the participant's usual work status immediately prior to their acute hospital admission during which they were enrolled in this trial. • If in doubt about the respondent's answer (e.g. as homemaker or unemployed), rely on the respondent's judgement of their work status. • There is no minimum number of hours per week that a respondent must work to qualify for the paid work category. Similarly, students need not be studying full-time in order to be classed as such.	All adult participants, in select regions

In the month before your hospitalisation were you receiving any treatment for anxiety or depression	• Select '**Yes**' if, in the month prior to the acute hospital admission in which the participant was enrolled in the trial, they were receiving any of the following:
	  • Medications prescribed for anxiety or depression
	  • Any other treatment for anxiety or depression, such as psychology or psychiatry
		All adult participants, in select regions

14.3.4 Paediatric Participants

14.3.4.1 EQ-5D-Y

Field / Question	Definition	Applies to
Was the EQ-5D-Y completed	• Select '**Yes**' if the patient or proxy completed all or some of the EQ-5D-Y questionnaire. • Note that a proxy version should be used for participants aged 4-7 years. Participants aged 8 and older may be completed by the participant themselves. • This questionnaire is not available for participants younger than 4 years of age.	All participants aged 4-18
EQ-5D-Y questionnaire	• The appropriate country- and age-specific instrument(s) will be provided by your regional coordinating centre. • Do not use the CRF or eCRF to administer the EQ-5D-Y questionnaire interview. Please use the appropriate follow-up instruments provided by your regional coordinating centre. • Everyone administering the EQ-5D-Y is expected to complete pre-interview training provided in the EQ-5D-Y manual. This manual will be provided by your regional coordinating centre.	All participants aged 4-18 who have completed the EQ-5D-Y

14.3.4.2 PedsQL SF15

This section of the Day-180 follow up consists of the 15-item short-form version of the Paediatric Quality of Life Inventory (PedsQL). There are different versions of this instrument for paediatric participants aged 2-4 years, 5-7 years, 8-12 years, and 13-18 years.

For participants aged 2-4, the questionnaire is completed by the participant's parents or guardians. For participants aged 5-12, the questionnaire is answered by both the participant and the participant; and for participants aged 13-18, it is answered by the participant.

Instructions for completing the PedsQL SF-15 are available from your regional coordinators.

Field / Question	Definition	Applies to
Was the PedsQL SF-15 completed	• Select '**Yes**' if the patient or proxy completed all or some of the PedsQL SF-15 questionnaire. • This questionnaire is not available for participants younger than 2 years of age.	All participants aged 2-18
PedsQL SF-15 questionnaire	• The appropriate country- and age-specific instrument(s) will be provided by your regional coordinating centre. • Do not use the CRF or eCRF to administer the PedsQL SF-15 questionnaire interview. Please use the appropriate follow-up instruments provided by your regional coordinating centre. • Everyone administering the PedsQL SF-15 is expected to complete pre-interview training provided in the PedsQL SF-15 manual. This manual will be provided by your regional coordinating centre.	All participants aged 2-18 who have completed the PedsQL SF-15

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15 Biological Sampling Forms

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- Influenza Antiviral Domain
- Influenza Immune Modulation Domain

15.1 Influenza Antiviral Domain

The following guidance relates to biological sampling for the Influenza Antiviral Domain. Not all sites that are participating in this domain will collect biological samples.

Field / Question	Definition	Applies to

Was a sample collected at the time point	• Select '**Yes**' if a sample was collected at the corresponding time period.
	• For this domain, there are three time points at which biological samples are to be collected at participating sites:
	  ◦ Baseline: collected on the day of randomisation to the Influenza Antiviral Domain.
	  ◦ Day 3: collected on Study Day 3 after randomisation to the Influenza Antiviral Domain, while the participant remains admitted to hospital.
	  ◦ Day 7: collected on Study Day 7 after randomisation to the Influenza Antiviral Domain, while the patient remains admitted to hospital.
		All participants with an allocation in the Influenza Antiviral Domain, at locations participating in biological sample collection

Date and time sample collected	• Enter the date and time that the sample was collected for each collection time point.	All participants with an allocation in the Influenza Antiviral Domain, at locations participating in biological sample collection

Field / Question	Definition	Applies to
Sample ID	• Enter the sample ID for the sample collected at each collection time point. • Contact your regional coordinating center for instructions on how to label samples.	All participants with an allocation in the Influenza Antiviral Domain, at locations participating in biological sample collection

15.2 Influenza Immune Modulation Domain

The following guidance relates to biological sampling for the Influenza Immune Modulation Domain. Not all sites that are participating in this domain will collect biological samples.

