NOTTINGHAM CLINICAL TRIALS UNIT

PROTECT-CH

Prophylactic Therapy in Care Homes Trial

Final analysis dummy tables
Final version 1.0
08-Oct-2021
Based on protocol version v2.0 (Date 01 Jul 2021)

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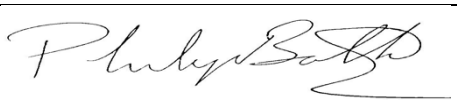
Approval

Name	Job title	Trial Role	Signature	Date
Philip Bath	Professor of Stroke Medicine	Chief Investigator		20/10/2021
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Amendments to versions

Version	Date	Change/comment	Statistician

1 Summary of Recruitment and Analysis Sets

1.1 Participant flow

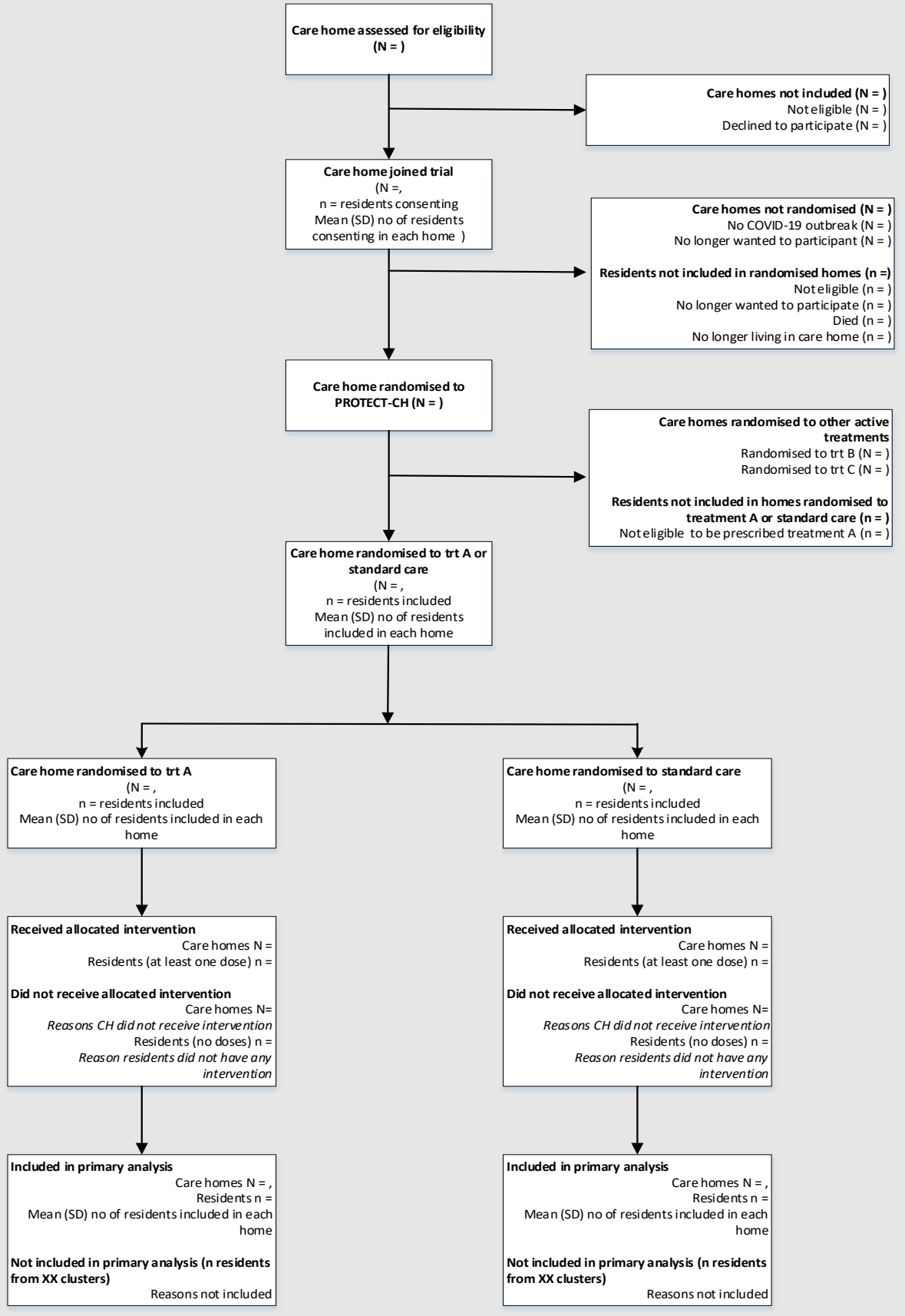

Figure 1: Participant flow diagram

1.2 Trial recruitment and analysis sets

Table 1: Number of care homes randomised in each group (contemporaneously randomised)

	Standard Care	Intervention A	Intervention B	Intervention C	Total
Care homes randomised	N = …	N = …	N = …	N = …	N = …

Table 2: Number of care homes and residents randomised in comparison of Intervention XX and Standard care

	Standard Care	Intervention Group	Total
Care homes randomised	N = …	N = …	N = …
Residents consenting (prior to randomisation)	n =	n =	n =
Residents included at point of randomisation	n = …	n = …	n = …
Residents excluded	n = …	n = …	n = …
Not eligible	(n = …)	(n = …)	(n = …)
No longer wishes to take part	(n = …)	(n = …)	(n = …)
Died prior to care home randomisation	(n = …)	(n = …)	(n = …)
No longer living in care home at randomisation	(n = …)	(n = …)	(n = …)

