



SNAP

STANDARDISED DERIVED VARIABLES

PREPARED BY: GRACE NORTON

VERSION: 2.0

DATE: 14 JANUARY 2026

1 CONTENTS

2 Changes since last version..... 3

3 Platform Study entry date 4

4 Domain..... 4

5 Silo..... 5

6 Silo misclassification..... 6

7 Randomised treatment..... 7

8 Age..... 8

9 Sex at birth 8

10 Weight..... 8

11 Acute Discharge date..... 9

12 Day differences 10

13 Withdrawal..... 10

13.1 Withdraw from all future study data collection..... 10

14 CRF open or required & values expected..... 11

14.1 Day 8 to 14 CRF 11

14.2 Day 6 to 14 value expected..... 12

15 Pitt Bacteremia Score..... 13

16 Vital Status & Date of death (Core Estimand 1/ Domain-specific Estimand A1.1/ Domain-specific Estimand B.1) 15

16.1 All cause mortality day 14 (Core Estimand 3) 16

16.2 All cause mortality day 28 (Core Estimand 4) 16

16.3 All cause mortality day 42 (Core Estimand 5)..... 17

16.4 Time to all-cause mortality censored at 90 days (Core Estimand 6)..... 17

17 Total index Hospitalisation (Core Estimand 7 & Core Estimand 9)..... 18

18 Acute Index hospitalisation (Core Estimand 8) 22

19 Microbiological Treatment Failure (Core Estimand 10)..... 23

20 Diagnosis of new focus/foci of infection (Core Estimand 11) 25

21 C. difficile (Core Estimand 12) 27

22 Return to usual level of function on the modified functional bloodstream infection score (FBIS) (Core Estimand 14)..... 27

23 Number of antibiotic days (Core Estimand 17) 29

24 Days alive free of antibiotics (Core Estimand 18)..... 29

25 Acute Kidney Injury (Domain-specific Estimand A1.2 & Domain-Specific Estimand B.6)..... 29

25.1 Baseline (Day 1) Creatine 29

25.2 Creatinine day 1 to 5 From acute and total discharge..... 30

25.3 Creatinine day 6 to 14 From acute and total discharge..... 33

25.4 Maximum creatinine between study days 6 and 14 35

25.5 Derived Acute Kidney Injury 36

25.6	Acute Kidney Injury Day 1 to 14	38
25.7	Acute Kidney Injury – composite Day 1 to 90	38
26	Renal replacement therapy (Domain-specific Estimand A1.3)	40
27	Ongoing renal replacement therapy at platform day 90 (Domain-specific Estimand A1.4)	40
28	Acute Liver Injury (Hepatotoxicity) (Domain-specific Estimand A1.5).....	40
28.1	Baseline ALT	40
28.2	Baseline GGT	41
28.3	ALT Day 1 to 5 from acute and total discharge	42
28.4	ALT Day 6 to 14 from acute and total discharge.....	43
28.5	GGT Day 1 to 5 from Acute and Total discharge	44
28.6	GGT Day 6 to 14 from Acute and Total discharge	45
28.7	ALT & GGT Day 1 to 5 from all sources.....	46
28.8	ALT & GGT Day 6 to 14 from all sources.....	47
28.9	Calculation of ALI from ALT	47
28.10	Calculation of ALI from GGT	50
28.11	Derived ALI.....	52
29	Serious adverse reaction	54
29.1	SAR any day 1 to 90	54
30	Change in assigned treatment (Backbone MSSA/PSSA)	54
30.1	Asked Question – Change in Assigned treatment	54
30.2	Change in assigned backbone treatment – day 1 to 90.....	59
30.3	Reason Change in assigned backbone treatment – day 1 to 90	61
31	Peripherally inserted central catheter (PICC)/other central venous catheter complications requiring line removal (Domain-specific Estimand A1.8).....	63
32	SAR related to backbone-domain.....	63
33	Protocol Adherent Adjunctive Domain	63
34	All-cause diarrhoea domain reveal to day 14 (Domain-specific Estimand B.2)	65
35	Change in C-Reactive Protein (CRP) (Domain-specific Estimand B.3)	66
36	Persistent bacteraemia at day 5 (Domain-specific Estimand B.4)	66
37	SIRS Criteria simultaneously on day 5 (Domain-specific Estimand B.5)	67
38	SAR related to adjunctive domain (Domain-specific Estimand B.7).....	67
39	Desirability Of Outcome Ranking category (DOOR1) – Adjunctive (Domain-specific Estimand B.8)	68
40	Desirability Of Outcome Ranking category (DOOR2) SNAP version – Adjunctive (Domain-specific Estimand B.9).....	68

2 CHANGES SINCE LAST VERSION

- Inconsistencies/ errors were noted in derived max_ggt_d1to5 and d14_pssaormssa_pd14highggt and updated
 - max_ggt_d1to5 included d1to7_btpd1highggt that should not have (d1to7_btpd1highggt is reserved as a baseline value)
 - max_ggt_d6to14 omitted d14_pssaormssa_pd14highggt that should not have
- <<acute hospital index with new_variable that is specific for those acute → acute >>
- <<change in assigned backbone treatment – new_var for those who had gap >>

3 PLATFORM STUDY ENTRY DATE

Platform randomisation date is considered platform study day 1 (i.e. count starts from 1 and not 0).

Derived variable		Variables and Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
platform_entry_date_local	Date component of variable	pt_randomisationdatetimelocal	Randomised local time	Participants enrolled export
platform_entry_date_utc	Date component of variable converted to UTC time from the local time zone (of site)	pt_randomisationdatetimelocal	Randomised local time	Participants enrolled export
		timezone	Time zone	Location Status
Notes: Date only component is used to calculate number of days to negate need for rounding in day difference calculations				

4 DOMAIN

Derived variable		Variables and Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
backbone_domain	Where revealoutcome is “Revealed” (i.e revealed/ enrolled into backbone domain) than 1, Otherwise 0	revealoutcome	Reveal Outcome	Backbone Eligibility
adj_domian	Where revealoutcome is “Revealed” (i.e revealed/ enrolled into adjunctive domain) than 1, Otherwise 0	revealoutcome	Reveal Outcome	Adjunctive Eligibility
eos_domain	Where revealoutcome is “Revealed” (i.e revealed/ enrolled into either EOS day 7 or EOS day 14 domain) than 1, Otherwise 0	revealoutcome	Reveal Outcome	EOS day 7 Eligibility
		revealoutcome	Reveal Outcome	EOS day 14 Eligibility
eos_d7_domain	Where revealoutcome is “Revealed” (i.e revealed/ enrolled into EOS day 7 domain) than 1, Otherwise 0	revealoutcome	Reveal Outcome	EOS day 7 Eligibility
eos_d14_domain	Where revealoutcome is “Revealed” (i.e revealed/ enrolled into EOS day 14 domain) than 1, Otherwise 0	revealoutcome	Reveal Outcome	EOD day 14 Eligibility
pct_domain	Where revealoutcome is “Revealed” (i.e revealed/ enrolled into PET/CT domain) than 1, Otherwise 0	revealoutcome	Reveal Outcome	PET/CT Eligibility
no_domain	Where backbone_domain is 0 and adj_domian is 0 and eos_domain is 0	backbone_domain	Derived variable	Derived variable – original value from Backbone Eligibility

	and pct_domain is 0	adj_domian	Derived variable	Derived variable – original value from Adjunctive Eligibility
	than 1, indicating participant is not enrolled into any domains,			
	otherwise where backbone_domain is 1 or adj_domian is 1 or eos_domain is 1 or pct_domain is 1	eos_domain	Derived variable	Derived variable – original values from EOS day 7 Eligibility and EOS day 14 Eligibility
	than 0, indicating that participant is enrolled into at least one domain	pct_domain	Derived variable	Derived variable – original value from PET/CT Eligibility
Notes: revealoutcome variable name is used in multiple exports for domain entry, use caution in using correct variable no_domain will be updated as new domains are added in the study no_domain having a value of 0 can also be an indication of not enrolled into any domains yet				

5 SILO

Those randomised into the backbone domain must have populated the ‘el_bb_bloodculture’ variable to be eligible and this value is used to randomise the patient into treatment arm. Therefore ‘el_bb_bloodculture’ is used as the priority source for silo for participants in the backbone domain.

For those not randomised in the backbone domain, ‘d1to7_silomedadminsilo’ is used as the priority source for silo. This is because the initial susceptibility result from ‘el_bb_bloodculture’ is often a preliminary one, and this is confirmed and finalised with further testing reported in ‘d1to7_silomedadminsilo’.

Derived variable		Variables and Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
silo	Where backbone_domain is 1 (i.e. participant has been enrolled into backbone domain), use el_bb_bloodculture to define silo	backbone_domain	Derived variable - Backbone Domain	Derived variable – original value from Backbone Eligibility
	Otherwise if backbone_domain is 0 (i.e. participant has not been enrolled into backbone domain), use d1to7_silomedadminsilo and if missing, then use el_bb_bloodculture	d1to7_silomedadminsilo	What is the participant's silo	Day 1 to 7
	Where remains missing, silo is missing.	el_bb_bloodculture	What is the antimicrobial susceptibility of <i>Staphylococcus aureus</i> in the index blood culture isolate	Backbone Eligibility
Notes: el_bb_bloodculture should never be missing for those enrolled into backbone domain, this is built into the database and checks should be run to ensure this is the case Silo categories are PSSA/ MSSA/ MRSA, where ‘PSSA - Automated testing only’ falls under PSSA. Silo missing may be due to participant withdrawn from future data collection before day 1-7 CRF opening, or prior to backbone screening, or withdrawn after day 1-7 CRF opening but the CRF was not completed prior to withdraw				

6 SILO MISCLASSIFICATION

Notes

Derived variable		Variables and Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
silod2	Where value is “MSSA - Methicillin susceptible S. aureus”, make “MSSA” "PSSA - Penicillin susceptible S. aureus", make "PSSA", "MRSA - Methicillin resistant S. aureus", make "MRSA"	d1to7_pd2bloodcultureresult	Result (Did the participant have a blood culture collected on Platform Day 2)	Day 1 to 7
silod5	Where value is “MSSA - Methicillin susceptible S. aureus”, make “MSSA” "PSSA - Penicillin susceptible S. aureus", make "PSSA", "MRSA - Methicillin resistant S. aureus", make "MRSA"	d1to7_pd5bloodcultureresult	Result (Did the participant have a blood culture collected on Platform Day 5)	Day 1 to 7
silomismatch	Where any of silod2, silod5 or silo_updated is not equal to silo, assigne value 1 indiation there is a mismatch of silo from baseline (initially recorded silo) to any later result of silo	silod2	Derived variable	Derived variable
		silod5	Derived variable	Derived variable
		silo_updated	Updated Silo	Silo Misclassification Log
		silo	Derived variable	Derived variable
any_updated_silo_mrsa	If any values in later confirmed silo is “MRSA” assign value 1, otherwise 0	silod2	Derived variable	Derived variable
		silod5	Derived variable	Derived variable
		silo_updated	Updated Silo	Silo Misclassification Log
Notes: silod2, silod5 are modified of original values to check match and mismatch of confirmed silo at baseline (derived variable ‘silo’). any_updated_silo_mrsa, used to handle mismatch of MSSA to PSSA which is allowable to be considered protocol adherent. Given MSSA at baseline can be later identified as MSSA or PSSA, the only non-allowable value for protocol non-adherence in MRSA any_updated_silo_mrsa where values are missing and none of the later confirmed values are “MRSA” then it is also assigned 0				

Derived variable		Variables and Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
silo_misclassification	Where silo is “MSSA” and silo_mismatch is 1 and any_updated_silo_mrsa is 1, then assign value 1 indicating silo misclassification,	silo	Derived variable	Derived variable
	Where silo is “PSSA” or silo is “MSSA” and silo_mismatch is 1, assign value 1 indicating silo misclassification,			
	Where silo is “MSSA” and (silo_mismatch is 0 or any_updated_silo_mrsa is 0), then assign value 0 indicating silo is not misclassified,	silo_mismatch	Derived variable	Derived variable
	Where silo is “PSSA” or silo is “MSSA” and silo_mismatch is 0, assign value 0 indicating silo is not misclassified	any_updated_silo_mrsa	Derived variable	Derived variable
Notes:				

7

RANDOMISED TREATMENT

Derived variable		Variables and Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
backbone_treatment	Where pt_interventionsenrolled contains “AP01” then assign value “(Flu)cloxacillin”, where pt_interventionsenrolled contains “AP02”, assign value “Penicillin”, where pt_interventionsenrolled contains “AM01”, assign value “(Flu)cloxacillin” where pt_interventionsenrolled contains “AM02”, assign value “Cefazolin” where pt_interventionsenrolled contains “AR01”, assign value “Vancomycin” where pt_interventionsenrolled contains “AR02”, assign value “Vancomycin + Cefazolin”	pt_interventionsenrolled	Interventions Enrolled	Participants enrolled
Notes: pt_interventionsenrolled contains intervention codes for all domains and will only contain one intervention code per domain				

8 AGE

Age is collected at time of platform screening, however when entered incorrectly it is updated in the database and appears correctly in participants enrolled export but remains incorrect in platform eligibility export. Therefore, age is derived using the following formula.

Derived variable		Variables and Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
age	Where value is available in pt_age, use that,	el_age	Age	Platform eligibility
	Otherwise where pt_age is missing, use el_age,	pt_age	Age	Participants enrolled
	Otherwise leave as missing			
Notes: age represents age at time of platform screening				

9 SEX AT BIRTH

Sex at birth is collected at time of platform screening, however when entered incorrectly it is updated in the database and appears correctly in both participants enrolled export and enrolment list export. Hence sex at birth can be used directly from the enrolment list export.

Variable	Label/ title	Data export / CRF
sex	Sex at birth	Enrolment list
Notes:		

10 WEIGHT

Weight is collected at baseline in kilograms (kgs) and additionally in grams (g) for participants under 5 years of age. Total weight in kgs is calculated by converting g to kg, then addition with reported kg weight, done directly in the database (but can also be completed using reported weight values).

Where weight is an impossible value (i.e total weight in kg is 0), it is coerced to missing. At time of document publication, data entries of impossible values were known to be entered in order to complete CRF and data base fix is in progress to allow 'unknown' option to resolve the issue (this will be applied to all participants in the database retrospectively and prospectively and data queries raised). In addition, as g is only available for some participants, calculation within the database ignores missing (e.g 3 kgs + missing g will produce a value of 3), hence when both kg and g value is missing, a value of 0.000 will be present.

Derived variable		Variables and Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
weight_kg_baseline	Where bas_vsweight is 0.000, make value missing, Otherwise uses value in bas_vsweight	bas_vsweight	Weight	Baseline

Notes:
 For calculating total weight in kg using values entered, use (bas_vsweightg * 0.001) + bas_vsweightkg, and coerce values of 0.000 to missing.

11 ACUTE DISCHARGE DATE

Acute discharge data date is the date timepoint of when data in the acute discharge form was collected until, e.g some questions will ask “Were there any new focus/foci of infection diagnosed between platform Day [last CRF completed time window] and acute discharge”, where ‘acute discharge’ is the relevant date field.

Derived variable		Variables and Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
adis_transfer_date	Use the relevant date (see notes) of adis_dateofdischarge or adis_dateofdischargeacutebed or adis_dateofdeath, otherwise leave missing, indicating no acute discharge has occurred	adis_dateofdischarge	Date of discharge from this (the enrolling) hospital	Acute Discharge
		adis_dateofdischargeacutebed	Date of discharge from acute care bed	Acute Discharge
		adis_dateofdeath	Date of death	Acute Discharge
adis_crf_data_date	Where adis_clinicaldatasubsequentacuteprovider is “Yes” and adis_dateoffinaldischargeacute care is available, use that, Otherwise use adis_transfer_date, Otherwise leave as missing (indicating no acute discharge has occurred)	adis_clinicaldatasubsequentacuteprovider	Will clinical data for this participant be made available by the subsequent acute care provider	Acute Discharge
		adis_dateoffinaldischargeacute care	Derived Variable	Derived Variable
		adis_dateoffinaldischargeacute care	Date of final discharge from Acute Care	Acute Discharge
adis_end_acute_				
daydiff_platform_entry_adis_transfer_date	Calculate n of days from platform_entry_date_local (considered day 1) to adis_transfer_date (local)	platform_entry_date_local	Derived Variable	Derived Variable – original value form participants enrolled
		adis_transfer_date	Derived Variable	Derived Variable – original values from Acute Discharge

Notes:
 Where participant has an acute discharge CRF, only one of adis_dateofdischarge, adis_dateofdischargeacutebed, adis_dateofdeath will have a value, based on where they were discharged to

adis_transfer_date reflects date participant was discharged from the acute bed of the enrolling hospital, it does not necessarily reflect whether patient has left acute care entirely or their acute index hospitalisation, these are dependent on where the participant was discharged to.

adis_crf_data_date reflects date of when data is relevant to in the acute discharge CRF, i.e. where questions asks time window platform day [x] to acute discharge, the tail of the time window ‘acute discharge’ is adis_crf_data_date

Dates are local to the site, and should be either used with other local date/ datetime variables to the site or converted to UTC (or other) time to use with other date/ datetime UTC (or other) variables.

adis_clinicaldatasubsequentacuteprovider is included in argument for adis_crf_data_date, due to residual data issues

12 DAY DIFFERENCES

General use day difference derived variables, not otherwise specific to other sections of this document.

Derived variable		Variables and Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
daydiff_platform_entry_tdis_dischargedate	Calculate n of days from platform_entry_date_local (considered day 1) to total discharge date	platform_entry_date_local	Derived Variable	Derived Variable – original value from participants enrolled
		tdis_dischargedate	Date of discharge from total index hospitalisation	Total Discharge
daydiff_platform_entry_data_download	Calculate n days from date of data download (utc) to platform_entry_date_utc	platform_entry_date_local	Derived Variable	Derived Variable – original value form participants enrolled
Notes: date of data download (utc) is the date in which data was downloaded from database converted to utc, and can be substituted for other relevant dates, e.g a data cut-off date				

13 WITHDRAWAL

Data collection will cease in the event where:

- Participant withdraws from all data collection

No further data is collected after this event. Any data collected before event remains part of the study data

13.1 WITHDRAW FROM ALL FUTURE STUDY DATA COLLECTION

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
wd_future_data_collection	Where - wd_withdrawalall is “Yes” - or - wd_contactfollowups is “Yes” and wd_medrectoday90 is “Yes”, than 1, indicating data collection has ceased due to withdrawal,	wd_withdrawalall	Withdraw from all aspects of the SNAP Trial	Consent Withdrawals
		wd_contactfollowups	Withdraw from being contacted for follow-up	Consent Withdrawals
		wd_medrectoday90	Withdraw from use of medical records to collect vital status, hospital	Consent Withdrawals

	otherwise 0, indicating data collection has not ceased due to withdrawal		discharge and day 90	
wd_data_collection_end_date	Where wd_future_data_collection is 1, use wd_dateofwithdrawal,	wd_future_data_collection	Derived Variable	Derived Variable
	Otherwise leave as missing, indicating no data collection end date due to withdrawal	wd_dateofwithdrawal	Derived Variable	Derived Variable
daydiff_platform_enrty_wd_dateofwithdrawal	Calculate n of days from platform_entry_date_local (considered day 1) to wd_data_collection_end_date	platform_entry_date_local	Derived Variable	Derived Variable – original value form participants enrolled
		wd_data_collection_end_date	Derived Variable	Derived Variable – original value form Withdraw
Notes: wd_future_data_collection represents where participant has withdrawn, and no further data is collected beyond time of participant withdrawal. Where wd_contactfollowups is “Yes” and wd_medrectoday90 <u>is not</u> “Yes” means participant will not have data collected for any remaining CRFs except for day 90 CRF where medical records <u>can</u> be accessed for day 90 data collection. Region UK has additional 6 and 12 month follow up points, withdrawal from data collection also covers these time points.				