Field / Question	Definition	Applies to

Was a sample collected at the time point	• Select '**Yes**' if a sample was collected at the corresponding time period.
	• For this domain, there are three time points at which biological samples are to be collected at participating sites:
	  ◦ Baseline: collected on the day of randomisation to the Influenza Immune Modulation Domain.
	  ◦ Day 3: collected on Study Day 3 after randomisation to the Influenza Immune Modulation Domain, while the participant remains admitted to hospital.
	  ◦ Day 7: collected on Study Day 7 after randomisation to the Influenza Immune Modulation Domain, while the patient remains admitted to hospital.
		All participants with an allocation in the Influenza Immune Modulation Domain, at locations participating in biological sample collection

Field / Question	Definition	Applies to
Date and time sample collected	• Enter the date and time that the sample was collected for each collection time point.	All participants with an allocation in the Influenza Immune Modulation Domain, at locations participating in biological sample collection
Sample ID	• Enter the sample ID for the sample collected at each collection time point. • Contact your regional coordinating center for instructions on how to label samples.	All participants with an allocation in the Influenza Immune Modulation Domain, at locations participating in biological sample collection

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16 Pregnancy Outcome Form

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- Pregnancy Outcome

16.1 Pregnancy Outcome

The following guidance relates to completion of the Pregnancy Outcome form. This form is only required for participants who are known to be pregnant at the time of randomisation to specific domains.

This form can be completed at any time, once the outcome of the pregnancy is known. The Pregnancy Outcome Form will be completed whenever the pregnancy outcome can be ascertained. If the patient is no longer pregnant at hospital discharge, the form should be completed from available medical records. For patients who remain pregnant at hospital discharge, the form should be completed at the time of the Day-180 follow-up unless it can be completed from available medical records at an earlier date (i.e., the patient should not be contacted to ascertain pregnancy outcome before Day 180 follow up). For patients who are still pregnant at the time of Day 180 follow-up, an additional follow up should be completed approximately six weeks after the estimated delivery date of delivery.

Field / Question	Definition	Applies to
Date follow-up completed	• Enter the date that the pregnancy outcome follow-up was completed.	All participants who were pregnant at randomisation to the Influenza Immune Modulation Domain

Follow up completed by	• Select the option that best describes how the information used to complete this form was ascertained:
	  • From available **medical records.**
	  • By interview with the **patient** who was a participant in this trial.
	  • By interview with a suitable **proxy** for the participant in this trial, who is familiar with the details of the pregnancy outcome.
		All participants who were pregnant at randomisation to the Influenza Immune Modulation Domain

Field / Question	Definition	Applies to

Neonatal outcome	• Select the option that best describes the outcome of the pregnancy:
	  • '**Liveborn**' refers to delivery of a foetus, irrespective of the duration of the pregnancy, which after separation shows signs of life, such as beating of the heart, breathing, pulsation of the umbilical cord, or definite movement of voluntary muscles.
	  • '**Miscarriage**' is defined as foetal loss prior to 20 weeks gestation.
	  • '**Termination of pregnancy**' refers to therapeutic abortion for any reason.
	  • '**Stillborn**' refers to foetal loss occurring before or during labour, post-20 weeks gestation.
	  • '**Other**' outcome not otherwise listed, such as ectopic / molar / blighted ovum.
		All participants who were pregnant at randomisation to the Influenza Immune Modulation Domain

Date of outcome	• Enter date of birth (liveborn or stillborn), or date of miscarriage or termination.	Patients with a pregnancy that resulted in liveborn or stillborn birth, miscarriage or termination
Birth weight	• Enter the infant's weight at birth	Patients with a pregnancy that resulted in liveborn birth
Infant sex	• Enter the infant's sex at birth. • Sex at birth is determined by physical sexual characteristics at the time of birth, not by gender identity. • Select '**intersex**' if the infant was born with sex characteristics that do not fit typical binary definitions for male or female bodies, including sexual anatomy, reproductive organs, hormonal patterns, and/or chromosome patterns.	Patients with a pregnancy that resulted in liveborn birth

Field / Question	Definition	Applies to

Did the infant require admission to Neonatal ICU (NICU) post-partum	• Select '**Yes**' if the infant required admission to a neonatal ICU (or equivalent) for more than 12 hours, within 96 hours post-partum.
	• Answer '**No**' if:
	  • the infant was never admitted to NICU;
	  • if they were admitted to NICU more than 96 hours after birth; or
	  • if they were admitted to NICU but their admission lasted less than 12 hours.
		Patients with a pregnancy that resulted in liveborn birth