Table 3: Analysis set definitions per comparison

Analysis set	Definition	Standard Care Group	Intervention Group	Total
Care homes randomised concurrently		N =	N =	N =
Number of residents included		n =	n =	n =
Primary	Residents eligible for the intervention prior to care home randomisation analysed according to the group their care home was randomly allocated.	n =	n =	n =
Supplementary	All residents with consent regardless of whether eligible/took part in treatment phase of trial, analysed according to the group their care home was randomly allocated.	n =	n =	n =

Each intervention group compared with residents in the standard care group care homes randomised concurrently

2 Study data

2.1 Baseline characteristics of care homes

Table 4: Baseline characteristics of care homes per comparison (minimisation factors highlighted)

Characteristic	Standard Care (N = …)	Intervention Group (N = …)	Total (N=…)
Care home type			
Residential	xx (xx)	xx (xx)	xx (xx)
Mixed residential and nursing	xx (xx)	xx (xx)	xx (xx)
Nursing	xx (xx)	xx (xx)	xx (xx)
Prior COVID-19 in care home			
No	xx (xx)	xx (xx)	xx (xx)
Yes	xx (xx)	xx (xx)	xx (xx)
Size of Care Home (total number of residents in care home)			
Small (≤30 residents)	xx (xx)	xx (xx)	xx (xx)
Medium (>30 and ≤50 residents)	xx (xx)	xx (xx)	xx (xx)
Large (>50 residents)	xx (xx)	xx (xx)	xx (xx)
Mean[SD]	xx (xx)	xx (xx)	xx (xx)
Median [25th, 75th centile]	xx (xx to xx)	xx (xx to xx)	xx (xx to xx)
Min, max	xx to xx	xx to xx	xx to xx
Care home has the capacity to give oxygen			
No	xx (xx)	xx (xx)	xx (xx)
Yes	xx (xx)	xx (xx)	xx (xx)
Any residents in care home received vaccination against COVID-19			
No	xx (xx)	xx (xx)	xx (xx)
Yes	xx (xx)	xx (xx)	xx (xx)
Any staff in care home received vaccination against COVID-19			
No	xx (xx)	xx (xx)	xx (xx)
Yes	xx (xx)	xx (xx)	xx (xx)
Country			
England	xx (xx)	xx (xx)	xx (xx)
Wales	xx (xx)	xx (xx)	xx (xx)
Scotland	xx (xx)	xx (xx)	xx (xx)
Northern Ireland	xx (xx)	xx (xx)	xx (xx)
Care home ownership			
Council	xx (xx)	xx (xx)	xx (xx)
Commercial	xx (xx)	xx (xx)	xx (xx)
Charity	xx (xx)	xx (xx)	xx (xx)
Other	xx (xx)	xx (xx)	xx (xx)
Registered for clients with learning disabilities			
No	xx (xx)	xx (xx)	xx (xx)
Yes	xx (xx)	xx (xx)	xx (xx)
Care home maximum capacity			
Mean[SD]	xx (xx)	xx (xx)	xx (xx)
Median [25th, 75th centile]	xx (xx to xx)	xx (xx to xx)	xx (xx to xx)
Min, max	xx to xx	xx to xx	xx to xx
CQC rating (or equivalent in devolved nations)			
Outstanding	xx (xx)	xx (xx)	xx (xx)
Good	xx (xx)	xx (xx)	xx (xx)
Requires improvement	xx (xx)	xx (xx)	xx (xx)
PEP only:			
Index case of SARS-Cov-2 in:			
Resident	xx (xx)	xx (xx)	xx (xx)
Member of staff	xx (xx)	xx (xx)	xx (xx)
Lag between positive index test for COVID-19 (resident/member of staff) and care home randomisation (days)			
Median [25th, 75th centile]	xx (xx to xx)	xx (xx to xx)	xx (xx to xx)
Min, max	xx to xx	xx to xx	xx to xx
Also present in categories (tbc)			

Characteristic	Standard Care (N = …)	Intervention Group (N = …)	Total (N=…)
Continuous characteristic			
Mean[SD]	xx (xx)	xx (xx)	xx (xx)
Median [25th, 75th centile]	xx (xx to xx)	xx (xx to xx)	xx (xx to xx)
Min, max	xx to xx	xx to xx	xx to xx
Missing	xx	xx	xx
Binary characteristic			
No	xx (xx)	xx (xx)	xx (xx)
Yes	xx (xx)	xx (xx)	xx (xx)
Missing	xx	xx	xx
Categorical characteristic			
Level 1	xx (xx)	xx (xx)	xx (xx)
Level 2	xx (xx)	xx (xx)	xx (xx)
Level 3	xx (xx)	xx (xx)	xx (xx)
Level 4	xx (xx)	xx (xx)	xx (xx)
Level 5	xx (xx)	xx (xx)	xx (xx)
Missing	xx	xx	xx

All data are N (%) unless otherwise indicated.