14 CRF OPEN OR REQUIRED & VALUES EXPECTED

14.1 DAY 8 TO 14 CRF

In the event where any of the following occurs before day 8 (i.e. on days 1 to 7):

- Participant is acute discharged (any of ‘acute discharged to’ options); or
- Participant was lost to follow up (patient voluntarily left hospital before end of treatment. This is captured in acute discharge CRF and entered as discharged home, but cannot be differentiated from those who were discharged home as per medical treatment); or
- Participant has died

or

- Participant is not yet at day 15 (when day 8 to 14 CRF usually opens)
- Participant withdrew (from all aspects of trial or from being contacted for follow-up) before day 15 (i.e on days 1 to 14, before CRF usually opens)

The day 8 to 14 CRF is not required/ not yet expected. Where multiple of these events occur, the first event is used to consider whether day 8 to 14 CRF is expected.

Note:

Day 8 to 14 CRF usually opens on day 15. Where a participant is acute discharged or total discharged on between days 8 to 14 (inclusive), day 8 to 14 CRF will open for completion.

Previous database logic allowed for day 8 to 14 CRF to be completed in some of the above events, however blanket decision was made to apply above ruling to all participants. Additionally, it is possible for some CRFs to be completed in non-sequential order, meaning some data may be present in day 8 to 14 CRF where it is not expected or required. Where data remains despite not being required, that data should be disregarded.

Derived variable	Variables and raw data
------------------	------------------------

Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
crf_d8to14_required	Where - daydiff_platform_entry_adis_transfer_date is less than 8 days (i.e day 1 to 7 CRF opens on event, but day 8 to 14 remains closed) or - daydiff_platform_entry_dod is less than 8 days (i.e day 1 to 7 CRF opens on event, but day 8 to 14 remains closed) or - daydiff_platform_entry_data_download is less than 15 days (CRF has not yet opened) or (wd_withdrawalall is “Yes” or wd_contactfollowups is “Yes”) and daydiff_platform_enrty_wd_dateofwithdrawal is less than 15 days (withdrew before CRF opens) code as 0, indicating day 1 to 8 CRF is not / not yet required Otherwise code as 1, indicating day 1 to 8 CRF is expected to have data entered	platform_entry_date_utc	Derived Variable	Derived Variable
		daydiff_platform_entry_adis_transfer_date	Derived Variable	Derived Variable
		wd_withdrawalall	Withdraw from all aspects of the SNAP Trial	Withdrawal
		wd_contactfollowups	Withdraw from being contacted for follow-up	Withdrawal
		daydiff_platform_enrty_wd_dateofwithdrawal	Derived Variable	Derived Variable
		daydiff_platform_entry_dod	Derived Variable	Derived Variable
		daydiff_platform_entry_discharge_full_data_collection_end_date	Derived Variable	Derived Variable
crf_adis_required	Where a discharge destination is present, code as 1, indicating an acute discharge CRF is expected, Otherwise code as 0 indicating no acute discharge from is expected	adis_discharge_dto	Where is the participant being discharged to	Acute Discharge
crf_tdis_required	Where - adis_dischargedto “Acute care” or “Non-acute care” or “Residential care facility (eg. Nursing home)” and - adis_ns_wastransferredtononacutebed is “Yes” then code as 1, indicated total discharge CRF is expected, otherwise code as 0 indicating indicated total discharge CRF is not required	adis_discharge_dto	Where is the participant being discharged to	Acute Discharge
		adis_ns_wastransferredtononacutebed	Was the participant transferred to a non-acute bed	Acute Discharge
Notes: adis_dischargedto is used as a proxy on whether participant has an acute discharge CRF. Acute discharge is always open when participant in study and data is only entered if the CRF needs to be completed. Acute discharge data collection date (adis_datacollectiondate) is not used as proxy as is an automated field which enters a date upon click, thus can contain a date where the CRF was simply clicked open by user but no acute discharge CRF was needed. crf_tdis_required; CRF may not yet be complete where it is expected as CRF is completed after total discharge has occurred				

14.2 DAY 6 TO 14 VALUE EXPECTED

In the case where a participant has been discharged (acute or total, if either occur) before day 6, including where patient has died, or withdrew from data collection before day 6, then no day 6 to 14 value is entered for ALT, GGT and Serum Creatinine. This should be considered in calculating cases.

Acute discharge date used is first date of acute discharge (not adis_dateoffinaldischargeacute care, where discharged to another hospital and further data available, as this date does not trigger whether day 8 to 14 CRF is opened).

The last of dates (total discharge, acute discharge), is used as a participant may be acute discharged before day 5, and later total discharged after day 5, where the total discharge would collect ALT, GGT and Serum Creatinine that would cover day 6 onwards.

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
adis_tdis_date	Where tdis_dischargedate is available, use that,	tdis_dischargedate	Date of discharge from total index hospitalisation	Total Discharge
	Otherwise use adis_transfer_date ,	adis_transfer_date	Derived Variable	Derived Variable – original value from acute discharge
daydiff_platform_entry_adis_tdis_date	Calculate n of days between platform entry (considered day 1) to adis_tdis_date	platform_entry_date_local	Derived Variable	Derived Variable – original value from participants enrolled
		adis_tdis_date	Derived Variable	Derived Variable – original value from acute or total discharge
d6to14_value_expected	Where daydiff_platform_entry_adis_tdis_date is equal to or less than 5,	daydiff_platform_entry_adis_tdis_date	Derived Variable	Derived Variable
	or	wd_future_data_collection	Derived Variable	Derived Variable – value based of those in Withdraw
	wd_future_data_collection is 1 and daydiff_platform_entry_wd_dateofwithdrawal is equal to or less than 5, code as 0 indicating no day 6 to 14 value is expected, Otherwise code as 1, indicating a day 6 to 14 value is expected	daydiff_platform_entry_wd_dateofwithdrawal	Derived Variable	Derived Variable – original value from Withdraw
Notes: adis_transfer_date derived variable is used, which does not consider the date where a patient was discharged to another hospital under acute care. Only the ‘first’ acute date determines open/ close of CRFS. Where a participant dies outside of CRFs opening for data to be entered, this is recorded in acute or total discharge forms, therefore acute and total discharge dates cover this event. Total discharge is used where available as the ‘final’ date, as data is collected until total discharge (where a total discharge is required). Total discharge date should always be a later date than acute discharge date, data checks are run to ensure this is the case. Although a day 6 to 14 value can be expected, it is possible for highest and latest values recorded in acute discharge and total discharge to not cover the day 6 to 14 window where acute and/or total discharge spans beyond the day 6 to 14 window, e.g acute discharge may occur on day 2 (meaning day 8 to 14 CRF remains locked and no data will be entered) and total discharge occurs on day 10, meaning total discharge spans from day 2 to day 10, where we expect to see last recorded values. However, the latest and highest values asked on total discharge may happen to be on day 4 and therefore no value is present for day 6 to 14 window.				

15 PITT BACTEREMIA SCORE

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF

pitt_temp_score_base line	Where, bas_mostemp is “36.1 - 38.9”, code as 0, Otherwise, where bas_mostemp is “35.1 - 36.0 or 39.0 - 39.9”, code as 1, Otherwise, where bas_mostemp is “≤ 35 or ≥ 40”, code as 2, Otherwise, leave as missing	bas_mostemp	Most abnormal temperature	Baseline
pitt_hypotension_scor e_baseline	Where bas_moslowsystolicbloodpressure is <90 or bas_mosvasopressors is “Yes”, then code as 2, Otherwise where bas_moslowsystolicbloodpressure > 90 and bas_mosvasopressors is “No”, doe as 0, Otherwise, leave as missing	bas_moslowsystolic bloodpressure	Lowest systolic blood pressure	Baseline
		bas_mosvasopresso rs	Use of vasopressors in the 48 hours prior to platform entry	Baseline
pitt_ventilation_score_ baseline	Where bas_mosmechanicalvent is “Yes”, code as 2, Otherwise where bas_mosmechanicalvent is “No”, code as 0, Otherwise, leave as missing	bas_mosmechanical vent	Mechanical ventilation required in the 48 hours prior to platform entry	Baseline
pitt_cardiac_score_ba seline	Where bas_moscardiacarrest is “Yes”, code as 4, Otherwise, where bas_moscardiacarrest is “No”, code as 0, Otherwise, leave as missing	bas_moscardiacarre st	Cardiac arrest in the 48 hours prior to platform entry	Baseline
pitt_mental_score_ba seline	Where bas_mosmentalstatus is “1 – Alert”, code as 0, Otherwise, where bas_mosmentalstatus is “2 – Disorientated”, code as 1, Otherwise, where bas_mosmentalstatus is “3 – Stuporous”, code as 2, Otherwise, where bas_mosmentalstatus is “4 - Comatose“, code as 4, Otherwise, leave as missing	bas_mosmentalstat us	Mental status	Baseline
Notes: bas_mosmentalstatus numeric values differ from validated item, pitt_mental_score_baseline uses correct item scoring				

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
pitt_score_baseline	Sum values of pitt_temp_score_baseline and	pitt_temp_score_ba seline	Derived Variable	Derived Variable

	pitt_hypotension_score_baseline and pitt_ventilation_score_baseline and pitt_cardiac_score_baseline and pitt_mental_score_baseline, Where any value is missing, sum should be missing, indicating score cannot be determined due to missingness	pitt_hypotension_score_baseline	Derived Variable	Derived Variable
		pitt_ventilation_score_baseline	Derived Variable	Derived Variable
		pitt_cardiac_score_baseline	Derived Variable	Derived Variable
		pitt_mental_score_baseline	Derived Variable	Derived Variable
Notes:				

16 VITAL STATUS & DATE OF DEATH (CORE ESTIMAND 1/ DOMAIN-SPECIFIC ESTIMAND A1.1/ DOMAIN-SPECIFIC ESTIMAND B.1)

Where a participant dies before day 90, this is captured in the relevant CRF for time point the participant is up to. This data is also entered in the day 90 CRF but may be entered at a later date. Therefore, for interim reporting, enter date of death from CRF in which it was recorded.

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
vitalstatus_d1to90	Where any of the values indicate “Dead” (note this will be “Died” in adis_dischargedto), then code as “Dead”, Otherwise where d90_vitalstatus is “Alive”, code as “Alive”, Otherwise leave as missing indicating vital status from day 1 to 90 not yet determined	d90_vitalstatus	Vital status on Platform Day 90 <Insert date D90>	Day 90
		d1to7_vitalstatus	Vital status at Day 7	Day 1 to 7
		d14_vitalstatus	Vital status at Day 14	Day 8 to 14
		d28_vitalstatus	Participant Status at Day 28	Day 28
		d42_vitalstatus	Vital status at Day 42 <Insert date of day 42>	Day 42
		adis_dischargedto	Where is the participant being discharged to	Acute Discharge
		tdis_dischargevitalstatus	Vital status at discharge	Total Discharge
dod_local	Where vitalstatus_d1to90is “Dead”, Check across variables, for date of death, where more than one value is entered, check dates match and use value (where values do not match leave as missing) Otherwise leave date of death as missing, indicating no date of death as patient is alive	d90_dod	Date of death	Day 90
		d1to7_dod	Date of death	Day 1 to 7
		d14_dod	Date of death	Day 8 to 14
		d28_dod	Date of death	Day 28
		d42_dod	Date of death	Day 42
		adis_dateofdeath	Date of death	Acute Discharge
		tdis_dateofdeath	Date of death	Total Discharge
daydiff_platform_entry_dod	Calculate n of days from platform_entry_date_local (considered day 1) to date of death	platform_entry_date_local	Derived Variable	Derived Variable – original value from participants enrolled
		dod	Derived Variable	Derived Variable – original from
date_lastknownalive_local	Check across variables, for date of last known alive, where more than one value is entered, use latest of dates,	d1to7_lastalive	Last known date alive	Day 1 to 7
		d14_lastalive	Last known date alive	Day 8 to 14

	Otherwise, leave date of last known alive as missing	d28_lastalive	Last known date alive	Day 28
		d42_lastalive	Last known date alive	Day 42
		adis_datelastknownalive	Last known date alive	Acute Discharge
		tdis_datelastknownalive	Last known date alive	Total Discharge
		d90_lastalive	Last known date alive	Day 90
Notes: Where date of death values do not match across variables, data query is raised with relevant region & site to correct data. date_lastknownalive_local can be non-matching across CRFs and still be valid, as date entered of last known alive can be true at one time point and at a later time point when more information is available can be a later date as participant may now be known to have been alive at a later date (e.g. may have had a healthcare appointment between time points).				

16.1 ALL CAUSE MORTALITY DAY 14 (CORE ESTIMAND 3)

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
died_d1to14_estimand	Where daydiff_platform_entry_dod is less than or equal to 14, then assign 1, Where daydiff_platform_entry_dod greater than 14 assign 0, Where vitalstatus_d1to90 is Alive, assign 0, d14_vitalstatus is Alive assign 0, d14_vitalstatus is Dead assign 1, d1to7_vitalstatus is Dead assign 1, d28_vitalstatus is Alive, assign 0, d42_vitalstatus is Alive, assign 0, daydiff_platform_entry_last_known_alive greater than 14, assign 0	daydiff_platform_entry_dod	Derived variable	Derived variable
		d90_vitalstatus	Vital status on Platform Day 90 <Insert date D90>	Day 90
		d1to7_vitalstatus	Vital status at Day 7	Day 1 to 7
		d14_vitalstatus	Vital status at Day 14	Day 8 to 14
		d28_vitalstatus	Participant Status at Day 28	Day 28
		d42_vitalstatus	Vital status at Day 42 <Insert date of day 42>	Day 42
		daydiff_platform_entry_last_known_alive	Derived variable	Derived variable
		Notes: **** reason why need to have all... ***		

16.2 ALL CAUSE MORTALITY DAY 28 (CORE ESTIMAND 4)

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
died_d1to28_estimand		daydiff_platform_entry_dod	Derived variable	Derived variable

Where daydiff_platform_entry_dod is less than or equal to 28, then assign 1, Where daydiff_platform_entry_dod greater than 28 assign 0, Where vitalstatus_d1to90 is Alive, assign 0, d28_vitalstatus is Alive assign 0, d28_vitalstatus is Dead assign 1, d1to7_vitalstatus is Dead assign 1, d42_vitalstatus is Alive, assign 0, daydiff_platform_entry_last_known_alive greater than 28, assign 0	d90_vitalstatus	Vital status on Platform Day 90 <Insert date D90>	Day 90
	d1to7_vitalstatus	Vital status at Day 7	Day 1 to 7
	d14_vitalstatus	Vital status at Day 14	Day 8 to 14
	d28_vitalstatus	Participant Status at Day 28	Day 28
	d42_vitalstatus	Vital status at Day 42 <Insert date of day 42>	Day 42
	daydiff_platform_entry_last_known_alive	Derived variable	Derived variable
Notes:			

16.3 ALL CAUSE MORTALITY DAY 42 (CORE ESTIMAND 5)

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
died_d1to42_estimand	Where daydiff_platform_entry_dod is less than or equal to 42, then assign 1, Where daydiff_platform_entry_dod greater than 42 assign 0, Where vitalstatus_d1to90 is Alive, assign 0, d42_vitalstatus is Alive, assign 0, d42_vitalstatus is Dead, assign 1, d1to7_vitalstatus is Dead assign 1, d14_vitalstatus is Dead assign 1, d28_vitalstatus is Dead assign 1, daydiff_platform_entry_last_known_alive greater than 42, assign 0	daydiff_platform_entry_dod	Derived variable	Derived variable
		d90_vitalstatus	Vital status on Platform Day 90 <Insert date D90>	Day 90
		d1to7_vitalstatus	Vital status at Day 7	Day 1 to 7
		d14_vitalstatus	Vital status at Day 14	Day 8 to 14
		d28_vitalstatus	Participant Status at Day 28	Day 28
		d42_vitalstatus	Vital status at Day 42 <Insert date of day 42>	Day 42
		daydiff_platform_entry_last_known_alive	Derived variable	Derived variable
Notes:				

16.4 TIME TO ALL-CAUSE MORTALITY CENSORED AT 90 DAYS (CORE ESTIMAND 6)

Derived variable	Variables and raw data
------------------	------------------------

Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
died_d1to90_estimand_tte	As above for vitalstatus_d1to90, but assigned 0 for alive (not died) and 1 for died			
died_d1to90_estimand_tte_last_known_alive	Where daydiff_platform_entry_last_known_alive < 90 days, make time daydiff_platform_entry_last_known_alive plus 1 day, Where daydiff_platform_entry_last_known_alive greater than or equal to 90 days, make time 90 days	daydiff_platform_entry_last_known_alive		
died_d1to90_estimand_tte				
died_d1to90_estimand				
Notes: daydiff_platform_entry_last_known_alive >= 90 days → allowable value + cleaning procedures				

17
TOTAL INDEX HOSPITALISATION (CORE ESTIMAND 7 & CORE ESTIMAND 9)

Total hospital index refers to consecutive time spent in hospital care from platform entry.

In the event where:

- Participant is discharged home (either at acute discharge or total discharge); or
- Participant is total discharged (no longer in an acute or non-acute care setting) during the study period; or
- Participant patient voluntarily left hospital before end of treatment. (This is captured in acute discharge CRF and entered as discharged home, but cannot be differentiated from those who were discharged home as per medical treatment); or
- Participant has died before day 90 (the study end day)

The participant is considered no longer in total hospital index. Where more than one of these events occur, the first event ends total hospital index.

Where none of the above occur during the study period, the patient is considered in hospital index for the entirety of the 90 days (study duration). Any re-admission after participant has left hospital in the above events, does not ‘re-start’ hospital index for study purposes.

End of hospital index informs time windows of interest for study outcomes and when some measures are captured until. E.g. in general, the time period of interest for study outcomes is platform entry until day 90 or until end of hospital index, whichever occurs first.

Note: It is possible for acute or total discharge CRFs to be filled out retrospectively, meaning full follow up data may be collected beyond when a participant had been discharged (in any one of the above events) that would not have been collected otherwise. When this occurs, only the expected data should be used. Data cleaning checks are run to eliminate these cases.