Neonatal status at one-month post-delivery	• Select the option that best describes the status of the infant at one month post-delivery. • '**Complications or sequelae**' in this context refer to ongoing health complications arising during gestation, during the delivery, or immediately post-partum.	Patients with a pregnancy that resulted in liveborn birth
Date of death	• Enter the participant's date of death. • If the precise date of death is unknown, select '**date unknown**'	Patients with a liveborn child who was deceased at one month post-delivery
Were anomalies identified in the neonatal period	• Select '**Yes**' if congenital anomalies were noted at the time of delivery.	Patients with a pregnancy that resulted in liveborn birth

Field / Question	Definition	Applies to

What is the suspected relationship of the pregnancy outcome to this patient's participation in the trial	• Select one option for each domains that are suspected to be related to one or more of the the following adverse pregnancy outcomes:
	  • Pregnancy resulting in stillborn birth, miscarriage, termination
	  • Liveborn infant requiring NICU admission, with documented anomalies at birth, or deceased at one month post-delivery
	• **Not related**: The investigator determines that the allocated intervention / participation had no effect on any of the adverse pregnancy outcomes reported.
	• **Unlikely**: it is possible but unlikely that the allocated intervention / participation made some contribution to any of the adverse pregnancy outcomes reported. There is another far more likely cause.
	• **Possibly**: The investigator determines that the allocated intervention / participation contributed to any of the adverse pregnancy outcomes reported, but may not be the prime cause. There is another contributing factor such as a co-morbid condition which has more likely caused all of the adverse outcomes.
	• **Probably**: The investigator determines that the allocated intervention / participation has more likely caused any of the adverse pregnancy outcomes reported than another factor.
	• **Definitely**: The investigator determines that the allocated intervention / participation caused any of the adverse pregnancy outcomes reported and there are no other factors which could have contributed. This would ordinarily include a strong temporal relationship.
	• If any of the adverse pregnancy outcomes are believed to be **possibly**, **probably**, or **definitely** related to study participation, you will be prompted to enter an SAE report for the event.
		Patients with a pregnancy with an adverse outcome

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17 Appendices

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17.1 Microbiological Testing

17.1.1 Alternate names of organisms

Organism name	Also reported as
Acinetobacter spp	• Acinetobacter species (e.g. A. baumannii) • Acinetobacter baumannii complex
Aspergillus	• Aspergillus species (e.g. A. fumigatus)
Bacillus spp	• May be documented as “B.” followed by the subtype (e.g. “B. thermophilus”) • Bacillus species does not include: o Gram-negative bacillus o Gram-positive bacillus
Burkholderia pseudomallei	• B. pseudomallei • Melioidosis
Chlamydophila pneumoniae	• C. pneumoniae • Chlamydophila (previously Chlamydia) pneumoniae

Organism name	Also reported as
Coagulase negative staphylococci	• Coagulase-Negative Staphylococci • CoNS or CNS • Any staphylococci other than S. aureus • Includes many species of staphylococci such as Staphylococcus epidermidis
(non-SARS-CoV-2) coronavirus	• Alpha Coronavirus (229E and NL63) • Beta Coronavirus (OC43, HKU1, SARS-CoV and MERS-CoV) • Severe Acute Respiratory Syndrome related coronavirus (SARS-CoV) • Middle East Respiratory Syndrome Coronavirus (MERS-CoV)
Corynebacterium	• May be documented as “C.” followed by the subtype (e.g. “C. pseudotuberculosis”, “C. coryneforms”, or “C. diphtheroids”)
Cryptococcus species	• Cryptococcus species (e.g. C. gattii)
Escherichia coli	• E. coli
Haemophilus influenzae	• H. influenzae • H. influenzae type b (Hib) • H. influenzae not typeable
Influenza A	• Influenza A (InfA or fluA) • A(H1N1)pdm09 • A(H1N1) • A(H3N2) • A(H5N1) • A(H7N9)
Influenza B	• Influenza B (InfB or fluB) • B/Yamagata/16/88 (can be recorded as – B-like virus) • B/Victoria/2/87
Klebsiella spp	• Klebsiella pneumoniae • K. pneumoniae • Klebsiella oxytoca