2.2 Baseline characteristics of residents

Table 5: Baseline characteristics of residents per comparison

Characteristic	Standard Care (n = …)	Intervention Group (n = …)	Total (n=…)
Age at randomisation			
<80	xx (xx)	xx (xx)	xx (xx)
80-89	xx (xx)	xx (xx)	xx (xx)
≥90	xx (xx)	xx (xx)	xx (xx)
Mean[SD]	xx (xx)	xx (xx)	xx (xx)
Median [25th, 75th centile]	xx (xx to xx)	xx (xx to xx)	xx (xx to xx)
Min, max	xx to xx	xx to xx	xx to xx
Missing	xx	xx	xx
Sex			
Male	xx (xx)	xx (xx)	xx (xx)
Female	xx (xx)	xx (xx)	xx (xx)
Missing	xx	xx	xx
Ethnicity			
White (British, Irish, any other white background)	xx (xx)	xx (xx)	xx (xx)
Mixed (White and Black Caribbean, White and Black African, White and Asian, any other mixed background)	xx (xx)	xx (xx)	xx (xx)
Indian	xx (xx)	xx (xx)	xx (xx)
Pakistani	xx (xx)	xx (xx)	xx (xx)
Bangladeshi	xx (xx)	xx (xx)	xx (xx)
Chinese	xx (xx)	xx (xx)	xx (xx)
Black Caribbean	xx (xx)	xx (xx)	xx (xx)
Black African	xx (xx)	xx (xx)	xx (xx)
Other ethnic group	xx (xx)	xx (xx)	xx (xx)
Not stated	xx (xx)	xx (xx)	xx (xx)
Not known	xx (xx)	xx (xx)	xx (xx)
Advance directive for no hospitalisation			
No	xx (xx)	xx (xx)	xx (xx)
Yes	xx (xx)	xx (xx)	xx (xx)
Missing	xx	xx	xx
Do Not Attempt Resuscitation order			
No	xx (xx)	xx (xx)	xx (xx)
Yes	xx (xx)	xx (xx)	xx (xx)
Missing	xx	xx	xx
Weight (kg)			
Mean[SD]	xx (xx)	xx (xx)	xx (xx)
Median [25th, 75th centile]	xx (xx to xx)	xx (xx to xx)	xx (xx to xx)
Min, max	xx to xx	xx to xx	xx to xx
Missing	xx	xx	xx
Body Mass Index (kg/m²)			
Mean[SD]	xx (xx)	xx (xx)	xx (xx)
Median [25th, 75th centile]	xx (xx to xx)	xx (xx to xx)	xx (xx to xx)
Min, max	xx to xx	xx to xx	xx to xx
Missing	xx	xx	xx
Co-morbidities			
Diabetes	xx (xx)	xx (xx)	xx (xx)
Heart disease	xx (xx)	xx (xx)	xx (xx)
Chronic lung disease	xx (xx)	xx (xx)	xx (xx)
Severe liver disease	xx (xx)	xx (xx)	xx (xx)
Severe kidney impairment	xx (xx)	xx (xx)	xx (xx)
Dementia	xx (xx)	xx (xx)	xx (xx)
Stroke	xx (xx)	xx (xx)	xx (xx)
Missing	xx	xx	xx
Smoking status			
Current smoker	xx (xx)	xx (xx)	xx (xx)
Previous smoker	xx (xx)	xx (xx)	xx (xx)
Never smoked	xx (xx)	xx (xx)	xx (xx)
Missing	xx	xx	xx
Previous positive test for COVID-19			
No	xx (xx)	xx (xx)	xx (xx)

Characteristic	Standard Care (n = …)	Intervention Group (n = …)	Total (n=…)
Yes	xx (xx)	xx (xx)	xx (xx)
Missing	xx	xx	xx
PEP trials only: Positive test for COVID-19 at randomisation			
No	xx (xx)	xx (xx)	xx (xx)
Yes	xx (xx)	xx (xx)	xx (xx)
Missing	xx	xx	xx
Received vaccination for COVID-19			
No	xx (xx)	xx (xx)	xx (xx)
Yes	xx (xx)	xx (xx)	xx (xx)
Missing	xx	xx	xx
If vaccinated:			
Partially vaccinated	xx (xx)	xx (xx)	xx (xx)
Fully vaccinated	xx (xx)	xx (xx)	xx (xx)
Time in care home (months)			
Mean[SD]	xx (xx)	xx (xx)	xx (xx)
Median [25th, 75th centile]	xx (xx to xx)	xx (xx to xx)	xx (xx to xx)
Min, max	xx to xx	xx to xx	xx to xx
Missing	xx	xx	xx
Type of consent			
Consent by resident	xx (xx)	xx (xx)	xx (xx)
Proxy consent by personal legal representative	xx (xx)	xx (xx)	xx (xx)
Electronic frailty index (eFI)			
Mean[SD]	xx (xx)	xx (xx)	xx (xx)
Median [25th, 75th centile]	xx (xx to xx)	xx (xx to xx)	xx (xx to xx)
Min, max	xx to xx	xx to xx	xx to xx
Missing	xx	xx	xx
Fit (0-0.12)	xx (xx)	xx (xx)	xx (xx)
Mild frailty (>0.12 – 0.24)	xx (xx)	xx (xx)	xx (xx)
Moderate frailty (> 0.24 – 0.36)	xx (xx)	xx (xx)	xx (xx)
Severe frailty (> 0.36)	xx (xx)	xx (xx)	xx (xx)
Continuous characteristic			
Mean[SD]	xx (xx)	xx (xx)	xx (xx)
Median [25th, 75th centile]	xx (xx to xx)	xx (xx to xx)	xx (xx to xx)
Min, max	xx to xx	xx to xx	xx to xx
Missing	xx	xx	xx
Binary characteristic			
No	xx (xx)	xx (xx)	xx (xx)
Yes	xx (xx)	xx (xx)	xx (xx)
Missing	xx	xx	xx
Categorical characteristic			
Level 1	xx (xx)	xx (xx)	xx (xx)
Level 2	xx (xx)	xx (xx)	xx (xx)
Level 3	xx (xx)	xx (xx)	xx (xx)
Level 4	xx (xx)	xx (xx)	xx (xx)
Level 5	xx (xx)	xx (xx)	xx (xx)
Missing	xx	xx	xx

All data are N (%) unless otherwise indicated.