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
end_total_hospital_in dex_alive	Where participant went Home from first acute bed (adis_dischargedto), assign value 1 (total hospital index ended during study 90 days),	adis_dischargedto		
	Where participant went to Residential care facility (adis_dischargedto) and was not transferred to non-acute bed (adis_ns_wastransferredtononacutebed), assign 1,	adis_ns_wastransferredtononacutebed		
		tdis_dischargeduring90days		
	Where participant was total discharged during 90 days (tdis_dischargeduring90days) and reported alive, assign value 1,	tdis_dischargevitalstatus		
	Where participant discharged from subsequent acute care provider assign 1 (discharged_subsequentacuteprovider),	discharged_subsequentacuteprovider		
		end_acute_hospital_index_alive		
	Where reported not discharged during 90 days after acute discharge (tdis_dischargeduring90days), assign value 0,	discharged_subsequentacuteprovider		
	Where acute hospital index did not end during study 90 days, assign value 0,			
end_total_hospital_in dex_alive_date	If died during total hospital index (died_during_acute_hospital_index, tdis_dischargevitalstatus) , assign value 2 (represents died during total hospital index)	died_during_acute_hospital_index		
daydiff_platform_entry_end_total_hospital_in dex_alive		tdis_discharge date		
		adis_dateofdischargeacutebed		
		adis_ns_wastransferredtononacutebed		
		adis_dateoffinaldischargeacute care		

end_total_hospital_in dex_alive_date_proxy				
end_total_hospital_in dex_alive_estimand				
end_total_hospital_in dex_alive_estimand_tt e				

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
end_hospital_index	Where adis_dischargedto is “Home” or adis_dischargedto is "Residential care facility (eg. Nursing home)" & adis_ns_wastransferredtononacutebed is "No" (went ‘home’ to residential care facility)	adis_dischargedto	Where is the participant being discharged to	Acute Discharge
	or vitalstatus_d1to90 is “Dead”	vitalstatus_d1to90	Derived variable	Derived variable

	or tdis_dischargeduring90days is "Yes - Enter data" (total discharge occurred in day 1 to 90 study window) then code as 1, indicating hospital index has ceased during the study window (day 1 to 90), otherwise, code as 0 indicating participant has not ceased hospital index	tdis_dischargeduring90days	Did total discharge occur in the 90 days of study enrolment to day 90	Total Discharge
end_hospital_index_event	Where - adis_dischargedto is "Home" or - adis_dischargedto is "Residential care facility (eg. Nursing home)" & adis_ns_wastransferredtononacutebed is "No" or - tdis_dischargeduring90days is "Yes - Enter data" & tdis_dischargevitalstatus is "Alive", make value "Home (including to residential care facility)", otherwise where vitalstatus_d1to90 is "Dead", make value "Died"	adis_dischargedto	Where is the participant being discharged to	Acute Discharge
		adis_ns_wastransferredtononacutebed	Was the participant transferred to a non-acute bed	Acute Discharge
		tdis_dischargeduring90days	Did total discharge occur in the 90 days of study enrolment to day 90	Total Discharge
		tdis_dischargevitalstatus	Vital status at discharge	Total Discharge
		vitalstatus_d1to90	Derived variable	Derived variable
adis_home_date	Where, adis_dischargedto is "Home" use value in adis_dateofdischargeacutebed, Otherwise leave as missing	adis_dischargedto	Where is the participant being discharged to	Acute Discharge
		adis_dateofdischargeacutebed	Date of discharge from acute care bed	Acute Discharge
adis_residential_care_date	Where adis_dischargedto is "Residential care facility (eg. Nursing home)", use value in adis_dateofdischargeacutebed, Otherwise leave as missing	adis_dischargedto	Where is the participant being discharged to	Acute Discharge
		adis_dateofdischargeacutebed	Date of discharge from acute care bed	Acute Discharge
tdis_home_date	Where tdis_dischargeduring90days is "Yes - Enter data" & tdis_dischargevitalstatus is "Alive", use value tdis_dischargedate, Otherwise leave as missing	tdis_dischargeduring90days	Did total discharge occur in the 90 days of study enrolment to day 90	Total Discharge
		tdis_dischargevitalstatus	Vital status at discharge	Total Discharge
		tdis_dischargedate	Date of discharge from total index hospitalisation	Total Discharge
end_hospital_index_date	Of adis_home_date, adis_residential_care_date, tdis_home_date, dod_local, Where adis_home_date is the minimins, use value adis_home_date, Otherwise, where adis_residential_care_date is the minimum, use value adis_residential_care_date,	adis_home_date	Derived variable	Derived variable
		adis_residential_care_date	Derived variable	Derived variable
		tdis_home_date	Derived variable	Derived variable

	Otherwise, where tdis_home_date is the minimum, use value tdis_home_date, Otherwise where dod_local is the minimum, use value, dod_local, Otherwise leave missing	dod_local	Derived variable	Derived variable
daydiff_platform_entry_end_hospital_index	Calculate n days between platform_entry_date_local (considered day 1) and end_hospital_index_date	platform_entry_date_local	Derived variable	Derived variable
		end_hospital_index_date	Derived variable	Derived variable
Notes: Where participant has reached day 90 and end_hospital_index is 0, this indicates participant was in hospital index for entire study window. Where participant has not yet reached day 90 and end_hospital_index is 0, this indicates participant is currently still in hospital index, but status may change up until patient reached day 90. Total discharge CRF does not collect whether a participant was discharged home or to residential care facility, hence home or residential care facility are grouped as one category in end_hospital_index_event				

18 ACUTE INDEX HOSPITALISATION (CORE ESTIMAND 8)

Acute index hospitalisation refers to consecutive time spent in acute hospital care from platform entry.

All participants start their study journey in acute care, hence the count for acute index hospitalisation starts on platform day 1 for all participants.

In the event where a participant is transferred from enrolling hospital acute care bed to non-acute care (non-acute bed as per study definition) or discharged from the enrolling hospital acute care bed directly to any of the above events ending index hospitalisation, the participant is no longer in acute care.

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
end_acute_hospital_index	Where - adis_dischargedto is empty - or - adis_dischargedto is "Acute care" & adis_ns_wastransferredtononacutebed is "No", code as 0, Otherwise, where - adis_dischargedto is "Acute care" & adis_ns_wastransferredtononacutebed is "Yes" - or - adis_dischargedto is "Home" - or - adis_dischargedto is "Died" - or - adis_dischargedto is "Non-acute care" - or - adis_dischargedto is "Residential care facility (eg. Nursing home)", code as 1	adis_dischargedto	Acute discharge	Acute discharge
		adis_ns_wastransferredtononacutebed	Was the participant transferred to a non-acute bed	Acute discharge
end_acute_hospital_index_event	Where adis_dischargedto is "Acute care" & adis_ns_wastransferredtononacutebed is "Yes", make value "Non-acute care",	adis_dischargedto	Where is the participant being discharged to	Acute discharge

	Otherwise use value from adis_dischargedto	adis_ns_wastransferre dtononacutebed	Was the participant transferred to a non-acute bed	Acute discharge
end_acute_hos pital_index_dat e	Where - adis_dischargedto is "Acute care" & adis_ns_wastransferredtononacutebe d is "Yes", use value in adis_dateoffinaldischargeacutecare, Otherwise where - adis_dischargedto is "Home" or - adis_dischargedto is "Non-acute care" or - adis_dischargedto is "Residential care facility (eg. Nursing home)", use value in adis_dateofdischargeacutebed, otherwise, where - adis_dischargedto is "Died", use value in adis_dateofdeath	adis_dischargedto	Where is the participant being discharged to	Acute discharge
		adis_ns_wastransferre dtononacutebed	Was the participant transferred to a non-acute bed	Acute discharge
		adis_dateoffinaldisch argeacutecare	Date of final discharge from Acute Care	Acute discharge
		adis_dateofdischarge acutebed	Date of discharge from acute care bed	Acute discharge
		adis_dateofdeath	Date of death	Acute discharge
daydiff_platfor m_entry_end_a cute_hospital_i ndex	Calculate n days between platform_entry_date_local (considered day 1) and end_acute_hospital_index_date	platform_entry_date_l ocal	Derived variable	Derived variable
		end_acute_hospital_in dex_date	Derived variable	Derived variable
Notes: crf_adis_required derived variable below end_acute_hospital_index is a dynamic variable, where a participant is within the 90 day study period a 0 indicates have not or have not yet ended acute index hospitalisation, where a participant has reached platform day 90 and a 0 indicates the participant was in acute care for the entirety of the 90 days scenario adis_dischargedto is "Acute care" & adis_ns_wastransferredtononacutebed is "Yes", indicates participant left the enrolling hospital to another acute care facility, and was later transferred to a non-acute bed daydiff_platform_entry_end_acute_hospital_index indicates number of days in acute care, for participants who did not die during their acute care. It is possible a participant has been recorded as leaving acute care and have a missing date of when acute hospital index ended, and therefore calculating number of days is not possible.				

19
MICROBIOLOGICAL TREATMENT FAILURE (CORE ESTIMAND 10)

Microbiological Treatment Failure is defined as a positive sterile site culture with the same silo as the index isolate (PSSA/MSSA/MRSA) between platform day 15 and 90 (inclusive).

Positive sterile site culture is collected in various CRFS and fields, dependant on the participants journey, i.e. whether acute discharged. Where a patient has an acute discharge, the question time window asked is based on date of acute discharge. Due to oversights in database design, some ‘time window’ errors exists, whereby if a participant is discharged prior to day 15 (i.e. before time window) and response to question on whether a positive sterile site culture between acute discharge date (e.g. day 3) and day 90 is ‘Yes’ and associated date is also prior to day 15 (i.e. before time window), it is not possible to determine what happened within time window to identify whether the endpoint was reach or not. For participants who fell under this scenario, additional data was collected under existing data fields that ask specific to the time window of interest.

adis_crf_data date/ daydiff_platform_entry_adis_crf_data,

- In coding (was not yet published), added “_d90” to follow convention, indicates what time point var relates too
- Add paedts, measured in separate variable and measured differently, but outcome/ meaning is the same
- Moved vital status to top (age does not matter) and so that write first before any others
 - o Checked previous and does not make diff

```
snap <- snap %>% mutate(fbis_baseline = case_when(bas_heleveloffunctionfbis == "0 - Unknown" | is.na(bas_heleveloffunctionfbis) ~ d90_he_fbisleveloffunction),
  fbis_baseline = case_when(fbis_baseline == "0 - Unknown" ~ NA,
    TRUE ~ as.integer(substr(bas_heleveloffunctionfbis, 1, 1)) ),
  fbis_d90 = case_when(d90_he_fbisparticipantsleveloffunction == "0 - Unknown" ~ NA,
    TRUE ~ as.integer(substr(d90_he_fbisparticipantsleveloffunction, 1, 1))),
  fbis_return_d90_previous = case_when(fbis_d90 >= fbis_baseline ~ 1,
    fbis_d90 < fbis_baseline | vitalstatus_d1to90 == "Dead" ~ 0),
  |
  fbis_return_d90 = case_when(vitalstatus_d1to90 == "Dead" ~ 0,
    age >= 18 & fbis_d90 >= fbis_baseline ~ 1,
    age >= 18 & fbis_d90 < fbis_baseline ~ 0,
    age <18 & d90_he_fbischildstatus == "Yes" ~ 1,
    age <18 & d90_he_fbischildstatus == "No" ~ 0))
```

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
micro_treatment_failure_d15to90	Where daydiff_platform_entry_end_acute_hospital_index is less than	daydiff_platform_entry_end_acute_hospital_index	Derived Variable	Derived Variable
		adis_sterilesiteculture	Was there a positive sterile site culture any time after platform Day 14 until acute hospital discharge with the same silo as the index isolate (PSSA/MSSA/MRSA)	Acute Discharge
		adis_sterilesiteculturedate	Date the first sterile culture was positive	Acute Discharge
		d90_d14tod90_sterilesiteculture	Was there a positive sterile site culture any time after platform Day 14 <insert date of day 14> up until platform Day 90 <insert date of day 90>, with the same silo as the index isolate (PSSA/MSSA/MRSA)	Day 90
		d90_d14tod90_sterilesiteculturedate	Date that first sterile site culture post Day 14 was collected	Day 90
		d90_adistod90_sterilesiteculture	Was there a positive sterile site culture any time after acute hospital discharge <insert date of ADIS> up until platform Day 90 <insert date of day 90> with the same silo as the index isolate (PSSA/MSSA/MRSA)	Day 90
		d90_adistod90_sterilesiteculturedate	Date the first sterile culture post Acute Discharge was collected	Day 90
Notes:				

20 DIAGNOSIS OF NEW FOCUS/FOCI OF INFECTION (CORE ESTIMAND 11)

Diagnosis of new focus/ foci of infection (foi/foci) is defined as a new foi/foci between platform day 15 to day 90 (inclusive).

New focus/ foci of infection is collected in various CRFS and fields, dependant on the participants journey, i.e. whether an acute discharge CRf is filled out. Where a patient has an acute discharge, the question time window asked is based on date of acute discharge (on day 90 crf d90_foi_adistod90newinfection).

Due to oversights in database design some errors exist. This includes: where a participant has an acute discharge prior to day 15 (i.e. before time window) and response to question on whether a new foi/foci between acute discharge date (e.g. day 3) and day 90 is either 'Yes', it is not possible to determine whether this occurred before or within the time window (there is no associated date variable). In the same scenario where the response is 'No' we can safely assume this also applies to the time window (i.e. no foi/foci for the entirety of window e.g. d3 to d90, which also covers time window of interest, d15 to d90). Where a participant has an acute discharge to another acute care facility and clinical data is available, the database incorrectly displays the first date. Sites are advised to enter data with the correct date. Where database oversight exists, all efforts have been made to collect data correct to time window of interest to reduce unnecessary missing. Derivation is used with the correct 'crf data' date.

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
new_foi_d15tod90	Where d90_foi_d15tod90newinfection is Yes, then assign 1,	adis_foi_pd15newinfection	Were there any new focus/foci of infection diagnosed between platform Day 15 <insert date of day 15> and acute discharge	
	Where d90_foi_d15tod90newinfection is No, assign 0,			
	Where daydiff_platform_entry_adis_crf_data_date is less than 15 days and adis_foi_pd15newinfection is No assign 0 (question displayed will be e.g. d3 to d90),	d90_foi_adistod90newinfection	Were there any NEW focus/foci of infection diagnosed between acute discharge <insert date of acute discharge> and platform Day 90 <insert date of day 90>	
	Where, daydiff_platform_entry_adis_crf_data_date is greater than or equal to 15 and (adis_foi_pd15newinfection or d90_foi_adistod90newinfection) are Yes, assign 1,	d90_foi_d15tod90newinfection	Were there any NEW focus/foci of infection diagnosed between platform Day 15 <insert date of day 15> and platform Day 90 <insert date of day 90>	
	Where daydiff_platform_entry_adis_crf_data_date & daydiff_platform_entry_adis_transfer_date are exactly d15 and d90_foi_d15tod90newinfection is missing, use value d90_foi_adistod90newinfection Yes to assign 1, No to assign 0,	daydiff_platform_entry_adis_crf_data_date		
	Where daydiff_platform_entry_adis_crf_data_date greater than or equal to 15, and adis_foi_pd15newinfection is No and d90_foi_adistod90newinfection is No (15 to adis, adis to d90), then assign 0,	daydiff_platform_entry_dod		
Where daydiff_platform_entry_adis_crf_data_date greater than or equal to 15 and daydiff_platform_entry_adis_crf_data_date is equal to daydiff_platform_entry_dod, use adis_foi_pd15newinfection Yes to assign 1, No assign 0 (IE 5)				
Notes: Data should be cleaned to ensure no impossible values (e.g. died before day 15) No associated date variables FOI CRF contain details of the foi/foci. All are asked details on the initial foi/foci. If a response of ‘Yes’ to the above, then it asks subsequent foi/foci details.				

21 C. DIFFICILE (CORE ESTIMAND 12)

(C. Difficile is collected in Day 90 CRF as well as Serious Adverse Reaction (SAR) log (currently outside of the database at time of document publication, which will be built into the database). For C. Difficile diarrhoea collected via the database only, please use d90_cdiffrhodiaany. For a composite variable, please use the below specifications.

Variables needed, not elsewhere specified

Variable	Label/ title	Data export / CRF
medra_term_llt	MedDRA term (LLT)	SNAP_SARLog_[date]
medra_code_llt	MedDRA code (LLT)	SNAP_SARLog_[date]
d90_cdiffrhodiaany	Did the participant have C. difficile diarrhoea determined by a clinical laboratory in the 90 days following platform entry	Day 90
Notes: LLT = Lowest Level Terms PT = Preferred Term		

		Criteria	Descriptor
cdiff_d1to90_com pсите	Considered a case, coded as 1, when any of the criteria boxes are met	medra_term_llt is “C.difficile diarrhea” or “C.difficile colitis”	Is a case when any source determines is a case
		medra_code_llt is “10006833” or “10006835”	
		d90_cdiffrhodiaany is “Yes”	
	Considered not a case, coded as 0, when all the criteria for case are not met and both non-case criteria boxes are met for	d90_cdiffrhodiaany is “No” (medra_term_llt is not “C.difficile diarrhea” or “C.difficile colitis”) ; or - medra_code_llt is not “10006833” or 10006835” or - no entry in SAR Log	AKI is confirmed not a case when Determined not a case in CRF and no entry in SAR log (either no entry at all or all entries for participant are not c.diff terms)
	Considered missing, value left blank, when values are missing and do not allow for calculation	d90_cdiffrhodiaany is missing	Unable to be calculated due to missingness
Notes: medra_term & medra_code should always match, however both applied in case of typo medra_term can contain upper and lower case C. difficile Diarrhoea is only collected in SAR log and in day 90 CRF			

22 RETURN TO USUAL LEVEL OF FUNCTION ON THE MODIFIED FUNCTIONAL BLOODSTREAM INFECTION SCORE (FBIS) (CORE ESTIMAND 14)

Return to usual level of function on the modified functional bloodstream infection score (FBIS) between baseline (platform entry) and 90 days after platform entry

- Adults and paed, measured differently

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
fbis_baseline	Where baseline collected fbis score is missing or reported as 'unknown', use retrospective value collected in day 90 CRF,	bas_heleveloffunctionfbis	Usual level of function	Baseline
	Where baseline remains reported as 'unknown', assign it as missing (this step is to ensure calculations are applied appropriately), Else assign the associated number score (e.g. '1 - Hospitalised (or equivalent, such as hospice' is 1)	d90_he_fbisleveoffunction	Which category best describes the participant's level of function at baseline, based on their best recollections	Day 90
fbis_d90	Where d90 score is reported as 'unknown', assign it as missing (this step is to ensure calculations are applied appropriately), Else assign the associated number score (e.g. '1 - Hospitalised (or equivalent, such as hospice' is 1)	d90_he_fbisparticipantsleveoffunction	Which category best describes the participant's level of function on Day 90	Day 90
fbis_return_d90	Where vital status at day 90 is dead assign 0,	vitalstatus_d1to90	Derived variable	Derived variable
	Where participant has withdrawn form data collection within study 90 days, assign missing,	daydiff_platform_entry_wd_data_collection_end_date	Derived variable	Derived variable
	Where participant is adult (18 years or older) and day 90 score is greater than or equal to baseline score, assign 1,	age	Derived variable	Derived variable
	Where participant is adult (18 years or older) and day 90 score is less than baseline score assign 0,	fbis_d90	Derived variable	Derived variable
	Where participant is paediatric (less than 18 years) and reported 'Yes' to return to usually level of activity, assign 1,	fbis_baseline	Derived variable	Derived variable
	Where participant is paediatric (less than 18 years) and reported 'No' to return to usually level of activity, assign 0	d90_he_fbischildstatus	Has your child returned to their usual level of activity	Day 90
Notes: - Possible to wd after d90 - Adult + paed measured diff, outcome is same - This way streamlines door2 deriving				

23 NUMBER OF ANTIBIOTIC DAYS (CORE ESTIMAND 17)

Clinician estimated number of antibiotic days (IV and/or oral/enteral) in the 90 days following platform entry.