Organism name	Also reported as
Legionella	• Legionella species (spp) • Legionellosis • Legionella pneumophila • Legionella longbeachae • Legionella (another species name)
Moraxella catarrhalis	• M. catarrhalis
Mucormycosis species	• Mucor • Rhizopuses
Mycoplasma pneumoniae	• Mycoplasma pneumoniae • M. pneumonia
Nocardia species	• Nocardia species (e.g. N. asteroids)
Non-tuberculosis mycobacteria	• Mycobacterium avium complex (MAC) • Mycobacterium species other than tuberculosis (e.g. M abscessus) • Mycobacteria other than tuberculosis (MOTT)
Pneumoncystis	• Pneumocystis jiroveci pneumonia (PJP) • Pneumocystis carinii pneumonia (PCP)
Pseudomonas aeruginosa	• P. aeruginosa
Respiratory Syncytial Virus	• RSV • RSV type A or type B • Human RSV (hRSV)
SARS-CoV-2	• SARS-CoV-2 • COVID-19 • Novel Coronavirus • 2019-nCoV

Organism name	Also reported as
Staphylococcus aureus	• S. aureus • MRSA • ca-MRSA • ha-MRSA • nm-MRSA • m-MRSA (multiresistant MRSA)
Streptococcus agalactiae	• Group B streptococcus • GBS • Streptococcus agalactiae
Streptococcus pneumoniae	• S. pneumoniae • Pneumococci or pneumococcus
Streptococcus pyogenes	• Group A streptococcus • Group A β-hemolytic streptococcus • GAS • S. pyogenes
Tuberculosis	• Mycobacterium tuberculosis • TB • MTB • Mycobacterium tuberculosis • M tuberculosis complex
Varicella zoster virus	• VZV • Chickenpox • Shingles

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17.1.2 Acceptable tests for organisms in lower respiratory tract or lung tissue specimens

Organism name	Type of test
Aspergillus	• A galactomannan test if reported as positive • Culture • Histopathology • PCR, NAT or GeneXpert
Cryptococcus species	• Culture • Histopathology • Microscopy • PCR, NAT or GeneXpert
Mucormycosis species	• Culture • Histopathology • Microscopy • PCR, NAT or GeneXpert
Nocardia species	• Culture • Histopathology • PCR, NAT or GeneXpert
Non-Tuberculosis mycobacteria	• Culture • PCR, NAT or GeneXpert
Pneumocystis	• Histopathology • PCR, NAT or GeneXpert
Tuberculosis	• Culture • MPT-64 antigen • PCR, NAT or GeneXpert
Varicella zoster virus	• PCR, NAT or GeneXpert

17.2 Multi-Resistant Organisms

17.2.1 Carbapenem resistance

The following table lists gram-negative organisms and resistance on antibiotic susceptibility testing that identifies them as Carbapenem-resistant gram-negative organisms.

Organism	Reported as resistant to
Acinetobacter	• Ceftazidime AND either meropenem or imipenem
Citrobacter	• Meropenem, or • Imipenem
E. coli	• Meropenem, or • Imipenem
Enterobacter	• Meropenem, or • Imipenem
Klebsiella	• Meropenem, or • Imipenem
Proteus	• Meropenem, or • Imipenem
Pseudomonas aeruginosa	• Ceftazidime AND either meropenem or imipenem
Serratia	• Meropenem, or • Imipenem

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17.3 Adverse Event Diagnostic Categories

High-level diagnostic category	Sub-category
Abnormal laboratory results	• Hyperkalaemia • Pancytopenia • Haemolytic anaemia • Thrombocytopaenia • Agranulocytosis • Rhabdomyolysis • Elevated ALT/AST • Elevated creatinine kinase • Serum glucose decreased • Other abnormal laboratory result
Bleeding	• Disseminated intravascular coagulation • Eye haemorrhage • Gastrointestinal haemorrhage • Intra-abdominal haemorrhage • Muscle haemorrhage • Intracranial haemorrhage • Spinal cord haemorrhage • Respiratory tract haemorrhage • Hemarthrosis • ENT haemorrhage • Bleeding from surgical site • Other bleeding
Cardiac disorders	• Cardiac arrest • Ventricular arrythmia • Atrial fibrillation • Electrocardiogram QT prolonged • Acute myocardial infarction • Other cardiac disorder

High-level diagnostic category	Sub-category
Drug reaction	• Heparin-induced thrombocytopaenia • Allergic reaction (non-anaphylactic) • Anaphylactic reaction • Stevens-Johnson Syndrome / Toxic Epidermal Necrosis • Angioedema • Drug-induced liver injury • Drug-induced hypotension • Other drug reaction
Gastrointestinal disorders	• Gastrointestinal obstruction • Gastrointestinal perforation • Mesenteric ischemia • Bowel ischemia • Nausea • Vomiting • Diarrhea • Other gastrointestinal disorder
Hepatobiliary disorders	• Cholestasis • Hepatitis • Drug-induced liver injury • Other hepatobiliary disorders
Infection	• Soft tissue infection • Respiratory tract infection • Abdominal infection • Intracranial infection • Meningitis • Bloodstream infection • Sepsis of unknown origin • Febrile neutropenia • Other infection