3 Adherence to allocated intervention

Table 6: Adherence to trial allocation (care homes)

	Standard Care (N = …)	Intervention (N = …)
Trial IMP dispatched to care home		
No	-	xx (xx)
Yes	-	xx (xx)
Care home received trial IMP		
No	-	xx (xx)
Yes	-	xx (xx)
Care home discontinued delivering trial treatment		
No	-	xx (xx)
Yes	-	xx (xx)
Reason if care home discontinued delivering trial treatment		
Care home no longer wanted to participate in trial	-	xx (xx)
Drug supply problems	-	xx (xx)
Care home Concerns over safety	-	xx (xx)
No staff capacity to deliver trial treatment	-	xx (xx)
False positive LFT triggered outbreak	-	xx (xx)
Other	-	xx (xx)

Table 7: Adherence to trial allocation (residents)

	Standard Care (n = …)	Intervention (n = …)
Resident received at least one dose of allocated intervention		
No	-	xx (xx)
Yes	-	xx (xx)
Missing	-	xx
If no, reason resident did not any receive allocated intervention		
Resident decision	-	xx (xx)
Primary care decision	-	xx (xx)
Care home staff decision	-	xx (xx)
Personal legal representative decision	-	xx (xx)
Lack of drug supply	-	xx (xx)
Admitted to hospital	-	xx (xx)
Death	-	xx (xx)
Other	-	xx (xx)
Time from care home randomisation to first dose (days)		
Median [25th, 75th centile]	-	xx (xx to xx)
Min, max	-	xx to xx
Missing	-	xx
Percentage of doses taken[1]		
Median [25th, 75th centile]	-	xx (xx to xx)
Min, max	-	xx to xx
Missing	-	xx
0%	-	xx (xx)
> 0% - < 25%	-	xx (xx)
≥ 25% - < 50%	-	xx (xx)
≥ 50% - < 75%	-	xx (xx)
≥ 75% - 100%	-	xx (xx)
Note categories used will depend on IMP and will be agreed prior to unblinding for that comparison		
Duration of treatment (days)		
Mean[SD]	-	xx (xx)
Median [25th, 75th centile]	-	xx (xx to xx)
Min, max	-	xx to xx

	Standard Care (n = …)	Intervention (n = …)
Allocated intervention permanently stopped early		
No	-	xx (xx)
Yes	-	xx (xx)
Missing	-	xx
Reason if allocated intervention permanently stopped early		
Resident decision	-	xx (xx)
Primary care decision	-	xx (xx)
Care home staff decision	-	xx (xx)
Personal legal representative decision	-	xx (xx)
Death	-	xx (xx)
Other	-	xx (xx)

1 - Number of doses taken collected for xx weeks after randomisation. *Add no of weeks information collected for depending on IMP. For ciclesonide and niclosamide will be 7 weeks.*

All data are N (%) unless otherwise indicated.

Table 8: Residents treated with steroid inhaler or oral steroids as part of routine care

	Standard Care (n = …)	Intervention (n = …)
Any steroid inhaler treatment		
No	xx (xx)	xx (xx)
Yes	xx (xx)	xx (xx)
Missing	xx	xx
Weeks from randomisation that steroid inhaler treatment first reported		
One	xx (xx)	xx (xx)
Two	xx (xx)	xx (xx)
etc		
Number of weeks steroid inhaler treatment reported		
Mean[SD]	xx (xx)	xx (xx)
Median [25th, 75th centile]	xx (xx to xx)	xx (xx to xx)
Min, max	xx to xx	xx to xx
Any oral steroid treatment		
No	xx (xx)	xx (xx)
Yes	xx (xx)	xx (xx)
Missing	xx	xx
Weeks from randomisation that oral steroid treatment first reported		
One	xx (xx)	xx (xx)
Two	xx (xx)	xx (xx)
etc		
Number of weeks oral steroid treatment reported		
Mean[SD]	xx (xx)	xx (xx)
Median [25th, 75th centile]	xx (xx to xx)	xx (xx to xx)
Min, max	xx to xx	xx to xx

All data are N (%) unless otherwise indicated.

4 Study quality summaries

Table 9: Completeness of follow up (care homes)

	Standard Care (N = …)	Intervention (N = …)
Data collected at 60 days following randomisation		
No	xx (xx)	xx (xx)
Yes	xx (xx)	xx (xx)
Reason if data not collected at 60 days following randomisation		
Care home withdrawn from trial	xx	xx
No staff capacity for data collection	xx	xx
Other	xx	xx

All data are N (%) unless otherwise indicated.