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
n_days_antibiotics_d1to90	Where n days known alive (died_d1to90_estimand_tte) is less than n days reported on antibiotics (i.e n days on antibiotics is more than n days known alive), then assign n days known alive, Else assign value in total days on antibiotics	died_d1to90_estimand_tte	Derived variable	Derived variable
		d90_daysonabs_totaldays	Total days on antibiotics	Day 90
Notes: - died_d1to90_estimand_tte is used purposely cos if IE handling				

24 DAYS ALIVE FREE OF ANTIBIOTICS (CORE ESTIMAND 18)

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
n_days_alive_free_antibiotics_d1to90	Calculate n days known alive minus n days on antibiotics	died_d1to90_estimand_tte	Derived variable	Derived variable
		n_days_antibiotics_d1to90	Derived variable	Derived variable
Notes: - died_d1to90_estimand_tte is used purposely cos if IE handling				

25 ACUTE KIDNEY INJURY (DOMAIN-SPECIFIC ESTIMAND A1.2 & DOMAIN-SPECIFIC ESTIMAND B.6)

Acute Kidney Injury (AKI) uses values of creatinine for derivation. A value of 0 is not allowable and should be removed prior to derivation.

25.1 BASELINE (DAY 1) CREATINE

	Derived variable	Variables and notes from Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
baseline_creatinine	Where d1to7_labresultspd1highserumcreatinine_as_umoll is available, use that,	d1to7_labresultspd1highserumcreatinine_as_umoll	Highest serum creatinine day 1 µmol/L	Day 1 to 7
		platform_entry_date_local	Derived variable: platform entry date	Derived variable:

Otherwise if d1to7_labresultspd1highserumcreatinine_as_umoll is missing and value available in adis_pssaormssa_highestserumcreatinine_as_umoll / adis_mrsa_highestserumcreatinine_as_umoll, collected on study day 1 use that, Otherwise if adis_pssaormssa_highestserumcreatinine_as_umoll / adis_mrsa_highestserumcreatinine_as_umoll missing and value available in tdis_pssaormssa_highestserumcreatinine_as_umoll / tdis_mrsa_latestserumcreatinine_as_umoll available on day 1, use that, Otherwise if tdis_pssaormssa_highestserumcreatinine_as_umoll / tdis_mrsa_latestserumcreatinine_as_umoll is missing, and value available in tdis_pssaormssa_latestserumcreatinine_date / dis_mrsa_latestserumcreatinine_as_umoll on day 1, use that Otherwise leave baseline as missing				original value from Participants enrolled export
	adis_pssaormssa_highestserumcreatinine_as_umoll	Highest serum creatinine µmol/L	Acute Discharge	
	adis_pssaormssa_highestserumcreatinine_date	Highest serum creatinine date	Acute Discharge	
	adis_mrsa_highestserumcreatinine_as_umoll	Highest serum creatinine µmol/L	Acute Discharge	
	adis_mrsa_highestserumcreatinine_date	Highest serum creatinine date	Acute Discharge	
	tdis_pssaormssa_highestserumcreatinine_as_umoll	Highest serum creatinine µmol/L	Total Discharge	
	tdis_pssaormssa_highestserumcreatinine_date	Highest serum creatinine date	Total Discharge	
	tdis_pssaormssa_latestserumcreatinine_as_umoll	Most recent serum creatinine µmol/L	Total Discharge	
	tdis_pssaormssa_latestserumcreatinine_date	Date of most recent result prior to total hospital discharge	Total Discharge	
	tdis_mrsa_highestserumcreatinine_as_umoll	Highest serum creatinine µmol/L	Total Discharge	
	tdis_mrsa_highestserumcreatinine_date	Date of highest recorded result	Total Discharge	
	tdis_mrsa_latestserumcreatinine_as_umoll	Most recent serum creatinine µmol/L	Total Discharge	
	tdis_mrsa_latestserumcreatinine_date	Date of most recent result prior to total hospital discharge	Total Discharge	

Notes:

Only highest serum creatinine is collected at acute discharge and not latest

Participant will only have a value in either adis_pssaormssa_highestserumcreatinine_as_umoll or adis_mrsa_highestserumcreatinine_as_umoll, depending on silo

Participant will only have a value in either tdis_pssaormssa_highestserumcreatinine_as_umoll or tdis_mrsa_latestserumcreatinine_as_umoll, depending on silo

25.2 CREATININE DAY 1 TO 5 FROM ACUTE AND TOTAL DISCHARGE

Derived variables to capture creatinine values from acute or total discharge with day 1 to 5

Acute Discharge				
Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
adis_highest_creatinine_d1to5	If n of study days between Highest serum creatinine date and platform entry is less than or equal to 5 days, then use Highest serum creatinine value, otherwise leave missing	adis_pssaormssa_highestserumcreatinine_as_umoll	Highest serum creatinine µmol/L	Acute Discharge
		adis_pssaormssa_highestserumcreatinine_date	Highest serum creatinine date	Acute Discharge
		platform_entry_date_local	Derived variable	Derived variable: original value from

				Participants enrolled export
	If n of study days between Highest serum creatinine date and platform entry date is less than or equal to 5 days, then use Highest serum creatinine value, otherwise leave missing	adis_mrsa_highestserumcreatinine_as_umoll	Highest serum creatinine μ mol/L	Acute Discharge
		adis_mrsa_highestserumcreatinine_date	Highest serum creatinine date	Acute Discharge
		platform_entry_date_local	Derived variable	Derived variable: original value from Participants enrolled export
Note that patients will only have a value in either (or none) based on silo (PSSA/MSSA/MRSA)				

Total Discharge				
Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
tdis_highest_creatinine_d1to5	If n of study days between Highest serum creatinine date and platform entry date is less than or equal to 5 days, then use Highest serum creatinine value, otherwise leave missing	tdis_pssaormssa_highestserumcreatinine_as_umoll	Highest serum creatinine μ mol/L	Total Discharge
		tdis_pssaormssa_highestserumcreatinine_date	Highest serum creatinine date	Total Discharge
		platform_entry_date_local	Derived variable	Derived variable - original value from Participants enrolled export
	If n of study days between Highest serum creatinine date and platform entry date is less than or equal to 5 days, then use Highest serum creatinine value, otherwise leave missing	tdis_mrsa_highestserumcreatinine_as_umoll	Highest serum creatinine μ mol/L	Total Discharge
		tdis_mrsa_highestserumcreatinine_date	Date of highest recorded result	Total Discharge
		platform_entry_date_local	Derived variable	Derived variable - original value from Participants enrolled export
	Note: patients will only have a value in one (or none) based on silo (PSSA/MSSA/MRSA)			
Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
tdis_latest_creatinine_d1to5	If n of study days between most recent serum creatinine date and platform entry date is less than or equal to 5 days, then use Highest serum creatinine value, otherwise leave missing	tdis_pssaormssa_latestserumcreatinine_as_umoll	Most recent serum creatinine μ mol/L	Total Discharge
		tdis_pssaormssa_latestserumcreatinine_date	Date of most recent result prior to total hospital discharge	Total Discharge
		platform_entry_date_local	Derived variable	Derived variable: original value from Participants enrolled export
	If n of study days between most recent serum creatinine date and platform	tdis_mrsa_latestserumcreatinine_as_umoll	Most recent serum	Total Discharge

	entry is less than or equal to 5 days, then use Highest serum creatinine value, otherwise leave missing		creatinine $\mu\text{mol/L}$	
		tdis_mrsa_latestserumcreatinine_date	Date of most recent result prior to total hospital discharge	Total Discharge
		platform_entry_date_local	Derived variable	Derived variable - original value from Participants enrolled export
Note: patients will only have a value in one (or none) based on silo (PSSA/MSSA/MRSA)				
tdisd14_highest_creatinine_d1to5	If n of study days between Highest serum creatinine date and platform entry date is less than or equal to 5 days, then use Highest serum creatinine value, otherwise leave missing	tdis_pssaormssa_highestserumcreatinine_d14_as_umoll	Highest serum creatinine $\mu\text{mol/L}$	Total Discharge
		tdis_pssaormssa_highestserumcreatinine_d14_date	Date of highest recorded result	Total Discharge
		platform_entry_date_local	Derived variable	Derived variable - original value from Participants enrolled export
	If n of study days between Highest serum creatinine date and platform entry date is less than or equal to 5 days, then use Highest serum creatinine value, otherwise leave missing	tdis_mrsa_highestserumcreatinine_d14_as_umoll	Highest serum creatinine $\mu\text{mol/L}$	Total Discharge
		tdis_mrsa_highestserumcreatinine_d14_date	Date of highest recorded result	Total Discharge
		platform_entry_date_local	Derived variable	Derived variable - original value from Participants enrolled export
Note: patients will only have a value in one (or none) based on silo (PSSA/MSSA/MRSA)				

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
max_creatinine_d1to5	highest of values	d1to7_pssaormssa_pd1to5highserumcreatinine_as_umoll	PSSAorMSSA Highest serum creatinine day 1 to 5 $\mu\text{mol/L}$	Day 1 to 7
		d1to7_pssaormssa_pd5highserumcreatinine_as_umoll	PSSAorMSSA Highest serum creatinine day 5 $\mu\text{mol/L}$	Day 1 to 7
		d1to7_mrsa_pd1to5highserumcreatinine_as_umoll	Highest serum creatinine level From platform Day 1 to platform Day 5 as $\mu\text{mol/L}$	Day 1 to 7
		d1to7_mrsa_pd5highserumcreatinine_as_umoll	Highest serum creatinine level on Day 5 as $\mu\text{mol/L}$	Day 1 to 7
		d1to7_adj_pd1to5highserumcreatinine_as_umoll	Highest serum creatinine level from platform Day 1 to platform Day 5 as $\mu\text{mol/L}$	Day 1 to 7
		d1to7_adj_pd5highserumcreatinine_as_umoll	Highest serum creatinine level on Day 5 as $\mu\text{mol/L}$	Day 1 to 7

		adis_highest_creatinine_d1to5	Derived variable	Derived variable – value from Acute Discharge
		tdis_highest_creatinine_d1to5	Derived variable	Derived variable – value from Total Discharge
		tdis_latest_creatinine_d1to5	Derived variable	Derived variable – value from Total Discharge
		tdisd14_highest_creatinine_d1to5	Derived variable	Derived variable – value from Total Discharge
Notes: Day 1 to 7 values don't have associated date variables d1to7_pssaormssa_pd5highserumcreatinine_as_umoll, was previously named d1to7_pssa_pd5highserumcreatinine_as_umoll d1to7_pssaormssa_pd5highserumcreatinine_as_umoll, was previously named d1to7_pssa_pd5highserumcreatinine_as_umoll				

25.3 CREATININE DAY 6 TO 14 FROM ACUTE AND TOTAL DISCHARGE

Derived variables to capture creatinine values within study days 6 to 14

Acute Discharge				
Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
adis_highest_creatinine_d6to14	If n of study days between Highest serum creatinine date and platform entry date is between 6 and 14 days (inclusive), then impute Highest serum creatinine value into [var name], otherwise leave missing	adis_pssaormssa_highestserumcreatinine_as_umoll	Highest serum creatinine µmol/L	Acute Discharge
		adis_pssaormssa_highestserumcreatinine_date	Highest serum creatinine date	Acute Discharge
		platform_entry_date_local	Derived variable: platform entry date	Derived variable: original value from Participants enrolled export
	If n of study days between Highest serum creatinine date and platform entry date is between 6 and 14 days (inclusive), then impute Highest serum creatinine value into [var name], otherwise leave missing	adis_mrsa_highestserumcreatinine_as_umoll	Highest serum creatinine µmol/L	Acute Discharge
		adis_mrsa_highestserumcreatinine_date	Highest serum creatinine date	Acute Discharge
		platform_entry_date_local	Derived variable: platform entry date	Derived variable: original value from Participants enrolled export
Note that patients will only have a value in either (or none) based on silo (PSSA/MSSA/MRSA)				
Total Discharge				
Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
tdis_highest_creatinine_d6to14	If n of study days between Highest serum creatinine date and platform entry date is between 6 and 14 days (inclusive), then use Highest serum creatinine value, otherwise leave missing	tdis_pssaormssa_highestserumcreatinine_as_umoll	Highest serum creatinine µmol/L	Total Discharge
		tdis_pssaormssa_highestserumcreatinine_date	Highest serum creatinine date	Total Discharge
		platform_entry_date_local	Derived variable:	Derived variable:

			platform entry date	original value from Participants enrolled export
	If n of study days between Highest serum creatinine date and platform entry date is between 6 and 14 days (inclusive), then use Highest serum creatinine value, otherwise leave missing	tdis_mrsa_highestserumcreatinine_as_umoll	Highest serum creatinine $\mu\text{mol/L}$	Total Discharge
		tdis_mrsa_highestserumcreatinine_date	Date of highest recorded result	Total Discharge
		platform_entry_date_local	Derived variable: platform entry date	Derived variable: original value from Participants enrolled export
Note: patients will only have a value in one (or none) based on silo (PSSA/MSSA/MRSA)				
Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
tdis_latest_creatinine_d6to14	If n of study days between most recent serum creatinine date and platform entry date is between 6 and 14 days (inclusive), then use Highest serum creatinine value, otherwise leave missing	tdis_pssaormssa_latestserumcreatinine_as_umoll	Most recent serum creatinine $\mu\text{mol/L}$	Total Discharge
		tdis_pssaormssa_latestserumcreatinine_date	Date of most recent result prior to total hospital discharge	Total Discharge
		platform_entry_date_local	Derived variable: platform entry date	Derived variable: original value from Participants enrolled export
	If n of study days between most recent serum creatinine date and platform entry date is between 6 and 14 days (inclusive), then use Highest serum creatinine value, otherwise leave missing	tdis_mrsa_latestserumcreatinine_as_umoll	Most recent serum creatinine $\mu\text{mol/L}$	Total Discharge
		tdis_mrsa_latestserumcreatinine_date	Date of most recent result prior to total hospital discharge	Total Discharge
		platform_entry_date_local	Derived variable: platform entry date	Derived variable: original value from Participants enrolled export
Note: patients will only have a value in one (or none) based on silo (PSSA/MSSA/MRSA)				
tdisd14_highest_creatinine_d6to14	If n of study days between Highest serum creatinine date and platform entry date is between 6 and 14 days (inclusive), then use Highest serum creatinine value, otherwise leave missing	tdis_pssaormssa_highestserumcreatinined14_as_umoll	Highest serum creatinine $\mu\text{mol/L}$	Total Discharge
		tdis_pssaormssa_highestserumcreatinined14_date	Date of highest recorded result	Total Discharge
		platform_entry_date_local	Derived variable: platform entry date	Derived variable: original value from Participants enrolled export
	If n of study days between Highest serum creatinine date and platform entry date is between 6 and 14 days	tdis_mrsa_highestserumcreatinined14_as_umoll	Highest serum creatinine $\mu\text{mol/L}$	Total Discharge

	(inclusive), then use Highest serum creatinine value, otherwise leave missing	tdis_mrsa_highestserumcreatinine_d14_date	Date of highest recorded result	Total Discharge
		platform_entry_date_local	Derived variable: platform entry date	Derived variable: original value from Participants enrolled export
Note: patients will only have a value in one (or none) based on silo (PSSA/MSSA/MRSA)				

25.4 MAXIMUM CREATININE BETWEEN STUDY DAYS 6 AND 14

Day 14 value, found on day 8 to 14 CRF has an allowance of +/- 3 days where day 14 result is not available, hence follow up period may not strictly adhere to platform day 1 to 14.

Derived variable		Variables and raw data		
Derived variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
max_creatinine_d6to14	highest value of variables	d14_pssaormssa_pd6to14highserumcreatinine_as_umoll	Highest serum creatinine day 6 to 14 µmol/L	Day 8 to 14
		d14_pssaormssa_pd14highserumcreatinine_as_umoll	Highest serum creatinine day 14 µmol/L	Day 8 to 14
		d14_mrsa_pd6to14highserumcreatinine_as_umoll	Highest serum creatinine day 6 to 14 µmol/L	Day 8 to 14
		d14_mrsa_pd14highserumcreatinine_as_umoll	Highest serum creatinine day 14 µmol/L	Day 8 to 14
		d14_adj_pd6to14highserumcreatinine_as_umoll	Highest serum creatinine day 6 to 14 µmol/L	Day 8 to 14
		d14_adj_pd14highserumcreatinine_as_umoll	Highest serum creatinine day 14 µmol/L	Day 8 to 14
		adis_highest_creatinine_d6to14	Derived variable	Derived variable – value from Acute Discharge
		tdis_highest_creatinine_d6to14	Derived variable	Derived variable – value from Acute Discharge
		tdis_latest_creatinine_d6to14	Derived variable	Derived variable – value from Acute Discharge
		tdisd14_highest_creatinine_d6to14	Derived variable	Derived variable – value from Acute Discharge
Note: Day 8 to 14 values don’t have associated date variables d14_pssaormssa_pd14highserumcreatinine_as_umoll notes “If day 14 result is not available, record highest level between days 11 to 17 inclusive”, hence follow up period may not strictly adhere to platform day 1 to 14				

25.5 DERIVED ACUTE KIDNEY INJURY

Derived variable name		Criteria	Descriptor
aki_d1to5	Considered a case, coded as 1, when any of the criteria boxes are met	Difference between max_creatinine_d1to5 and baseline_creatinine is greater than or equal to 26.5 (i.e. max_creatinine_d1to5 - baseline_creatinine ≥ 26.5)	Baseline creatinine has an increase of ≥ 26.5 μmol/L within 5 days
		max_creatinine_d1to5 divided by baseline_creatinine is equal to or greater than 1.5	Baseline creatinine increases 1.5 times at follow up
	Considered not a case, coded as 0, when all the criteria for case are not met and any of the non-case criteria boxes are met	Difference between max_creatinine_d1to5 and baseline_creatinine is less than 26.5 (i.e. max_creatinine_d1to5 - baseline_creatinine < 26.5)	Baseline creatinine does not have an increase ≥ 26.5 μmol/L within 5 days
		max_creatinine_d1to5 divided by baseline_creatinine is less than 1.5	Baseline creatinine does not increase 1.5 times within 5 days
	Considered missing, value left blank, when values are missing and do not allow for calculation	baseline_creatinine is missing and/or max_creatinine_d1to5 is missing	Unable to be calculated due to missingness
aki_d1to5_stage	Considered not a case, coded as 0, has been confirmed not a case	aki_d1to5 is 0	Not case of AKI by binary derivation
	Considered stage 1, coded as 1, when either of the criteria box are met	max_creatinine_d1to5 divided by baseline_creatinine is equal to or greater than 1.5 and less than 2.0	Creatinine increases to 1.5 and less than 2 between baseline and follow up
		Difference between max_creatinine_d1to5 and baseline_creatinine is greater than or equal to 26.5 (i.e. max_creatinine_d1to5 - baseline_creatinine ≥ 26.5) AND max_creatinine_d1to5 divided by baseline_creatinine is less than 2.0	Creatinine difference between baseline and follow up has a value of 26.5 or higher and creatinine increase between baseline and follow up is less than 2
	Considered stage 2 coded as 2, when the criteria box are met	max_creatinine_d1to5 divided by baseline_creatinine is equal to or greater than 2.0 and less than 3.0	Creatinine increases to 2 and less than 3 between baseline and follow up
	Considered stage 3, coded as 3, when either of the criteria box are met	max_creatinine_d1to5 divided by baseline_creatinine is equal to or greater than 3.0	Creatinine increases to 2 and less than 3 between baseline and follow up
		max_creatinine_d1to5 greater than or equal to 354	Follow up creatinine has a value of 354 or higher
Notes: ‘within 5 days’ count starts from day 1 (and not day 1 plus 5 days)			