High-level diagnostic category	Sub-category
Nervous system disorders	• Neuromyopathy • Seizure • Cerebral ischemia • Irritability • Other nervous system disorder
Renal disorders	• Acute kidney injury • Other renal disorder
Respiratory disorders	• Pneumothorax • Respiratory distress • Other respiratory disorder
Thromboembolic disorders	• Pulmonary embolism • Acute myocardial infarction • Deep vein thrombosis • Cerebral ischemia • Thrombosis • Mesenteric ischemia • Bowel ischemia • Other thromboembolic disorders
Transfusion reaction	• Acute haemolytic transfusion reaction • Anaphylactic transfusion reaction • Transfusion-related acute lung injury • Transfusion-related circulatory overload • Other transfusion reaction
Pregnancy or birth complication	• Foetal loss • Congenital anomaly • Other birth complication
Other	• Multi-organ failure • Other not specified elsewhere

17.4 Ventilator Modes

Ventilatory mode in CRF	Drager	Maquet	Hamilton	CareFusion	Covidien / Medtronic	GE	Phillips
Volume-controlled ventilation	VC-CMV VC-AC IPPV / CMV $IPPV_{assist}$ / CMV_{assist}	VC Automode : VC-VS	Volume-CMV (s)CMV	Volume A/C	A/C VC A/C Volume	A/C VC	
Synchronized intermittent mandatory ventilation	VC_SIMV PC-SIMV PC-BIPAP SIMV BIPAP / PCV+	SIMV SIMV (VC) + PS SIMV (PC) + PS SIMV (PRVC) + PS	Volume-SIMV Pressure-SIMV SIMV P-SIMV+ APV_{simv} / SIMV+ Adaptive-SIMV PSIMV+ (incl. P_{sync})	Volume SIMV Pressure SIMV PRVC SIMV	SIMV SIMV-VC+	SIMV VC SIMV PC SIMV PRVC	
Pressure-regulated volume-controlled	VC-CMV Autoflow	PRVC Automode : PRVC-VS	APV_{cmv} / (S)CMV+ Adaptive-CMV	PRVC A/C	VC+	A/C PRVC PCV-VG	AVAPS
Mandatory minute ventilation	VC-MMV MMV						

Ventilatory mode in CRF	Drager	Maquet	Hamilton	CareFusion	Covidien / Medtronic	GE	Phillips
Pressure-controlled ventilation	PC-CMV PC-AC $BIPAP_{assist}$ / $PCV+_{assist}$	PC Automode : PC-PS	Pressure-CMV PCV+	Pressure A/C	A/C PC A/C Pressure BiLevel	A/C PC	PCV
Airway pressure release ventilation	PC-ARPV APRV	Vi-Vent APRV BV	APRV DuoPap	APRV APRV / BiPhasic	BiLevel	APRV BiLevel BiLevel VG	
Pressure support ventilation	PC-PSV SPN-CPAP/PS Variable PS PS CPAP/ ASB CPAP/PS SPN-CPAP CPN-CPAP/VS	PS/CPAP VS	Pressure Support Spont VS	CPAP PSV	SPONT PS VS	CPAP/PS VS	
Proportional assist ventilation	SPN-PPS PPS				PAV+		PPV
Adaptive support ventilation			ASV INTELLiVENT-ASV				
Other		NAVA					

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18 Change log

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18.1 Summary of changes

The following table lists changes to the Data Completion Guidelines over time.

Date	Version	Summary of Changes
12- AUG-2025	15	REMAP-CAP Data Completion Guidelines (V15) released. These correspond to an updated CRF, which has undergone substantial revision over the past year. As a result of this review, major changes have been made throughout the CRF. These were intended to to reflect changes to Core Protocol V4, and follow from a thorough review of the data that were being collected for this Platform. Due to the extensive changes, it is strongly recommended that research staff at all participating sites refamiliarize themselves with the Data Completion Guidelines prior to commencing data collection using the updated CRF. Participants enrolled under Core Protocol V3 or V3.1 will continue to use the corresponding CRF and Data Completion Guidelines (V14).
24-NOV-2025	15.1	Updated to coincide with release of CRF relating to Core Protocol V4. Minor modifications to fix typographical errors on Baseline CRF. Organ failure support definitions moved into a separate table under General Definitions.

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