Table 10: Completeness of follow up (residents)

(a) eCRF

	Standard Care (n = …)	Intervention (n = …)
Data collected for 60 days following randomisation		
No	xx (xx)	xx (xx)
Yes	xx (xx)	xx (xx)
Reason if data not collected for 60 days following randomisation		
Resident died	xx	xx
Participant/personal legal representative decision	xx	xx
Clinical decision	xx	xx
Resident no longer lives at care home	xx	xx
Not known	xx	xx
Other	xx	xx

All data are N (%) unless otherwise indicated.

(b) Routine data sources

	Standard Care (n = …)	Intervention (n = …)
Adequate data available for primary outcome		
No	xx (xx)	xx (xx)
Yes	xx (xx)	xx (xx)
Reason if data not available for primary outcome		
Participant/personal legal representative chose to discontinue from data collection	xx	xx
Participant withdrew consent (or consent withdrawn) for all trial related activities	xx	xx
Unable to link to routine datasets	xx	xx
Other	xx	xx

Table 11: Vaccination status at 60-day follow-up (residents)

	Standard Care (n = …)	Intervention (n = …)
Received vaccination for COVID-19		
No	xx (xx)	xx (xx)
Yes	xx (xx)	xx (xx)
Missing	xx	xx
If vaccinated:		
Partially vaccinated	xx (xx)	xx (xx)
Fully vaccinated	xx (xx)	xx (xx)

All data are N (%) unless otherwise indicated.

Note summarise booster vaccines in the above table if introduced during the trial.

Table 12: Summary of protocol violations (resident level)

	Standard Care (n = …)	Intervention (n = …)
At least one protocol violation		
No	xx (xx)	xx (xx)
Yes	xx (xx)	xx (xx)
Type of protocol violation		
Treatment without consent	xx	xx
Ineligible resident received treatment	xx	xx
Primary outcomes measures not reported	xx	xx
Serious adverse event not reported	xx	xx
Other	xx	xx

Protocol violations are listed in the appendix

5 Primary and secondary outcomes

5.1 Primary analysis for the primary outcome

Table 13: Primary outcome between group comparisons

	Standard Care (n = …)	Intervention (n = …)	Adjusted common odds ratio[1] (95% CI), p-value	ICC
Primary endpoint – most serious event experienced during the 60 days post-randomisation				
1) No SARS-CoV-2 infection	xx (xx)	xx (xx)	xx (xx.x to xx.x)	0.xxx
2) SARS-CoV-2 infection but remained in the care home	xx (xx)	xx (xx)	p = 0.xxx	
3) Admission to hospital (all cause)	xx (xx)	xx (xx)		
4) Death (all cause)	xx (xx)	xx (xx)		
Missing	xx	xx		

Data are n (%) unless otherwise indicated.

[1]Adjusted by all cluster-level minimisation factors and individual-level factors including age, sex, and vaccination status where technically possible.

Figure 2: Primary ordinal outcome by treatment group

Stacked bar graph to show percentages in each level of ordinal outcome by group for each pairwise comparison

5.2 Sensitivity analysis for the primary outcome

Table 14: Primary outcome between group comparisons with inclusion of symptomatic residents without a positive test in the "SARS-CoV-2 infection but resident remains in care home" level

	Standard Care (n = …)	Intervention (n = …)	Adjusted common odds ratio[1] (95% CI)	ICC
Primary endpoint – most serious event experienced during the 60 days post-randomisation				
1) No SARS-CoV-2 infection or symptoms	xx (xx)	xx (xx)	xx (xx.x to xx.x)	0.xxx
2) SARS-CoV-2 infection but remained in the care home (positive test or symptomatic)	xx (xx)	xx (xx)		
3) Admission to hospital (all cause)	xx (xx)	xx (xx)		
4) Death (all cause)	xx (xx)	xx (xx)		
Missing	xx	xx		

Data are n (%) unless otherwise indicated.
[1]Adjusted by all cluster-level minimisation factors and individual-level factors including age, sex, and vaccination status where technically possible.

Table 15: Primary outcome between group comparisons with further adjustment for xxx

	Standard Care (n = …)	Intervention (n = …)	Adjusted common odds ratio[1] (95% CI)	ICC
Primary endpoint – most serious event experienced during the 60 days post-randomisation				
1) No SARS-CoV-2 infection	xx (xx)	xx (xx)	xx (xx.x to xx.x)	0.xxx
2) SARS-CoV-2 infection but remained in the care home	xx (xx)	xx (xx)		
3) Admission to hospital (all cause)	xx (xx)	xx (xx)		
4) Death (all cause)	xx (xx)	xx (xx)		
Missing	xx	xx		

Data are n (%) unless otherwise indicated.
[1]Adjusted by all cluster-level minimisation factors and individual-level factors including age, sex, and vaccination status (where technically possible) and xxx due to marked imbalance at baseline.