Derived variable name		Criteria	Descriptor
-----------------------	--	----------	------------

aki_d6to14	Considered a case, coded as 1, when any of the criteria boxes are met	max_creatinine_d6to14 divided by baseline_creatinine is equal to or greater than 1.5	Creatinine increases 1.5 times within from baseline to follow up
		max_creatinine_d6to14 divided by max_creatinine_d1to5 is equal to or greater than 1.5	
	Considered not a case, coded as 0, when all the criteria for case are not met and either of the non-case criteria boxes are met	max_creatinine_d6to14 divided by baseline_creatinine is less than 1.5	Baseline creatinine does not increase 1.5 times to time of follow up
		max_creatinine_d6to14 divided by max_creatinine_d1to5 is less than 1.5	
	Considered missing, value left blank, when values are missing and do not allow for calculation	baseline_creatinine is missing and/ or max_creatinine_d1to5 is missing and/or max_creatinine_d6to14 is missing not allowing for calculations	Unable to be calculated due to missingness
aki_d6to14_stage	Considered not a case, coded as 0, has been confirmed not a case	aki_d6to14is 0	Not case of AKI by binary derivation
	Considered stage 1, coded as 1, when any of the criteria box are met	max_creatinine_d6to14 divided by baseline_creatinine is equal to or greater than 1.5 and less than 2.0	Creatinine increases to 1.5 and less than 2 between baseline and follow up
		max_creatinine_d6to14 divided by max_creatinine_d1to5 is equal to or greater than 1.5 and less than 2.0	
		Difference between max_creatinine_d6to14 and baseline_creatinine is greater than or equal to 26.5 (i.e. max_creatinine_d6to14 - baseline_creatinine ≥ 26.5) AND max_creatinine_d6to14 divided by baseline_creatinine is less than 2.0	Creatinine difference between baseline and follow up has a value of 26.5 or higher and creatinine increase between baseline and follow up is less than 2
		Difference between max_creatinine_d6to14 and max_creatinine_d1to5 is greater than or equal to 26.5 (i.e. max_creatinine_d6to14 - max_creatinine_d1to5 ≥ 26.5) AND max_creatinine_d6to14 divided by max_creatinine_d1to5 is less than 2.0	
	Considered stage 2 coded as 2, when either of the criteria box are met	max_creatinine_d6to14 divided by baseline_creatinine is equal to or greater than 2.0 and less than 3.0	Creatinine increases to 2 and less than 3 between baseline and follow up
		max_creatinine_d6to14 divided by max_creatinine_d1to5 is equal to or greater than 2.0 and less than 3.0	
	Considered stage 3, coded as 3, when either of the criteria box are met	max_creatinine_d6to14 divided by baseline_creatinine is equal to or greater than 3.0	Creatinine increases to 2 and less than 3 between baseline and follow up
		max_creatinine_d6to14 divided by max_creatinine_d1to5 is equal to or greater than 3.0	
		max_creatinine_d6to14 is greater than or equal to 354	Follow up creatinine has a value of 354 or higher
Notes: 'within 14 days' count starts from day 1 (and not day 1 plus 14 days) Baseline refers to time 1 (can be baseline or day 1 to 5 value) relative to time to 2 (day 1 to 5 value or day 6 to 14 value, respectively) Scenarios for confirming non-case (as well cases cases) are mutually exclusive, hence why only one of the scenarios needs to be met (along with not meeting criteria for a case)			

--

25.6 ACUTE KIDNEY INJURY DAY 1 TO 14

Derived variable name		Criteria	Descriptor
aki_d1to14	Considered a case, coded as 1, when any of the criteria boxes are met	aki_d1to5 is 1	AKI is detected from baseline (day 1) to day 1 to 5
		aki_d6to14 is 1	AKI is detected from baseline or day 1 to 5 to day 6 to 14
	Considered not a case, coded as 0, when both criteria for case are not met and either criteria for non-case are met	aki_d1to5 is 0 and (aki_d6to14 is 0 or missing)	AKI is confirmed not a case when day 1 to 5 window is not a case and day 6 to 14 window is not a case or missing, or vice versa. This is because clinically if it is not picked up by one, it is very unlikely to be picked up by the other, in addition many labs do not report out GGT
		(aki_d1to5 is 0 is missing) and aki_d6to14 is 0	
	Considered missing, value left blank, when values are missing and do not allow for calculation	aki_d1to5 is missing and aki_d6to14 is missing	AKI cannot be confirmed either way due to missingness
aki_d1to14_satge	Considered not a case, coded as 0, has been confirmed not a case	aki_d1to14 is 0	Not case of AKI by binary derivation
	Stage is max stage found across, aki_d1to5_stage and aki_d6to14_stage	aki_d1to5_stage	Maximum stage found across all time window comparisons
		aki_d6to14_stage	
Notes: AKI is detected ‘within 14 days’, where count starts from day 1 (and not day 1 plus 14 days)			

25.7 ACUTE KIDNEY INJURY – COMPOSITE DAY 1 TO 90

Below is a composite variable, also taking cases from the Serious Adverse Reaction (SAR) log (i.e. log that is kept when a SAR is reported only, SAR log does not collect information in the absence of an SAR).

Variable	Label/ title	Data export / CRF
medra_term_llt	MedDRA term (LLT)	SNAP_SARLog_[date]
medra_code_llt	MedDRA code (LLT)	SNAP_SARLog_[date]
Notes: LLT = Lowest Level Terms PT = Preferred Term		

		Criteria	Descriptor
--	--	----------	------------

aki_d1to90_compi site	Considered a case, coded as 1, when any of the criteria boxes are met	aki_d1to14 is 1 or medra_term_llt is “acute kidney injury” or medra_term_llt is “stage 1 acute kidney injury” or medra_term_llt is “stage 2 acute kidney injury” or medra_term_llt is “stage 3 acute kidney injury” or medra_code is “10069339” or medra code is “10080266” or medra code is “10080269” or medra code is “10080271”	AKI is a case when any source determines is a case
	Considered not a case, coded as 0, when all the criteria for case are not met and any of the non-case criteria boxes are met	aki_d1to14 is 0 (medra_term_llt is no “acute kidney injury” or medra_term_llt is not “stage 1 acute kidney injury” or medra_term_llt is not “stage 2 acute kidney injury” or medra_term_llt is not “stage 3 acute kidney injury”) and (medra_code is not “10069339” or medra code is not “10080266” or medra code is not “10080269” or medra code is not “10080271”) or no entry in SAR Log	AKI is confirmed not a case when all sources determine not a case
	Considered missing, value left blank, when values are missing and do not allow for calculation	aki_d1to14 is missing	Unable to be calculated due to missingness

Notes:

medra_term_llt & associated medra_code_llt should always match, however both applied in case of typo
 medra_term_llt can contain upper and lower case, e.g either “Acute Kidney Injury” and “acute kidney injury” should be considered a case and coded as 1

aki_d1to90 currently does not capture full scope of possible derivations from database (creatinine is collected at later timepoints, but not currently included in derivation). aki_d1to90 reflects AKI derived from day 1 to day 14 available values in the database, with the SAR log which captures SARs from day 1 to day 90.

26 RENAL REPLACEMENT THERAPY (DOMAIN-SPECIFIC ESTIMAND A1.3)

Receipt of renal replacement therapy (RRT) between Platform day 1 and Platform day 90.

Derived variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
rrt_d1to90	Where response in acute discharge and day 90 match, assign the matching value (e.g. if both 'Yes' assign 'Yes'),	adis_requirerrt_priordischarge	Did the participant require RRT any time prior to acute discharge	
	Where there is no observation in acute discharge, use value recorded at day 90,	d90_requirerrt_priord90	Did the participant require RRT any time in the 90 days following platform entry	
Notes: - Asked for those not ESKD at baseline				

27 ONGOING RENAL REPLACEMENT THERAPY AT PLATFORM DAY 90 (DOMAIN-SPECIFIC ESTIMAND A1.4)

Notes – as above because it uses derived rrt_d1to90== “No” then, rrt_postd90 = “No” – means ‘No’s include where participant may not have reached d90. ‘Yes’ only ever asked when d1to90 is ‘yes’

28 ACUTE LIVER INJURY (HEPATOTOXICITY) (DOMAIN-SPECIFIC ESTIMAND A1.5)

ALI (Heptatoxicity) is considered a case when baseline value is within the range of normal (i.e less than or equal to ULN) and the follow up value is greater than 2.5 times the ULN or baseline value is above ULN (greater than ULN) and the follow up value is 2.5 times the baseline value or baseline value is missing and follow up value reaches 5 times ULN (greater than or equal to 5 times ULN).

ALI (Heptatoxicity) uses values of ALT and GGT. Where a value is reported as 0, usually this indicates a value of <1 reported by the lab and entered into the database as 0, hence values of 0 are allowable.

28.1 BASELINE ALT

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
baseline_alt	Where value is available in d1to7_btpd1highalt, use that,	d1to7_btpd1highalt	Highest ALT	Day 1 to 7
	otherwise if d1to7_btpd1highalt missing	adis_pssaormssa_highalt	Highest ALT from platform day 1 to acute discharge	Acute Discharge
	and value is available in	adis_pssaormssa_highalt_date	Highest ALT date	Acute Discharge

adis_pssaormssa_highalt collected on study day 1, use that, otherwise if adis_pssaormssa_highalt missing and value is available in adis_pssaormssa_latestalt collected on study day 1, use that, otherwise if adis_pssaormssa_highalt missing and value is available in tdis_pssaormssa_highalt collected on study day 1, use that, otherwise if tdis_pssaormssa_highalt missing and value is available in tdis_pssaormssa_latestalt collected on study day 1, use that, otherwise leave baseline as missing	adis_pssaormssa_highalt	platform_entry_date_local	derived variable: platform entry date	Derived variable: original value from Participants enrolled export
	adis_pssaormssa_highalt	adis_pssaormssa_latestalt	Most recent ALT from platform day 1 to acute discharge	Acute Discharge
	adis_pssaormssa_highalt	adis_pssaormssa_latestalt_date	Most recent ALT date	Acute Discharge
	adis_pssaormssa_highalt	tdis_pssaormssa_highalt	Highest value from acute discharge [date of adis] until total hospital discharge	Total Discharge
	adis_pssaormssa_highalt	tdis_pssaormssa_highalt_date	Date of highest recorded result	Total Discharge
	adis_pssaormssa_highalt	tdis_pssaormssa_latestalt	Most recent test result from acute discharge until total hospital discharge	Total Discharge
	adis_pssaormssa_highalt	tdis_pssaormssa_latestalt_date	Date of most recent result from acute discharge until total hospital discharge	Total Discharge
Notes: Latest value should not be higher than highest value within the same CRF, data quality checks are run to ensure this is not the case, however during interim reporting quality updates may not have yet been applied				

28.2 BASELINE GGT

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Derived Variable name	Derived Variable logic descriptor	Derived Variable name
baseline_ggt	Where value is available in d1to7_btpd1highggt, use that,	d1to7_btpd1highggt	Highest GGT	Day 1 to 7
	otherwise, if d1to7_btpd1highggt missing and value is available in adis_pssaormssa_highggt collected on study day 1, use that,	adis_pssaormssa_highggt	Highest value from platform day 1 [date] until hospital discharge	Acute Discharge
	otherwise, if adis_pssaormssa_highggt is missing and value is available in adis_pssaormssa_latestggt collected on study day 1, use that,	adis_pssaormssa_highggt_date	Highest GGT date	Acute Discharge
	otherwise, if adis_pssaormssa_latestggt is missing and value is available	platform_entry_date_local	Derived variable: platform entry date	Derived variable: original value from Participants enrolled export
		adis_pssaormssa_latestggt	Most recent GGT	Acute Discharge

in tdis_pssaormssa_highggt collected on study day 1, use that, otherwise, if tdis_pssaormssa_highggt is missing and value is available in tdis_pssaormssa_latestggt collected on study day 1, use that, otherwise leave baseline as missing	adis_pssaormssa_latestggt_date	Most recent GGT date	Acute Discharge
	tdis_pssaormssa_highggt	Highest value from acute discharge <insert date of adis> until total hospital discharge	Total Discharge
	tdis_pssaormssa_highggt_date	Date of highest recorded result	Total Discharge
	platform_entry_date_local	Derived variable: platform entry date	Derived variable: original value from Participants enrolled export
	tdis_pssaormssa_latestggt	Most recent test result, prior to total hospital discharge	Total Discharge
Notes: Latest value should not be higher than highest value within the same CRF, data quality checks are run to ensure this is not the case, however during interim reporting quality updates may not have yet been applied			

28.3 ALT DAY 1 TO 5 FROM ACUTE AND TOTAL DISCHARGE

Derived variables to capture any ALT values within first 14 study days in acute discharge and total discharge CRFs.

- Corresponding dates of ALT and GGT variables are the date of which the measure was taken (and not data entry date)
- Dates used below are both local to the site

Acute Discharge				
Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ Descriptor	Data export / CRF
adis_highest_alt_d1to5	If n of study days between Highest ALT date and platform entry date (considered day 1) is less than or equal to 5 days, then use adis_pssaormssa_highalt , otherwise leave missing	adis_pssaormssa_highalt	Highest ALT from platform day 1 to acute discharge	Acute Discharge
		adis_pssaormssa_highalt_date	Highest ALT date	Acute Discharge
		platform_entry_date_local	derived variable: platform entry date	Derived variable: original value from Participants enrolled export
adis_latest_alt_d1to5	If n of study days between most recent ALT date and platform entry date (considered day 1) is less than or equal to 5 days, use adis_pssaormssa_latestalt, otherwise leave missing	adis_pssaormssa_latestalt	Most recent ALT	Acute Discharge
		adis_pssaormssa_latestalt_date	Most recent ALT date	Acute Discharge
		platform_entry_date_local	Derived variable: platform entry date	Derived variable: original value from Participants enrolled export

Total Discharge	
Derived variable	Variables and raw data

Derived Variable name	Derived Variable logic descriptor	Variable	Label/ Descriptor	Data export / CRF
tdis_highest_alt_d1to5	If n of study days between Highest ALT date and platform entry date is less than or equal to 5 days, then use tdis_pssaormssa_highalt, otherwise leave missing	tdis_pssaormssa_highalt	Highest value from acute discharge [date of adis] until total hospital discharge	Total Discharge
		tdis_pssaormssa_highalt_date	Date of highest recorded result	Total Discharge
		platform_entry_date_local	Derived variable: platform entry date	Derived variable: original value from Participants enrolled export
tdis_latest_alt_d1to5	If n of study days between most recent ALT date and platform entry date is less than or equal to 5 days, then use tdis_pssaormssa_latestalt, otherwise leave missing	tdis_pssaormssa_latestalt	Most recent test result from acute discharge until total hospital discharge	Total Discharge
		tdis_pssaormssa_latestalt_date	Date of most recent result from acute discharge until total hospital discharge	Total Discharge
		platform_entry_date_local	Derived variable: platform entry date	Derived variable: original value from Participants enrolled export

28.4 ALT DAY 6 TO 14 FROM ACUTE AND TOTAL DISCHARGE

Acute Discharge				
Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ Descriptor	Data export / CRF
adis_highest_alt_d6to14	If n of study days between Highest ALT date and platform entry date (considered day 1) is between 6 and 14 days (inclusive), use adis_pssaormssa_highalt, otherwise leave missing	adis_pssaormssa_highalt	Highest ALT from platform day 1 to acute discharge	Acute Discharge
		adis_pssaormssa_highalt_date	Highest ALT date	Acute Discharge
		platform_entry_date_local	derived variable: platform entry date	Derived variable: original value from Participants enrolled export
adis_latest_alt_d6to14	If n of study days between most recent ALT date and platform entry date (considered day 1 is between 6 and 14 days (inclusive), use adis_pssaormssa_latestalt, otherwise leave missing	adis_pssaormssa_latestalt	Most recent ALT	Acute Discharge
		adis_pssaormssa_latestalt_date	Most recent ALT date	Acute Discharge
		platform_entry_date_local	Derived variable: platform entry date	Derived variable: original value from Participants enrolled export

Total Discharge				
Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ Descriptor	Data export / CRF
tdis_highest_alt_d6to14	If n of study days between Highest ALT date and platform entry date is	tdis_pssaormssa_highalt	Highest value from acute discharge [date of adis] until	Total Discharge

	between 6 and 14 days (inclusive), then use tdis_pssaormssa_highalt, otherwise leave missing		total hospital discharge	
		tdis_pssaormssa_highalt_date	Date of highest recorded result	Total Discharge
		platform_entry_date_local	Derived variable: platform entry date	Derived variable: original value from Participants enrolled export
tdis_latest_alt_d6to14	If n of study days between most recent ALT date and platform entry date is between 6 and 14 days (inclusive), use tdis_pssaormssa_latestalt, otherwise leave missing	tdis_pssaormssa_latestalt	Most recent test result from acute discharge until total hospital discharge	Total Discharge
		tdis_pssaormssa_latestalt_date	Date of most recent result from acute discharge until total hospital discharge	Total Discharge
		platform_entry_date_local	Derived variable: platform entry date	Derived variable: original value from Participants enrolled export
tdis_highest_alt_d14	If n of study days between highest d14 date and platform entry is between 6 and 14 days (inclusive), then use tdis_pssaormssa_highaltd14_enteredvalue, otherwise leave missing	tdis_pssaormssa_highaltd14_enteredvalue	Highest value from acute discharge [date of adis] and platform day 14 (inclusive) [date of platform day 14]	Total Discharge
		tdis_pssaormssa_highaltd14_date	Date of highest recorded result	Total Discharge
		platform_entry_date_local	Derived variable: platform entry date	Derived variable: original value from Participants enrolled export

28.5 GGT DAY 1 TO 5 FROM ACUTE AND TOTAL DISCHARGE

Acute Discharge				
Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title in form (as per data descriptor)	Data export / CRF
adis_highest_ggt_d1to5	If n of study days between Highest GGT date and platform entry date is less than or equal to 5 days, then use adis_pssaormssa_highggt, otherwise leave missing	adis_pssaormssa_highggt	Highest value from platform day 1 [date] until hospital discharge	Acute Discharge
		adis_pssaormssa_highggt_date	Highest GGT date	Acute Discharge
		platform_entry_date_local	Derived variable: platform entry date	Derived variable: original value from Participants enrolled export
adis_latest_ggt_d1to5	If n of study days between Highest GGT date and platform entry date is less than or equal to 5 days, then use adis_pssaormssa_latestggt, otherwise leave missing	adis_pssaormssa_latestggt	Most recent GGT	Acute Discharge
		adis_pssaormssa_latestggt_date	Most recent GGT date	Acute Discharge
		platform_entry_date_local	Derived variable: platform entry date	Derived variable: original value from Participants enrolled export