5.3 Subgroup analysis for the primary outcome

Table 16: Subgroup analysis of primary outcome (most serious event experienced in the 60 days post randomisation)

	Standard Care (n = …)	Intervention (n = …)	Adjusted common odds ratio[1] (95% CI)	Adjusted interaction effect[1] (95% CI)	p-value for interaction
Type of care home				xx (xx.x to xx.x)	0.xxx
Residential	(n = …)	(n = …)			
1) No SARS-CoV-2 infection	xx (xx)	xx (xx)	xx (xx.x to xx.x)		
2) SARS-CoV-2 infection but remained in the care home	xx (xx)	xx (xx)			
3) Admission to hospital (all cause)	xx (xx)	xx (xx)			
4) Death (all cause)	xx (xx)	xx (xx)			
Missing	xx	xx			
Residential/nursing	(n = …)	(n = …)			
1) No SARS-CoV-2 infection	xx (xx)	xx (xx)	xx (xx.x to xx.x)		
2) SARS-CoV-2 infection but remained in the care home	xx (xx)	xx (xx)			
3) Admission to hospital (all cause)	xx (xx)	xx (xx)			
4) Death (all cause)	xx (xx)	xx (xx)			
Missing	xx	xx			
Nursing	(n = …)	(n = …)			
1) No SARS-CoV-2 infection	xx (xx)	xx (xx)	xx (xx.x to xx.x)		
2) SARS-CoV-2 infection but remained in the care home	xx (xx)	xx (xx)			
3) Admission to hospital (all cause)	xx (xx)	xx (xx)			
4) Death (all cause)	xx (xx)	xx (xx)			
Missing	xx	xx			
Prior COVID-19 in the care home				xx (xx.x to xx.x)	0.xxx
Prior COVID-19 in the care home	(n = …)	(n = …)			
1) No SARS-CoV-2 infection	xx (xx)	xx (xx)	xx (xx.x to xx.x)		
2) SARS-CoV-2 infection but remained in the care home	xx (xx)	xx (xx)			
3) Admission to hospital (all cause)	xx (xx)	xx (xx)			
4) Death (all cause)	xx (xx)	xx (xx)			
Missing	xx	xx			
No prior COVID-19 in the care home	(n = …)	(n = …)			
1) No SARS-CoV-2 infection	xx (xx)	xx (xx)	xx (xx.x to xx.x)		
2) SARS-CoV-2 infection but remained in the care home	xx (xx)	xx (xx)			
3) Admission to hospital (all cause)	xx (xx)	xx (xx)			
4) Death (all cause)	xx (xx)	xx (xx)			
Missing	xx	xx			
Care home size				xx (xx.x to xx.x)	0.xxx
Small (≤30 residents)	(n = …)	(n = …)			
1) No SARS-CoV-2 infection	xx (xx)	xx (xx)	xx (xx.x to xx.x)		
2) SARS-CoV-2 infection but remained in the care home	xx (xx)	xx (xx)			
3) Admission to hospital (all cause)	xx (xx)	xx (xx)			
4) Death (all cause)	xx (xx)	xx (xx)			
Missing	xx	xx			
Medium (>30 and ≤50 residents)	(n = …)	(n = …)			
1) No SARS-CoV-2 infection	xx (xx)	xx (xx)	xx (xx.x to xx.x)		
2) SARS-CoV-2 infection but remained in the care home	xx (xx)	xx (xx)			
3) Admission to hospital (all cause)	xx (xx)	xx (xx)			
4) Death (all cause)	xx (xx)	xx (xx)			
Missing	xx	xx			
Large (>50 residents)	(n = …)	(n = …)			
1) No SARS-CoV-2 infection	xx (xx)	xx (xx)	xx (xx.x to xx.x)		
2) SARS-CoV-2 infection but remained in the care home	xx (xx)	xx (xx)			
3) Admission to hospital (all cause)	xx (xx)	xx (xx)			
4) Death (all cause)	xx (xx)	xx (xx)			
Missing	xx	xx			