Total Discharge

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title in form (as per data descriptor)	Data export / CRF
tdis_highest_ggt_d1to5	If n of study days between Highest GGT date and platform entry date is less than or equal to 5 days, then use tdis_pssaormssa_highggt, otherwise leave missing	tdis_pssaormssa_highggt	Highest value from acute discharge <insert date of adis> until total hospital discharge	Total Discharge
		tdis_pssaormssa_highggt_date	Date of highest recorded result	Total Discharge
		platform_entry_date_local	Derived variable: platform entry date	Derived variable: original value from Participants enrolled export
tdis_latest_ggt_d1to5	If n of study days between latest GGT date and platform entry date is less than or equal to 5 days, then use tdis_pssaormssa_latestggt, otherwise leave missing	tdis_pssaormssa_latestggt	Most recent test result, prior to total hospital discharge	Total Discharge
		tdis_pssaormssa_latestggt_date	Date of most recent result prior to total hospital discharge	Total Discharge
		platform_entry_date_local	Derived variable: platform entry date	Derived variable: original value from Participants enrolled export
tdis_highest_ggt_d5	If n of study days between Highest GGT date and platform entry date is less than or equal to 5 days, then use tdis_pssaormssa_highggt_d14_enteredvalue, otherwise leave missing	tdis_pssaormssa_highggt_d14_enteredvalue	Highest value from acute discharge <insert date of adis> and platform day 14 (inclusive) [date of platform day 14]	Total Discharge
		tdis_pssaormssa_highggt_d14_date	Date of highest recorded result	Total Discharge
		platform_entry_date_local	Derived variable: platform entry date	Derived variable: original value from Participants enrolled export

28.6 GGT DAY 6 TO 14 FROM ACUTE AND TOTAL DISCHARGE

Acute Discharge				
Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title in form (as per data descriptor)	Data export / CRF
adis_highest_ggt_d6to14	If n of study days between Highest GGT date and platform entry date is between 6 and 14 days (inclusive), then use adis_pssaormssa_highggt, otherwise leave missing	adis_pssaormssa_highggt	Highest value from platform day 1 [date] until hospital discharge	Acute Discharge
		adis_pssaormssa_highggt_date	Highest GGT date	Acute Discharge
		platform_entry_date_local	Derived variable: platform entry date	Derived variable: original value from Participants enrolled export
adis_latest_gtt_d6to14	If n of study days between Highest GGT date and platform entry date is between 6 and 14 days (inclusive), then use adis_pssaormssa_lates tgggt, otherwise leave missing	adis_pssaormssa_latestggt	Most recent GGT	Acute Discharge
		adis_pssaormssa_latestggt_date	Most recent GGT date	Acute Discharge
		platform_entry_date_local	Derived variable: platform entry date	Derived variable: original value from Participants enrolled export
Total Discharge				

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title in form (as per data descriptor)	Data export / CRF
tdis_highest_ggt_d6to14	If n of study days between Highest GGT date and platform entry date is between 6 and 14 days (inclusive), then use tdis_pssaormssa_highggt, otherwise leave missing	tdis_pssaormssa_highggt	Highest value from acute discharge <insert date of adis> until total hospital discharge	Total Discharge
		tdis_pssaormssa_highggt_date	Date of highest recorded result	Total Discharge
		platform_entry_date_local	Derived variable: platform entry date	Derived variable: original value from Participants enrolled export
tdis_latest_ggt_d6to14	If n of study days between latest GGT date and platform entry date is between 6 and 14 days (inclusive), then use tdis_pssaormssa_latestggt, otherwise leave missing	tdis_pssaormssa_latestggt	Most recent test result, prior to total hospital discharge	Total Discharge
		tdis_pssaormssa_latestggt_date	Date of most recent result prior to total hospital discharge	Total Discharge
		platform_entry_date_local	Derived variable: platform entry date	Derived variable: original value from Participants enrolled export
tdis_highest_ggt_d14	If n of study days between Highest GGT date and platform entry date is between 6 and 14 days (inclusive), then use tdis_pssaormssa_highggt_d14_enteredvalue, otherwise leave missing	tdis_pssaormssa_highggt_d14_enteredvalue	Highest value from acute discharge <insert date of adis> and platform day 14 (inclusive) [date of platform day 14]	Total Discharge
		tdis_pssaormssa_highggt_d14_date	Date of highest recorded result	Total Discharge
		platform_entry_date_local	Derived variable: platform entry date	Derived variable: original value from Participants enrolled export

28.7 ALT & GGT DAY 1 TO 5 FROM ALL SOURCES

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title in form (as per data descriptor)	Data export / CRF
max_alt_d1to5	highest value of variables	d1to7_pssaormssa_pd1to5highalt	PSSA or MSSA Highest ALT day 1 to 5	Day 1 to 7
		adis_highest_alt_d1to5	Derived variable	Derived variable – value from Acute Discharge
		adis_latest_alt_d1to5	Derived variable	Derived variable – value from Acute Discharge
		tdis_highest_alt_d1to5	Derived variable	Derived variable – value from Total Discharge
		tdis_latest_alt_d1to5	Derived variable	Derived variable – value from Total Discharge
max_ggt_d1to5	highest value of variables	d1to7_pssaormssa_pd1to7highggt	PSSA or MSSA Highest GGT day 1 to 5	Day 1 to 7
		adis_highest_ggt_d1to5	Derived variable	Derived variable – value from Acute Discharge
		adis_latest_ggt_d1to5	Derived variable	Derived variable – value from Acute Discharge

		tdis_highest_ggt_d1to5	Derived variable	Derived variable – value from Total Discharge
		tdis_latest_ggt_d1to5	Derived variable	Derived variable – value from Total Discharge
Notes: d1to7_pssaormssa_pd1to5highalt, was previously called d1to7_pssa_pd1to5highalt d1to7_pssaormssa_pd1to7highggt, variable naming convention suggests value considers day 1 to 7, however question text and value if for platform day 1 to 5				

28.8 ALT & GGT DAY 6 TO 14 FROM ALL SOURCES

Day 14 values, found on day 8 to 14 CRF have allowance of +/- 3 days, hence follow up period may not strictly adhere to platform day 1 to 14.

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title in form (as per data descriptor)	Data export / CRF
max_alt_d6to14	Highest of values	d14_pssaormssa_pd6to14highalt	Highest ALT from platform Day 6 to platform Day 14 inclusive	Day 8 to 14
		d14_pssaormssa_pd14highalt	Highest ALT on platform Day 14	Day 8 to 14
		adis_highest_alt_d6to14	Derived variable	Derived variable – value from Acute Discharge
		adis_latest_alt_d6to14	Derived variable	Derived variable – value from Acute Discharge
		tdis_highest_alt_d6to14	Derived variable	Derived variable – value from Total Discharge
		tdis_latest_alt_d6to14	Derived variable	Derived variable – value from Total Discharge
		tdis_highest_alt_d14	Derived variable	Derived variable – value from Total Discharge

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Derived Variable name	Derived Variable logic descriptor	Data export / CRF
max_ggt_d6to14	Highest of values	d14_pssaormssa_pd6to14highggt	Highest GGT from platform Day 6 to platform Day 14 inclusive	Day 8 to 14
		d14_pssaormssa_pd14highggt	Highest GGT on platform Day 14	Day 8 to 14
		adis_highest_ggt_d6to14	Derived variable	Derived variable – value from Acute Discharge
		adis_latest_gtt_d6to14	Derived variable	Derived variable – value from Acute Discharge
		tdis_highest_ggt_d6to14	Derived variable	Derived variable – value from Total Discharge
		tdis_latest_ggt_d6to14	Derived variable	Derived variable – value from Total Discharge
		tdis_highest_ggt_d14	Derived variable	Derived variable – value from Total Discharge
Notes: d14_pssaormssa_pd14highalt and d14_pssaormssa_pd6to14highggt notes “If day 14 result is not available, record highest level between days 11 to 17 inclusive”, hence follow up period may not strictly adhere to platform day 1 to 14.				

28.9 CALCULATION OF ALI FROM ALT

ALI from ALT measures are calculated by comparing baseline and follow up values against an Upper Limit of Normal (ULN), 2.5 times the (2.5*ULN) and 5 times the ULN (5*ULN).

Upper Limit of Normal (ULN) for ALT is stratified by sex at birth as ULN is lower in females, compared to males.

Where sex at birth is male:

- ULN is defined as 30
- 2.5 times the ULN is 75
- 5 times the ULN is 150

Where sex at birth is female:

- ULN is defined as 19
- 2.5 times the ULN is 47.5
- 5 times the ULN is 95

		Criteria	Descriptor
ali_alt_d1to5	Considered a case, coded as 1, when any of the criteria boxes are met	baseline_alt less than or equal to ULN and max_alt_d1to5 is greater than or equal to 2.5*ULN	Baseline is equal to or below ULN and follow up is greater than 2.5 times ULN
		baseline_alt greater than ULN and max_alt_d1to5 divided by baseline_alt is equal to or greater than 2.5	Baseline is above ULN and follow up is 2.5 times or more than baseline
		baseline_alt missing and max_alt_d1to5 equal to or greater than or equal to 5*ULN	Baseline is not available and follow up is equal to or greater than or 5 times ULN
	Considered not a case, coded as 0, when all the criteria for case are not met and any of the non-case criteria boxes are met	baseline_alt less than or equal to ULN and max_alt_d1to5 less than 2.5*ULN	Baseline is equal to or below ULN and follow up is less than 2.5 times ULN
		baseline_alt is greater than ULN and max_alt_d1to5 divided by baseline_alt is less than 2.5	Baseline is above ULN and follow up is less than 2.5 times baseline
		baseline_alt is missing and max_alt_d1to5 less than 5*ULN	Baseline is missing and follow up is less than 5 times ULN
	Considered missing, value left blank, when values are missing and do not allow for the calculation	baseline_alt and max_alt_d1to5 are missing	Unable to be calculated due to missingness
Notes: Scenarios for confirming non-case (as well cases cases) are mutually exclusive, hence why only one of the scenarios needs to be met (along with not meeting criteria for a case)			

Day 6 to 14 calculation considers difference between baseline (day 1) to day 6 to 14 window, as well as difference between day 1 to 5 window to day 6 to 14 window. ‘Baseline’ in descriptor column below refers to first comparator time point (either baseline or day 1 to 5 window) and follow up refers to day 6 to 14 window.

		Criteria	Descriptor
ali_alt_d6to14	Considered a case, coded as 1, when any of the criteria boxes are met	baseline_alt less than or equal to ULN and max_alt_d6to14 greater than or equal to 2.5*ULN	Baseline is equal to or below ULN and follow up is greater than 2.5 times ULN
		max_alt_d1to5 less than or equal to ULN and max_alt_d6to14 greater than or equal to 2.5*ULN	
		baseline_alt greater than ULN and max_alt_d6to14 divided by baseline_alt is equal to or greater than 2.5	Baseline is above ULN and follow up is 2.5 times or more than baseline
		max_alt_d1to5 greater than ULN and max_alt_d6to14 divided by baseline_alt is equal to or greater than 2.5	
		baseline_alt missing and max_alt_d6to14 equal to or greater than or equal to 5*ULN	Baseline is not available and follow up is greater than or equal to 5 times ULN
	Considered not a case, coded as 0, when all the criteria for case are not met and non-case criteria boxes are met for all comparisons between time points (i.e baseline to d1to5, baseline to d6to14 and d1to5 to d6to14 scenarios confirm non case)	baseline_alt less than or equal to ULN and max_alt_d6to14 less than 2.5*ULN	Baseline is or below ULN and follow up is less than 2.5 times ULN
		max_alt_d1to5 less than or equal to ULN and max_alt_d6to14 less than 2.5*ULN	
		baseline_alt is greater than ULN and max_alt_d6to14 divided by baseline_alt is less than 2.5	Baseline is above ULN and follow up is less than 2.5 times baseline (or day 1 to 5)
		max_alt_d1to5 is greater than ULN and max_alt_d6to14 divided by baseline_alt is less than 2.5	
		baseline_alt is missing and max_alt_d6to14 less than 5*ULN	Baseline is missing and follow up is less than 5 times ULN
		max_alt_d1to5 is missing and max_alt_d6to14 less than 5*UL	
	Considered missing, value left blank, when values are missing and do not allow for the calculation	baseline_alt and/or max_alt_d1to5 and/or max_alt_d6to14 are not available to calculate above criteria	Unable to be calculated due to missingness
Notes:			

Missing is simply 'left as missing' (i.e. where values do not allow for outcome of 1 or 0, leave as missing) no explicit code run to code for missing

Baseline refers to time 1 (can be baseline or day 1 to 5 value) relative to time to 2 (day 1 to 5 value or day 6 to 14 value, respectively)

_d6to14 suffix on this variable does not follow convention, it is not representative of the time period observed, rather it reflects the time window of the last follow up window

28.10 CALCULATION OF ALI FROM GGT

ALI from GGT measures are calculated by comparing baseline and follow up values against an Upper Limit of Normal (ULN), 2.5 times the (2.5*ULN) and 5 times the ULN (5*ULN).

ULN for GGT is stratified by sex at birth as ULN is lower in females, compared to males.

Where sex at birth is male:

- ULN is defined as 60
- 2.5 times the ULN is 150
- 5 times the ULN is 300

Where sex at birth is female:

- ULN is defined as 40
- 2.5 times the ULN is 100
- 5 times the ULN is 200

		Criteria	Descriptor
ali_ggt_d1to5	Considered a case, coded as 1, when any of the criteria boxes are met	baseline_ggt less than or equal to ULN and max_ggt_d1to5 is greater than or equal to ULN*2.5	Baseline is equal to or below ULN and follow up is greater than 2.5 times ULN
		baseline_ggt is greater than ULN and max_ggt_d1to5 divided by baseline_ggt is equal to or greater than 2.5	Baseline is above ULN and follow up is 2.5 times or more than baseline
		baseline_ggt is missing and max_ggt_d1to5 is greater than or equal to 5*ULN	Baseline is missing and follow up is greater than or equal to 5 times ULN
	Considered not a case, coded as 0, when all the criteria for case are not met and any of the non-case criteria boxes are met	baseline_ggt less than or equal to ULN and max_ggt_d1to5 is less than 2.5*ULN	Baseline is equal to or below ULN and follow up is less than 2.5 times ULN
		baseline_ggt is greater than ULN and max_ggt_d1to5 divided by baseline_ggt is less than 2.5	Baseline is above ULN and follow up is less than 2.5 times baseline

		baseline_ggt is missing and max_ggt_d1to5 is less than 5*ULN	Baseline is missing and follow up is less than 5 times ULN
	Considered missing, value left blank, when values are missing and do not allow for the calculation	baseline_ggt and/or max_ggt_d1to5 and/or are not available to calculate above criteria	Unable to be calculated due to missingness
Notes: Scenarios for confirming non-case (as well cases cases) are mutually exclusive, hence why only one of the scenarios needs to be met (along with not meeting criteria for a case)			

Day 6 to 14 calculation considers difference between baseline (day 1) to day 6 to 14 window, as well as difference between day 1 to 5 window to day 6 to 14 window. ‘Baseline’ in descriptor column below refers to first comparator time point (either baseline or day 1 to 5 window) and follow up refers to day 6 to 14 window.

		Criteria	Descriptor
ali_ggt_d6to14	Considered a case, coded as 1, when any of the criteria boxes are met	baseline_ggt less than or equal to ULN and max_ggt_d6to14 is greater than or equal to 2.5*ULN	Baseline is equal to or below ULN and follow up is greater than 2.5 times ULN
		max_ggt_d1to5 less than or equal to ULN and max_ggt_d6to14 is greater than or equal to 2.5*ULN	
		baseline_ggt is greater than ULN and max_ggt_d6to14 divided by baseline_ggt is equal to or greater than 2.5	Baseline is above ULN and follow up is 2.5 times or more than baseline
		max_ggt_d1to5 is greater than ULN and max_ggt_d6to14 divided by baseline_ggt is equal to or greater than 2.5	
		baseline_ggt is missing and max_ggt_d6to14 is greater than or equal to 5*ULN	Baseline is missing and follow up is greater than or equal to 5 times ULN
		max_ggt_d1to5 is missing and max_ggt_d6to14 is greater than or equal to 5*ULN	
	Considered not a case, coded as 0, when all the criteria for case are not met and non-case criteria boxes are met for all comparisons between time points (i.e baseline to d1to5, baseline to d6to14 and d1to5 to d6to14 scenarios confirm non case)	baseline_ggt less than or equal to ULN and max_ggt_d6to14 is less than 2.5*ULN	Baseline is or below ULN and follow up is less than 2.5 times ULN
		max_ggt_d1to5 less than or equal to ULN and max_ggt_d6to14 is less than 2.5*ULN	
		baseline_ggt is greater than ULN and max_ggt_d6to14 divided by baseline_ggt is less than 2.5	Baseline is above ULN and follow up is less than 2.5 times baseline
		max_ggt_d1to5 is greater than ULN and max_ggt_d6to14 divided by baseline_ggt is less than 2.5	
		baseline_ggt is missing and max_ggt_d6to14 is less than 5*ULN	Baseline is missing and follow up is less than 5 times ULN

		max_ggt_d1to5 is missing and max_ggt_d6to14 is less than 5*ULN	
	Considered missing, value left blank, when values are missing and do not allow for the calculation	baseline_ggt and/or max_ggt_d1to5 and/or max_ggt_d6to14 and/or are not available to calculate above criteria	Unable to be calculated due to missingness
Notes: Missing is simply 'left as missing' (i.e. where values do not allow for outcome of 1 or 0, leave as missing) no explicit code run to code for missing _d6to14 suffix on this variable does not follow convention, it is not representative of the time period observed, rather it reflects the time window of the last follow up window			

28.11 DERIVED ALI

ALI considering both ALT and GGT

		Criteria	Descriptor
ali_d1to5	Considered a case, coded as 1, when either of the criteria boxes for case are met	ali_alt_d1to5 is 1	ALI is detected be either ALT or GGT measurements
		ali_ggt_d1to5 is 1	
	Considered not a case, coded as 0 when both criteria boxes for case are not met, and either of the criteria for non-case are met	ali_alt_d1to5 is 0 and (ali_ggt_d1to5 is 0 or missing)	ALI is confirmed not a case when ALI from ALT is confirmed not a case and ALI from GGT is either confirmed not a case or missing, or vice versa.
		(ali_alt_d1to5 is 0 or missing) and ali_ggt_d1to5 is 0	
		Considered missing, value left blank, when missing values do not allow clear indication of case or not case	ali_alt_d1to5 is missing and ali_ggt_d1to5 is missing
	Notes:		

		Criteria	Descriptor
ali_d6to14	Considered a case, coded as 1, when either of the criteria boxes for case are met	ali_alt_d6to14 is 1	ALI is detected be either ALT or GGT measurements
		ali_ggt_d6to14is 1	
	Considered not a case, coded as 0 when both criteria boxes for case are not met, and either of the criteria for non-case are met	ali_alt_d6to14 is 0 and ali_ggt_d6to14 is 0 or missing	ALI is confirmed not a case when ALI from ALT is confirmed not a case and ALI from GGT is either confirmed not a case or missing, or vice versa. This is because clinically if it is not picked up by one, it is very unlikely to be picked up by the other, in addition many labs do not report out GGT
		ali_alt_d6to14is 0 or missing and ali_ggt_d6to14 is 0	

	Considered missing, value left blank, when missing values do not allow clear indication of case or not case	ali_alt_d6to14 is missing and ali_ggt_d6to14 is missing	ALI cannot be confirmed due to missingness
Notes: _d6to14 suffix on this variable does not follow convention, it is not representative of the time period observed, rather it reflects the time window of the last follow up window			

		Criteria	Descriptor
ali_d1to14	Considered a case, coded as 1, when either of the criteria boxes for case are met	ali_d1to5 is 1	ALI is detected during day 1 to 5 window or 6 to 14 window
		ali_d6to14 is 1	
	Considered not a case, coded as 0 when both criteria boxes for case are not met, and either of the criteria for non-case are met	ali_d1to5 is 0 and ali_d6to14 is 0 or missing	ALI is confirmed not a case when day 1 to 5 window is not a case and day 6 to 14 is not a case or missing, or vice versa.
		ali_d1to5 is 0 or missing and ali_d6to14 is 0	This is because clinically if it is not picked up by one, it is very unlikely to be picked up by the other, in addition many labs do not report out GGT
	Considered missing, value left blank, when missing values do not allow clear indication of case or not case	ali_d1to5 is missing and ali_d6to14 is missing	ALI cannot be confirmed due to missingness
Notes: In the case participant has died before day 8 (when day 1 to 7 CRF usually opens), day 1 to 7 CRF opens to be completed where baseline and some follow up ALT & GGT values are collected, and additionally death is recorded in acute discharge which also collects ALT & GGT values. In the case where participant dies between day 8 and 14 (inclusive; i.e where day 8 to 14 CRF opens on day 15), day 8 to 14 CRF opens to be completed where baseline and some follow up ALT & GGT values are collected, and additionally death is recorded in acute discharge which also collects ALT & GGT values. In the case participant withdraws before day 8, unless an acute discharge form has been completed, no data will be available for ALT & GGT baseline or follow up values (baseline and some follow up are collected on day 1 to 7 CRF which opens on day 8). In the case participant withdraws between day 8 and 14 (inclusive; i.e where day 8 to 14 CRF opens on day 15), day 1 to 7 CRF would have been available for completion where baseline and some follow up values are collected for ALT & GGT. In the case participant has an acute or total discharge before day 8 (when day 1 to 7 CRF usually opens), day 1 to 7 CRF opens to be completed where baseline and some follow up ALT & GGT values are collected, and additionally ALT & GGT values are collected in acute and total discharge. In the case participant has an acute or total discharge before day 8 and 14, (inclusive; i.e where day 8 to 14 CRF opens on day 15), day 8 to 14 CRF opens to be completed where baseline and some follow up ALT & GGT values are collected, and additionally ALT & GGT values are collected in acute and total discharge.			

Missingness may be due to:

- ALT or GGT measurements not being done, where this is the case, the original variable will have a value “n/a” (this will not be the case for derived values).
- Measurements not taken due to silo in which participant is enrolled in
- Measurements not entered due to variable not available due to protocol participant was enrolled under
- Participant withdrew before data was collected on ALT and GGT values in relevant CRFs

29 SERIOUS ADVERSE REACTION

Serious Adverse Reactions (SARs) are currently collected in a log outside of the database. SARs will be collected in the database (and data retrospectively entered) once the database SAR CRF build is complete. Hence, in the transitional time derived SAR will use the SAR log. The current derivation will not consider values within the database. SARs are reported in the database as a binary yes/no, thereafter an additional two additional questions (both yes/no) are asked to confirm it is a true SAR. Only after both review questions are answered with ‘Yes’, then is the event truly considered an SAR. At time of this first document publication, a data base bug has been noted, where exports are not as expected, and hence derivation via database fields will not be valid.

29.1 SAR ANY DAY 1 TO 90

Derived variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
sar_any_d1to90	Where sar is “Yes”, code as 1, indicating an SAR has occurred, Otherwise code as 0, indicating no SAR has been reported	sar	SAR	SAR log
Notes: SAR log does not collect information in the absence of an SAR sar_any_d1to90 indicates any SAR occurred, where multiple SARs exist for 1 participant sar_any_d1to90 should still be 1, indicating at least 1 SAR occurred				

30 CHANGE IN ASSIGNED TREATMENT (BACKBONE MSSA/PSSA)

Change in assigned treatment broadly refers to an unplanned change in randomised backbone domain assigned treatment.

For those enrolled into backbone domain in PSSA or MSSA silo, time window of interest is platform entry (i.e day 1) until day 90 or hospital index ends, whichever occurs first.

For those enrolled into backbone domain in MRSA silo, time window of interest is platform entry (i.e day 1) until day 7 or hospital index ends, whichever occurs first.

For those enrolled into the EOS domain, time window of interest is platform entry (i.e day 1) until day 28 or hospital index ends, whichever occurs first.

30.1 ASKED QUESTION – CHANGE IN ASSIGNED TREATMENT

Change in assigned treatment is asked in various CRFs. The participant’s hospital journey (i.e. whether acute or total discharged or patient died) and silo (PSSA/ MSSA/ MRSA) dictates were change in assigned treatment question is asked and captured or if asked at all (i.e. question does not need to be asked if no longer in

hospital index or variable is not asked for domain participant is in). Hence, indicator variables are created to capture whether data is truly missing.

The logic applied to indicator variables indicates where the question should have been asked and where the value would be expected to be pulled from. Due to oversights in the database design or updates, some scenarios exist where the question is asked where it is not needed (e.g. d14_pssaormssa_assignedantibiochange asked, when d1to7_pssaormssa_assignedantibiochange has been answered as “Yes”) or should have been asked but was not (e.g. when acute discharged to subsequent acute care hospital and remains in acute care for entire study duration or when acute discharge warrants Total Discharge to be complete and total discharge does not occur during study period, day 90 CRF should display ‘was there a change...’ question, but does not).

Where question was asked, but was not needed, this data is not used. In the example above, if change occurred and captured in day 1 to 7, a subsequent question again asking ‘was there a change...’ can be interpreted in various ways (e.g. was there an additional change, was there a change to new treatment schedule applied, was there a change to the original treatment schedule and respond yes even if it has already occurred). Additionally, change in assigned treatment is a singular end point related to randomised treatment (either change from randomised treatment occurs or does not).

Where question was not asked (due to oversights in database design or update) and is needed, all efforts have been made with collecting datapoints at time of v1 publication of this document.

30.1.1 DAY 1 TO 7 CRF - ‘WAS THERE A CHANGE IN ASSIGNED BACKBONE ANTIBIOTIC FROM PLATFORM DAYS 1-7’

Variable: d1to7_pssaormssa_assignedantibiochange

Derived variable				
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
asked_d1to7_pssaormssa_assignedantibiochange	If - backbone_domain is 1 and - silo is “MSSA” or “PSSA” than 1, otherwise 0	backbone_domain	Derived variable	Derived variable – original value from Backbone Eligibility
		silo	Derived variable	Derived variable – original value from Backbone Eligibility or Day 1 to 7
Notes: Even in cases where event (acute or total discharge, patient dies) question is always asked as CRF will open on event (even when on day 1). Where the patient withdraws (wd_withdrawalall or wd_contactfollowups) before day 7, the day 1 to 7 CRF will remain locked and question is not available to answer.				

30.1.2 DAY 8 TO 14 CRF - ‘WAS THERE A CHANGE IN ASSIGNED BACKBONE ANTIBIOTIC FROM PLATFORM DAYS 8-14’

Variable: d14_pssaormssa_assignedantibiochange

Derived variable				
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
asked_d14_pssaormssa_assignedantibiochange	Where - backbone_domain is 1 and - silo is (“MSSA” or “PSSA”) and - crf_d8to14_required is 1 and - d1to7_pssaormssa_assignedantibiochange is “No” or missing (i.e not “Yes”; change has not already occurred) then code as 1, indicating question is shown, otherwise, code as 0, indicating question not shown under circumstances where it would not be expected/ required	backbone_domain	Derived variable	Derived variable – original value from Backbone Eligibility
		silo	Derived variable	Derived variable – original value from Backbone Eligibility or Day 1 to 7
		tdis_dischargedate	Date of discharge from total index hospitalisation (Discharge from a non-acute bed)	Total discharge
		d90_dod	Date of death	Day 90
		platform_entry_date_local	Derived variable	Derived variable – original value from Participants enrolled export
Notes: d14_pssaormssa_assignedantibiochange does not contain differences based on protocol version number				

30.1.3 ACUTE DISCHARGE CRF - 'WAS THERE A CHANGE IN ASSIGNED BACKBONE ANTIBIOTIC FROM PLATFORM DAY 15 <DATE> TO ACUTE DISCHARGE?'

Variable: adis_pssaormssa_anyantibiotic

This variable is specific to those in the PSSA / MSSA silo, under the backbone domain and asked when acute discharge occurs on day 15 or later.

Where an acute discharge occurs on day 1 to 7 and patient is still in hospital index, where ‘Was there a change..’ question is still expected, this is captured in day 1 to 7 CRF (CRF opens on event) and later in the Total Discharge CRF that covers from acute discharge date to Total Discharge date (i.e total hospital index).

Where an acute discharge occurs on day 8 to 14 and patient is still in hospital index, where ‘Was there a change..’ question is still expected, this is captured in day 1 to 7 CRF (opens automatically on day 8), day 8 to 14 CRF (opens on event) and in Total Discharge CRF that covers from acute discharge date to Total Discharge date (i.e total hospital index).

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
asked_adis_pssaormssa_anyantibiotic	Where - backbone_domain is 1 and - silos (“MSSA” or “PSSA”) and - daydiff_platform_entry_adis_transfer_date is equal to or greater than 15 days and - d1to7_pssaormssa_assignedantibiochange is “No” or missing (i.e not “Yes”; change has not already occurred days 1 to 7) and - d14_pssaormssa_assignedantibiochange is “No” or missing (i.e not “Yes”; change has not already occurred days 8 to 14) then code as 1, indicating question is shown, otherwise, code as 0, indicating question not shown under circumstances where it would not be expected/ required	backbone_domain	Derived variable	Derived variable – original value from Backbone eligibility
		silos	Derived variable	Derived variable – original value from Backbone Eligibility or Day 1 to 7
		daydiff_platform_entry_adis_transfer_date	Derived variable	Derived variable – original value from Acute Discharge
		d1to7_vitalstatus	Vital status at Day 7	Day 1 to 7
		d14_vitalstatus	Vital status at Day 14	Day 8 to 14
		Notes: daydiff_platform_entry_adis_transfer_date criteria will remove where acute discharge form is not filled out (ie not needed) as these will contain missing values and therefore will not meet criteria and hence be coded as 0 adis_pssaormssa_anyantibiotic is also only asked where d1to7_vitalstatus & d14_vitalstatus is “Alive” or “Unknown”, not when missing or “Died”. This however is handled by data cleaning checks. Where patient dies in days 1 to 14, this is also captured in acute discharge form, and change question will not be shown as daydiff_platform_entry_adis_transfer_date will be less than 15 days. Data claning checks ensure no data entry issues, as it is possible for data entered to be a mismatch between day 1 to 7 and day 8 to 14 crfs, vital status and date of death.		

30.1.4 TOTAL DISCHARGE CRF - 'WAS THERE A CHANGE IN ASSIGNED BACKBONE ANTIBIOTIC FROM ACUTE DISCHARGE <DATE> TO TOTAL HOSPITAL DISCHARGE <DATE>'

Variable: tdis_pssaormssa_assignedantibioticchange

This variable is specific to those in the PSSA / MSSA silo, under the backbone domain and asked when acute discharge warrants a Total Discharge CRF to be completed (see derived variable crf_tdis_required above for cases in which Total Discharge CRF is required).

This variable captures change in assigned backbone treatment from acute discharge to total discharge (i.e. total hospital index). Prior to acute discharge, change is captured in the Day 1 to 7 CRF. If acute discharge occurs on day 8 or later is change is captured additionally in the day 8 to 14 CRF (opens on event if acute discharge is day 8 to 14 or automatically opens day 15 onwards). If acute discharge occurs on day 15 or later, change is captured additionally in the Acute Discharge CRF. Hence total hospital index is covered in the event of an acute discharge that warrants a total discharge.

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
asked_tdis_pssaormssa_assignedantibiotic change	Where, - backbone_domain is 1 and - silo is (“MSSA” or “PSSA”) and - crf_tdis_required is 1 and - d1to7_pssaormssa_assignedantibiotic change is “No” or missing (i.e not “Yes”; change has not already occurred days 1 to 7) and - d14_pssaormssa_assignedantibiotic change is “No” or missing (i.e not “Yes”; change has not already occurred days 8 to 14) and - adis_pssaormssa_anyantibiotic is “No” or missing (i.e not “Yes”; change has not already occurred in days 15 to acute discharge day) then code as 1, indicating question is shown, otherwise, code as 0, indicating question not shown under circumstances where it would not be expected/ required	backbone_domain	Derived variable	Derived variable – original value from Backbone eligibility
		silo	Derived variable	Derived variable – original value from Backbone Eligibility or Day 1 to 7
		crf_tdis_required	Derived variable	Derived variable
		d1to7_pssaormssa_assignedantibiotic change	Was there a change in assigned backbone antibiotic from platform Days 1-7	Day 1 to 7
		d14_pssaormssa_assignedantibiotic change	Was there a change in assigned backbone antibiotic from platform Days 8-14	Day 8 to 14
		adis_pssaormssa_anyantibiotic	Was there a change in assigned backbone antibiotic from platform Day 15 <insert date> to acute discharge	Acute Discharge
		Notes: Day difference between entry and total discharge date does not matter, even when on platform day 1 question will show		

30.1.5 DAY 90 CRF – ‘WAS THERE A CHANGE IN ASSIGNED BACKBONE ANTIBIOTIC FROM PLATFORM DAY 15 TO PLATFORM DAY 90’

Variable: d90_pssaormssa_assignedantibioticchange

This variable should be asked to those in the backbone domain under the PSSA or MSSA silo for patients who have reached day 90, have not been reported as dead, and still in hospital index (total index hospitalisation) at day 90.

In hospital index (total index hospitalisation) at day 90 means the participant:

- has not died during the study period
- has not been acute discharge home during study period
- total discharge has not occurred during the study period

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
asked_d90_pssaormssa_assignedantibioticchange	Where - backbone_domain is 1 and - silos is (“MSSA” or “PSSA”) and - daydiff_platform_entry_data_download is equal to or greater than 90 days and - end_acute_hospital_index is 0 (i.e. still hospital index) or tdis_dischargeduring90days is "No - Close form" and - d1to7_pssaormssa_assignedantibiochange is “No” or missing (i.e not “Yes”; change has not already occurred days 1 to 7) and - d14_pssaormssa_assignedantibiochange is “No” or missing (i.e not “Yes”; change has not already occurred days 8 to 14) and - adis_pssaormssa_anyantibiotic is “No” or missing (i.e not “Yes”; change has not already occurred in days 15 to acute discharge day) and - tdis_pssaormssa_assignedantibioticchange is “No” or missing (i.e not “Yes”; change has not already occurred in days 15 to acute discharge day) then code as 1, indicating question is shown, otherwise, code as 0, indicating question not shown under circumstances where it would not be expected/ required	backbone_domain	Derived variable	Derived variable – original value from Backbone eligibility
		silos	Derived variable	Derived variable – original value from Backbone Eligibility or Day 1 to 7
		daydiff_platform_entry_data_download	Derived variable	Derived variable
		end_hospital_index	Derived variable	Derived variable
		d1to7_pssaormssa_assignedantibiochange	Was there a change in assigned backbone antibiotic from platform Days 1-7	Day 1 to 7
		d14_pssaormssa_assignedantibiochange	Was there a change in assigned backbone antibiotic from platform Days 8-14	Day 8 to 14
		adis_pssaormssa_anyantibiotic	Was there a change in assigned backbone antibiotic from platform Day 15 <insert date> to acute discharge	Acute Discharge
		tdis_pssaormssa_assignedantibioticchange	Was there a change in assigned backbone antibiotic from acute discharge <insert date> to total hospital discharge <insert date>	Total Discharge
Notes: tdis_dischargedate used as proxy to indicate patient was not totally discharged before reached day 90 d90_dod is empty used as proxy to indicated patient was alive at day 90, day_dod if filled when dod is recored elsewhere in the database				

30.2 CHANGE IN ASSIGNED BACKBONE TREATMENT – DAY 1 TO 90

This variable captures change in assigned backbone treatment for the entire study period, or in the case where a patient event occurs (e.g. discharged home), the total hospital index.

Notes:

Some missingness may occur due to oversights in the database design or update where question was not asked and should have; see intro text above in section beginning ‘Asked question – Change in assigned treatment’ for details on when question expected.

Currently this variable only captures change in assigned backbone treatment for those in the MSSA/ PSSA silo. MRSA silo will be added. Due to time demands with publishing this document as an associate document with the SAP for the MSSA and PSSA silos in the backbone domain, those domains were prioritised.