	Standard Care (n = …)	Intervention (n = …)	Adjusted common odds ratio[1] (95% CI)	Adjusted interaction effect[1] (95% CI)	p-value for interaction
Care home has capacity to give oxygen				xx (xx.x to xx.x)	0.xxx
Does have capacity					
1) No SARS-CoV-2 infection	xx (xx)	xx (xx)	xx (xx.x to xx.x)		
2) SARS-CoV-2 infection but remained in the care home	xx (xx)	xx (xx)			
3) Admission to hospital (all cause)	xx (xx)	xx (xx)			
4) Death (all cause)	xx (xx)	xx (xx)			
Missing	xx	xx			
Does not have capacity					
1) No SARS-CoV-2 infection	xx (xx)	xx (xx)	xx (xx.x to xx.x)		
2) SARS-CoV-2 infection but remained in the care home	xx (xx)	xx (xx)			
3) Admission to hospital (all cause)	xx (xx)	xx (xx)			
4) Death (all cause)	xx (xx)	xx (xx)			
Missing	xx	xx			
Age group				xx (xx.x to xx.x)	0.xxx
<80 years old	(n = …)	(n = …)			
1) No SARS-CoV-2 infection	xx (xx)	xx (xx)	xx (xx.x to xx.x)		
2) SARS-CoV-2 infection but remained in the care home	xx (xx)	xx (xx)			
3) Admission to hospital (all cause)	xx (xx)	xx (xx)			
4) Death (all cause)	xx (xx)	xx (xx)			
Missing	xx	xx			
80-89 years old	(n = …)	(n = …)			
1) No SARS-CoV-2 infection	xx (xx)	xx (xx)	xx (xx.x to xx.x)		
2) SARS-CoV-2 infection but remained in the care home	xx (xx)	xx (xx)			
3) Admission to hospital (all cause)	xx (xx)	xx (xx)			
4) Death (all cause)	xx (xx)	xx (xx)			
Missing	xx	xx			
≥ 90 years old	(n = …)	(n = …)			
1) No SARS-CoV-2 infection	xx (xx)	xx (xx)	xx (xx.x to xx.x)		
2) SARS-CoV-2 infection but remained in the care home	xx (xx)	xx (xx)			
3) Admission to hospital (all cause)	xx (xx)	xx (xx)			
4) Death (all cause)	xx (xx)	xx (xx)			
Missing	xx	xx			
Sex				xx (xx.x to xx.x)	0.xxx
Female					
1) No SARS-CoV-2 infection	xx (xx)	xx (xx)	xx (xx.x to xx.x)		
2) SARS-CoV-2 infection but remained in the care home	xx (xx)	xx (xx)			
3) Admission to hospital (all cause)	xx (xx)	xx (xx)			
4) Death (all cause)	xx (xx)	xx (xx)			
Missing	xx	xx			
Male					
1) No SARS-CoV-2 infection	xx (xx)	xx (xx)	xx (xx.x to xx.x)		
2) SARS-CoV-2 infection but remained in the care home	xx (xx)	xx (xx)			
3) Admission to hospital (all cause)	xx (xx)	xx (xx)			
4) Death (all cause)	xx (xx)	xx (xx)			
Missing	xx	xx			
Resident vaccination status prior to randomisation					
Fully vaccinated					
1) No SARS-CoV-2 infection	xx (xx)	xx (xx)	xx (xx.x to xx.x)		
2) SARS-CoV-2 infection but remained in the care home	xx (xx)	xx (xx)			
3) Hospitalised (all cause)	xx (xx)	xx (xx)			
4) Death (all cause)	xx (xx)	xx (xx)			
Missing	xx	xx			
Partially vaccinated					
1) No SARS-CoV-2 infection	xx (xx)	xx (xx)	xx (xx.x to xx.x)		
2) SARS-CoV-2 infection but remained in the care home	xx (xx)	xx (xx)			
3) Hospitalised (all cause)	xx (xx)	xx (xx)			
4) Death (all cause)	xx (xx)	xx (xx)			
Missing	xx	xx			
Not vaccinated					
1) No SARS-CoV-2 infection	xx (xx)	xx (xx)	xx (xx.x to xx.x)		
2) SARS-CoV-2 infection but remained in the care home	xx (xx)	xx (xx)			
3) Hospitalised (all cause)	xx (xx)	xx (xx)			
4) Death (all cause)	xx (xx)	xx (xx)			
Missing	xx	xx			

Data are n (%) unless otherwise indicated.

[1]Adjusted by all cluster-level minimisation factors and individual-level factors including age, sex, and vaccination status where technically possible.

Figure 3: Forest plot showing adjusted common odds ratio for primary outcome according to subgroup

5.4 Secondary outcomes

Table 17: Secondary outcomes related to COVID-19 during the 60 days post randomisation

	Standard Care (n = …)	Intervention (n = …)	Adjusted hazard ratio[1] (95% CI)
Healthcare referral for COVID-19[2]			
No	xx (xx)	xx (xx)	xx (xx.x to xx.x)
Yes	xx (xx)	xx (xx)	
Missing	xx	xx	
Received dexamethasone in care home for COVID-19			
No	xx (xx)	xx (xx)	xx (xx.x to xx.x)
Yes	xx (xx)	xx (xx)	
Missing	xx	xx	
Received oxygen in care home for COVID-19 (for care homes with capacity to give oxygen)			
No	xx (xx)	xx (xx)	xx (xx.x to xx.x)
Yes	xx (xx)	xx (xx)	
Missing	xx	xx	
SARS-CoV-2 infection with symptoms of COVID-19			
No	xx (xx)	xx (xx)	
Yes	xx (xx)	xx (xx)	xx (xx.x to xx.x)
Missing	xx	xx	
SARS-CoV-2 infection without symptoms of COVID-19			
No	xx (xx)	xx (xx)	
Yes	xx (xx)	xx (xx)	xx (xx.x to xx.x)
Missing	xx	xx	
Any SARS-CoV-2 infection (with or without symptoms of COVID-19)			
No	xx (xx)	xx (xx)	
Yes	xx (xx)	xx (xx)	xx (xx.x to xx.x)
Missing	xx	xx	

Data are n (%) unless otherwise indicated.
[1]Adjusted by all cluster-level minimisation factors and individual-level factors including age, sex, and vaccination status where technically possible.
[2]*e.g.* discussion outside of care home with GP (excluding routine visit), 111, 999 paramedic or Emergency Department assessment (without admission), remote hospital consultation.

Figure 4: Estimated cumulative incidence function for time to healthcare referral for COVID-19

Figure 5: Estimated cumulative incidence function for time to receiving dexamethasone in the care home for COVID-19

Figure 6: Estimated cumulative incidence function for time to receiving oxygen in the care home for COVID-19

Figure 7: Estimated cumulative incidence function for time to SARS-CoV-2 infection with symptoms of COVID-19

Figure 8: Estimated cumulative incidence function for time to SARS-CoV-2 infection without symptoms of COVID-19

Figure 9: Estimated cumulative incidence function for time to any SARS-CoV-2 infection with/without symptoms of COVID-19

Table 18: Secondary outcomes related to hospitalisation during the 60 days post randomisation