Variables used, not already specified

Variable	Label/ title	Data export / CRF
d1to7_pssaormssa_assignedantibiochange	Was there a change in assigned backbone antibiotic from platform Days 1-7	Day 1 to 7
d14_pssaormssa_assignedantibiochange	Was there a change in assigned backbone antibiotic from platform Days 8-14	Day 8 to 14
adis_pssaormssa_anyantibiotic	Was there a change in assigned backbone antibiotic from platform Day 15 [date] to acute discharge	Acute Discharge
adis_pssaormssa_anyantibiotic_reasonwhy	Reason why	Acute Discharge
tdis_pssaormssa_assignedantibioticchange	Was there a change in assigned backbone antibiotic from acute discharge [date] to total hospital discharge [date]	Total Discharge
tdis_pssaormssa_assignedantibioticchange why	Reason why	Total Discharge
d90_pssaormssa_assignedantibioticchange	Was there a change in assigned backbone antibiotic from platform Day 15 [date] to platform Day 90 [date]	Day 90
d90_pssaormssa_assignedantibioticchange why	Reason why	Day 90

Derived Variable name	Derived Variable logic descriptor	Criteria	Descriptor
change_assigned_treatment_backbone_d1to90	Considered a case, coded as 1, when any of the criteria boxes are met	asked_d1to7_pssaormssa_assignedantibiochange is 1 and d1to7_pssaormssa_assignedantibiochange is “Yes”	Change in backbone treatment is reported as “Yes” at any timepoint
		asked_d14_pssaormssa_assignedantibiochange is 1 and d14_pssaormssa_assignedantibiochange is “Yes”	
		asked_adis_pssaormssa_anyantibiotic is 1 and adis_pssaormssa_anyantibiotic is “Yes”	
		asked_tdis_pssaormssa_assignedantibioticchange is 1 and tdis_pssaormssa_assignedantibioticchange is “Yes”	
		asked_d90_pssaormssa_assignedantibioticchange is 1 and d90_pssaormssa_assignedantibioticchange is “Yes”	
	Considered not a case, coded as 0, when all the criteria for case are not met and all non-case criteria boxes are met	asked_d1to7_pssaormssa_assignedantibiochange is 0 or d1to7_pssaormssa_assignedantibiochange is “No”	Change in backbone treatment is reported as “No” in all time points where question was expected (see intro text above in section beginning ‘Asked question – Change in assigned treatment’)
		asked_d14_pssaormssa_assignedantibiochange is 0 or d14_pssaormssa_assignedantibiochange is “No”	
		asked_adis_pssaormssa_anyantibiotic is 0 or adis_pssaormssa_anyantibiotic is “No”	
		asked_tdis_pssaormssa_assignedantibioticchange is 0 or tdis_pssaormssa_assignedantibioticchange is “No”	
		asked_d90_pssaormssa_assignedantibioticchange is 0 or d90_pssaormssa_assignedantibioticchange is “No”	

	Considered missing, value left blank, when values are missing and do not allow for calculation	asked_d1to7_pssaormssa_assignedantibiochange is 1 and d1to7_pssaormssa_assignedantibiochange is missing or asked_d14_pssaormssa_assignedantibiochange is 1 and d14_pssaormssa_assignedantibiochange is missing or asked_adis_pssaormssa_anyantibiotic is 1 and adis_pssaormssa_anyantibiotic is missing or asked_tdis_pssaormssa_assignedantibioticchange is 1 and tdis_pssaormssa_assignedantibioticchange is missing or asked_d90_pssaormssa_assignedantibioticchange is 1 and d90_pssaormssa_assignedantibioticchange is missing	Change in backbone treatment is missing in any of the time points where question was expected and therefore cannot confirm whether change occurred or not (see intro text above in section beginning ‘Asked question – Change in assigned treatment’ for details on when question expected)
Notes:			

30.3 REASON CHANGE IN ASSIGNED BACKBONE TREATMENT – DAY 1 TO 90

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
reason change_assigned_treatment_backbone_d1to90	Where asked_d1to7_pssaormssa_assignedantibioticchange is 1 and d1to7_pssaormssa_assignedantibioticchange is “Yes”, then use value in d1to7_pssaormssa_assignedantibioticchangewhy, Otherwise, where asked_d14_pssaormssa_assignedantibioticchange is 1 and d14_pssaormssa_assignedantibioticchange is “Yes”, then use value in d14_pssaormssa_assignedantibioticchangewhy, Otherwise, where asked_adis_pssaormssa_anyantibiotic is 1 and adis_pssaormssa_anyantibiotic is “Yes”, then use value in adis_pssaormssa_anyantibiotic_reasonwhy, Otherwise, where asked_tdis_pssaormssa_assignedantibioticchange is 1 and tdis_pssaormssa_assignedantibioticchange is “Yes”, use value in tdis_pssaormssa_assignedantibioticchangewhy, Otherwise, where asked_d90_pssaormssa_assignedantibioticchange is 1 and d90_pssaormssa_assignedantibioticchange is “Yes”, use value in d90_pssaormssa_assignedantibioticchangewhy, Otherwise leave missing indicating either no change had occurred or change reason is missing	asked_d1to7_pssaormssa_assignedantibioticchange	Derived Variable	Derived Variable
		d1to7_pssaormssa_assignedantibioticchange	Was there a change in assigned backbone antibiotic from platform Days 1-7	Day 1 to 7
		d1to7_pssaormssa_assignedantibioticchangewhy	Reason why	Day 1 to 7
		asked_d14_pssaormssa_assignedantibioticchange	Derived Variable	Derived Variable
		d14_pssaormssa_assignedantibioticchange	Was there a change in assigned backbone antibiotic from platform Days 8-14	Day 8 to 14
		d14_pssaormssa_assignedantibioticchangewhy	Reason why	Day 8 to 14
		asked_adis_pssaormssa_anyantibiotic	Derived Variable	Derived Variable
		adis_pssaormssa_anyantibiotic	Was there a change in assigned backbone antibiotic from platform Day 15 <insert date> to acute discharge	Acute Discharge
		adis_pssaormssa_anyantibiotic_reasonwhy	Reason why	Acute Discharge
		asked_tdis_pssaormssa_assignedantibioticchange	Derived Variable	Derived Variable
		tdis_pssaormssa_assignedantibioticchange	Was there a change in assigned backbone antibiotic from acute discharge <insert date> to total hospital discharge <insert date>	Total Discharge
		tdis_pssaormssa_assignedantibioticchangewhy	Reason why	Total Discharge
		asked_d90_pssaormssa_assignedantibioticchange	Derived Variable	Derived Variable

		d90_pssaormssa_assignedantibioticchange	Was there a change in assigned backbone antibiotic from platform Day 15 <insert date> to platform Day 90 <insert date>	Day 90
		d90_pssaormssa_assignedantibioticchange why	Reason why	Day 90
Notes:				

31
PERIPHERALLY INSERTED CENTRAL CATHETER (PICC)/OTHER CENTRAL VENOUS CATHETER COMPLICATIONS REQUIRING LINE REMOVAL (DOMAIN-SPECIFIC ESTIMAND A1.8)

Peripherally inserted central catheter (PICC)/other central venous catheter complications requiring line removal during the total index hospitalisation

Derived variable		Variables and Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
picc_total_hosp_index				
Notes:				

32
SAR RELATED TO BACKBONE-DOMAIN

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
sar_assigned_treatment_backbone	Where an SAR is logged, that is related to backbone treatment and association is definitely, probably or possibly, assign 1 (has experienced at least 1 SAR related to assigned backbone treatment), else assign 0 (no evidence to indicate had SAR related to backbone, presumed not to have experienced)	which_protocol_treatment	Which protocol treatment	SAR log
		association_with_protocol_treatment	Association with protocol treatment	SAR log
Notes:				

33
PROTOCOL ADHERENT ADJUNCTIVE DOMAIN

Derived variable		Variables and Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
adjunctive_randomised_treatment_adherent	Where participant is enrolled into adjunctive domain, calculate n of non-missing doses.	adj_domain	Derived variable	
		d1to7_adj_ivclindamycindoses		Day 1 to 7
		d1to7_adj_oralclindamycindoses		Day 1 to 7
		d1to7_adj_lincomycindoses		Day 1 to 7
		d1to7_adj_linezolidoses		Day 1 to 7
		d1to7_adj_twoormoredosesnoadjdom		
	Where randomised to receive Adjunctive Clindamycin and total does is 10 or more, assign 1 (is treatment adherent), else where randomised to receive Adjunctive Clindamycin and total does is less than 10, assign 0 (not treatment adherent), Where randomised to receive No Adjunctive Clindamycin and d1to7_adj_twoormoredosesnoadjdom is No, assign 1 (adherent did not receive more than 2 does), else where randomised to receive No Adjunctive Clindamycin and d1to7_adj_twoormoredosesnoadjdom is Yes, assign 0 (not treatment adherent)	adj_randomised_treatment	Derived variable	Derived variable
adj_treatment_observable_7_days	Where participant died before day 7, day 7 vital status is unknown, withdrew before day 7 or went to another acute care provider where clinical data unavailable before day 7, then assign 0 (not observable for 7 days), else assign 1 (no evidence to indicate not observable, presumed to be observable for 7 days)	daydiff_platform_entry_dod		Derived variable
		vitalstatus_d1to7		Derived variable
		daydiff_platform_entry_wd_data_collection_end_date		Derived variable
		adis_dischargedto		Acute Discharge
		adis_clinicaldatasubsequentacuteprovider		Acute Discharge
		daydiff_platform_entry_adis_crf_data		Derived variable
pd_not_eligible_adj	Where a protocol deviation is logged and type of deviation is "Randomisation (into the core platform or a domain) of ineligible participant" and is related to Adjunctive domain, then assign 1 (indicates randomised into adjunctive but evidence after randomisation indicated that this participant was ineligible)	pd_typeofdeviation		
protocol_adherent_adjunctive	Where evidence indicates participant was not enrolled when ineligible and are observable for 7 days and are adj treatment adherent and silo is not misclassified, then assign 1 are protocol adherent, else assign 0 (lack of evidence to confirm adherence, presumed to be non-adherent to protocol)	pd_domain_related		
		pd_not_eligible_platform		
		pd_not_eligible_adj		
		adj_treatment_observable_7_days		
		adjunctive_randomised_treatment_adherent		
		silo_misclassification		
Notes: Where type of deviation is "Randomisation (into the core platform or a domain) of ineligible participant" and is related to core, this distinguishes whether randomisation with later evidence indicating participant was ineligible was for the core or domain. Domain related is not mutually exclusive can be both. Recommendation for protocol_adherent_adjunctive to be set to 'NA' when not in adjunctive domain, to avoid potential confusion and misuse				

Adjunctive protocol adherent =

- Silo not misclassified
- Not randomised when should not have been
 - pd_not_eligible_platform – should be with backbone as orig

- pd_not_eligible_adj
- Observable for 7 days
- Treatment adherent

34 ALL-CAUSE DIARRHOEA DOMAIN REVEAL TO DAY 14 (DOMAIN-SPECIFIC ESTIMAND B.2)

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
diarrhoea_d1 to14	Where d1to7_adj_diarrhoea or d14_adj_diarhoea is Yes, assign 1, Where both d1to7_adj_diarrhoea and d14_adj_diarhoea are No, assign 0	d1to7_adj_diarrhoea	Did the participant have diarrhoea any time from platform Day 1 <Insert date of Day 1> to Day 7 <Insert date of Day 7> inclusive	Day 1 to 7
		d14_adj_diarhoea	Did the participant have diarrhoea any time from platform Day 8 to Day 14 (inclusive)	Day 8 to 14
diarrhoea_d1 to7	Where d1to7_adj_diarrhoea is Yes, assign 1, Where d1to7_adj_diarrhoea is No, assign 0	d1to7_adj_diarrhoea	Did the participant have diarrhoea any time from platform Day 1 <Insert date of Day 1> to Day 7 <Insert date of Day 7> inclusive	Day 1 to 7
		d14_adj_diarhoea	Did the participant have diarrhoea any time from platform Day 8 to Day 14 (inclusive)	Day 8 to 14
diarrhoea_d1 to14_estimated	Where died whilst in acute care on or before day 7, use value in diarrhoea_d1to7, Where died in acute care on or after day 8, use value in value in diarrhoea_d1to14 Where acute discharge data date is less than or equal to 7, use value in diarrhoea_d1to7, else if acute discharge data date is day 8 or later, use value in value in diarrhoea_d1to14, Where did not leave acute care during study 90 days, use value in diarrhoea_d1to14, Where withdrew on or before 7 days, use value diarrhoea_d1to7, else if withdrew day 8 or later, use diarrhoea_d1to14	end_acute_hospital_index_alive	Derived Variable	Derived Variable
		daydiff_platform_entry_dod	Derived Variable	Derived Variable
		daydiff_platform_entry_adis_crf_data_date	Derived Variable	Derived Variable
		withdrew_during_acute_hospital_index	Derived Variable	Derived Variable
		daydiff_platform_entry_wd_data_collection_end_date	Derived Variable	Derived Variable
		diarrhoea_d1to7	Derived Variable	Derived Variable
		diarrhoea_d1to14	Derived Variable	Derived Variable
Notes:				

35 CHANGE IN C-REACTIVE PROTEIN (CRP) (DOMAIN-SPECIFIC ESTIMAND B.3)

Change in C-Reactive Protein (CRP) from platform day 1 until day 5 (+/-1 day).

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
crp_difference_d1to5	Day 5 value minus day 1 value	d1to7_adj_d5highcrp_as_mgl	Highest CRP day 1	Day 1 to 7
		d1to7_bt看pd1highcrp_as_mgl	Highest CRP day 5	Day 1 to 7
Notes: Impossible values should be cleaned out, i.e where died or withdrew before day 4 (day 4 as day 5 measurement has allowance of plus or minus 1 day)				

36 PERSISTENT BACTERAEMIA AT DAY 5 (DOMAIN-SPECIFIC ESTIMAND B.4)

Persistent bacteraemia at

- Does have allowance +/-1

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
blood_culture_d2	Where indicates a positive result (MSSA, PSSA, MRSA or Susceptibility not tested), assign value "Positive",	d1to7_pd2bloodculturecollected	Did the participant have a blood culture collected on Platform Day 2 <date of platform entry +1> +/- 1 day	
	Where d1to7_pd2bloodculturecollected is No, assigned value "Blood Culture not collected", Else leave as value in result (will be missing or "No growth of S. aureus")	d1to7_pd2bloodcultureresult	Result	
blood_culture_d5	Where indicates a positive result (MSSA, PSSA, MRSA or Susceptibility not tested), assign value "Positive",	d1to7_pd5bloodcultureresult	Did the participant have a blood culture collected on Platform Day 5 <date of platform entry +5> +/- 1 day	
	Where d1to7_pd2bloodculturecollected is No, assigned value "Blood Culture not collected", Else leave as value in result (will be missing or No growth of S. aureus)	d1to7_pd5bloodcultureresult	Result	
persistent_bacteraemia_d5	Where blood culture d5 indicates positive, assign value 1, where blood culture d5 indicates No growth of S. aureus, assign 0,	blood_culture_d2	Derived variable	
	Where blood culture d5 is not collected on missing (no value available) and blood culture on day 2 is No growth of S. aureus, assign 0, Else leave as missing	blood_culture_d5	Derived variable	
Notes: Impossible values should be cleaned out, i.e where died or withdrew before day 4 (day 4 as day 5 measurement has allowance of plus or minus 1 day)				

37 SIRS CRITERIA SIMULTANEOUSLY ON DAY 5 (DOMAIN-SPECIFIC ESTIMAND B.5)

- day 5 does not have an allowance of +/- 1 day unlike many other measured outcomes.
- Data entry rules if go home

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
sirs_d5	Where participant died before day 5, went to subsequent acute care provider where clinical data unavailable or withdrew before day 5, assigned value NA (missing, excluded as per SAP), Where participant was discharged home on or before day 5, assign value 0 (follows data entry rules), Where SIRS response is Yes, assign 1 (met 2 or more SIRS criteria), else where SIRS response is No, assign 0 (did not meet 2 or more SIRS criteria)	d1to7_sirscriteria	Did the participant satisfy 2 or more SIRS criteria at any single time point during calendar day 5 <insert date of Day 5>	Day 1 to 7
		daydiff_platform_entry_dod	Derived Variable	
		adis_dischargedto	Derived Variable	Acute Discharge
		adis_clinicaldata subsequentacuteprovider	Derived Variable	Acute Discharge
		daydiff_platform_entry_adis_crf_data_date	Derived Variable	
		daydiff_platform_entry_wd_data_collection_end_date	Derived Variable	
		end_total_hospital_index_alive	Derived Variable	
		daydiff_platform_entry_end_total_hospital_index_alive	Derived Variable	
Notes: Impossible values should be cleaned out, i.e where died or withdrew before day 4 (day 4 as day 5 measurement has allowance of plus or minus 1 day)				

38 SAR RELATED TO ADJUNCTIVE DOMAIN (DOMAIN-SPECIFIC ESTIMAND B.7)

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
sar_assigned_treatment_adj_d1to90	Where an SAR is logged, that is related to adjunctive treatment and association is definitely, probably or possibly, assign 1 (has experienced at least 1 SAR related to assigned adjunctive treatment), else assign 0 (no evidence to indicate had SAR related to adjunctive, presumed not to have experienced)	which_protocol_treatment		SAR log
		association_with_protocol_treatment		
Notes:				

39 DESIRABILITY OF OUTCOME RANKING CATEGORY (DOOR1) – ADJUNCTIVE (DOMAIN-SPECIFIC ESTIMAND B.8)

Desirability Of Outcome Ranking category Modified Antibacterial Resistance Leadership Group (ARLG) version is also referred to as DOOR 1. DOOR 1 excludes ranking by the modified FBIS score (quality of life) as detailed in SAP (all versions). DOOR1 for Adjunctive domain is modified, collapsing new focus of infection from day 15 to day 90 and SAR related to the adjunctive domain. This is due to nature of study arms for adjunctive domain (adjunctive treatment and no adjunctive treatment) where SARs are only observable in the treatment arm. Therefore, the ranking for DOOR2 adjunctive is 1, 2, 3 or 4, where:

- 4 = not alive at 90 days
- 3 = alive and 2/2 (micro treatment failure, infectious complication/SAR)
- 2 = alive and 1/2 (micro treatment failure, infectious complication/SAR)
- 1 = alive and 0/2 (micro treatment failure, infectious complication/SAR)

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
door_arlg_adj_infectious_complication_or_sar	Where either of new_foi_d15tod90 or sar_assigned_treatment_adj are 1, then assign 1,	new_foi_d15tod90	Derived variable	
	Else if both new_foi_d15tod90 and sar_assigned_treatment_adj are 0, than 0,	sar_assigned_treatment_adj	Derived variable	
	Else leave as missing			
door_arlg_adj	Where vitalstatus_d1to90 is “Dead”, assign rank 4, else sum across alive_at_90_days, micro_treatment_failure_d15to90, door_arlg_adj_infectious_complication_or_sar for ranking. Where any components are missing, leave as missing.	vitalstatus_d1to90	Derived variable	
		alive_at_90_days	Derived variable	
		micro_treatment_failure_d15to90	Derived variable	
		door_arlg_adj_infectious_complication_or_sar	Derived variable	
Notes:				

40 DESIRABILITY OF OUTCOME RANKING CATEGORY (DOOR2) SNAP VERSION – ADJUNCTIVE (DOMAIN-SPECIFIC ESTIMAND B.9)

Desirability Of Outcome Ranking SNAP version is also referred to as DOOR 2. DOOR 2 excludes ranking by hospital length of index admission as detailed in SAP (all versions).

Derived variable		Variables and raw data		
Derived Variable name	Derived Variable logic descriptor	Variable	Label/ title	Data export / CRF
door_snap_adj_sar_safety_outcome	Where any of SAR or safety outcomes is 1, assign 1, where all are 0, assign 0, else leave as missing (i.e cases where combination of 0 and NA)	sar_assigned_treatment_adj_d1to90	Derived variable	
		aki_d1to90_composite	Derived variable	
		rrt_d1to90	Derived variable	
		rrt_postd90	Derived variable	
		cdiff_d1to90_composite	Derived variable	
door_snap_adj	Where vital status at 90 days is Dead, assign 5,	vitalstatus_d1to90	Derived variable	
	Where alive and did return to usual level of function and no SAR or safety outcome is not met, assign 1,	fbis_return_d90	Derived variable	
	Where alive and did return to usual level of function and SAR or safety outcome is met, assign 2,	door_snap_adj_sar_safety_outcome	Derived variable	
	Where alive and did not return to usual level of function and SAR or safety outcome is not met, assign 3,			
	Where alive and did not return to usual level of function and SAR or safety outcome is met, assign 4,			
	Where rank cannot be calculated due to missing, leave as missing			
Notes:				