	Standard Care (n = …)	Intervention (n = …)	Adjusted effect estimate (95% CI)		ICC
Admission to hospital (all-cause)			**Adjusted hazard ratio for time to admission[1] (95% CI)**		
No	xx (xx)	xx (xx)			
Yes	xx (xx)	xx (xx)	xx (xx.x to xx.x)		
Missing	xx	xx			
Total number of hospital admissions	xx	xx			
Cause specific reasons:					
Covid-19	xx (xx)	xx (xx)			
Stroke	xx (xx)	xx (xx)			
Myocardial infarction	xx (xx)	xx (xx)			
…	xx (xx)	xx (xx)			
….	xx (xx)	xx (xx)			
Days alive and not in hospital			**Adjusted difference in means[1] (95% CI)**		
Mean[sd]	xx (xx)	xx (xx)	xx (xx.x to xx.x)	0.xxx	
Median [25th, 75th centile]	xx (xx to xx)	xx (xx to xx)			
Min, max	xx to xx	xx to xx			
Missing	xx	xx			

Data are n (%) unless otherwise indicated.
[1]Adjusted by all cluster-level minimisation factors and individual-level factors including age, sex, and vaccination status where technically possible.

Figure 10: Estimated cumulative incidence function for time to admission to hospital

Table 19: Secondary outcomes related to death during the 60 days post randomisation

	Standard Care (n = …)	Intervention (n = …)	Adjusted hazard ratio for time to death (95% CI)	ICC
Death (all-cause)				
No	xx (xx)	xx (xx)		
Yes	xx (xx)	xx (xx)	xx (xx.x to xx.x)	
Missing	xx	xx		
Cause specific reasons:				
Covid-19	xx (xx)	xx (xx)		
Stroke	xx (xx)	xx (xx)		
Pulmonary embolism	xx (xx)	xx (xx)		
Myocardial infarction	xx (xx)	xx (xx)		
…	xx (xx)	xx (xx)		
….	xx (xx)	xx (xx)		

Figure 11: Kaplan Meier curves for time to death

Table 20: Secondary outcome - electronic frailty index at 60 days

	Standard Care (n = …)	Intervention (n = …)	Adjusted common odds ratio[1] (95% CI)	ICC
Electronic frailty index (eFI)				
Fit (0-0.12)	xx (xx)	xx (xx)	xx (xx.x to xx.x)	0.xxx
Mild frailty (>0.12 – 0.24)	xx (xx)	xx (xx)		
Moderate frailty (> 0.24 – 0.36)	xx (xx)	xx (xx)		
Severe frailty (> 0.36)	xx (xx)	xx (xx)		
Resident died	xx (xx)	xx (xx)		
Missing	xx	xx		
Summary of eFI for residents alive at 60 days				
Mean[sd]	xx (xx)	xx (xx)		
Median [25th, 75th centile]	xx (xx to xx)	xx (xx to xx)		
Min, max	xx to xx	xx to xx		
n	xx	xx		
Missing	xx	xx		

Data are n (%) unless otherwise indicated.
[1]Adjusted by all cluster-level minimisation factors and individual-level factors including baseline eFI, age, sex, and vaccination status where technically possible.

Table 21: Secondary ordinal outcome during the 120 days post randomisation

	Standard Care (n = …)	Intervention (n = …)	Adjusted common odds ratio[1] (95% CI)	ICC
Most serious event experienced during the 120 days post-randomisation				
1) No SARS-CoV-2 infection	xx (xx)	xx (xx)	xx (xx.x to xx.x)	0.xxx
2) SARS-CoV-2 infection but remained in the care home	xx (xx)	xx (xx)		
3) Admission to hospital (all cause)	xx (xx)	xx (xx)		
4) Death (all cause)	xx (xx)	xx (xx)		
Missing	xx	xx		

Data are n (%) unless otherwise indicated.
[1]Adjusted by all cluster-level minimisation factors and individual-level factors including age, sex, and vaccination status where technically possible.

Figure 12: Secondary ordinal outcome during the 120 days post randomisation by treatment group

Stacked bar graph to show percentages in each level of ordinal outcome by group for each pairwise comparison

Table 22: Total number of SARS-CoV-2 infections in the care home during the 60 days post-randomisation (care home level data also including residents not participating in PROTECT)

	Standard Care (N =)	Intervention (N =)	Adjusted difference in rates[1] (95% CI)	Adjusted rate ratio[1] (95% CI)
Total number of SARS-CoV-2 infections in care home during the 60 days post-randomisation				
Mean[sd]	xx (xx)	xx (xx)		
Median [25th, 75th centile]	xx (xx to xx)	xx (xx to xx)		
Min, max	xx to xx	xx to xx		
Missing	xx	xx		
SARS-CoV-2 infections per resident during the 60 days post-randomisation				
Mean[sd]	xx (xx)	xx (xx)	xx (xx to xx)	xx (xx to xx)
Median [25th, 75th centile]	xx (xx to xx)	xx (xx to xx)		
Min, max	xx to xx	xx to xx		
Missing	xx	xx		

[1]Adjusted by all cluster-level minimisation factors

5.5 Subgroup analysis for secondary outcome

Table 23: Subgroup analysis of all-cause mortality

	Standard Care Group n / N (%)	Intervention Group n / N (%)	Adjusted hazard ratio for time to death[1] (95% CI)	Adjusted interaction effect[1] (95% CI)	p-value for interaction
Type of care home				xx (xx.x to xx.x)	0.xxx
Residential	xx / xx (xx)	xx / xx (xx)	xx (xx.x to xx.x)		
Missing	xx	xx			
Residential/nursing	xx / xx (xx)	xx / xx (xx)	xx (xx.x to xx.x)		
Missing	xx	xx			
Nursing	xx / xx (xx)	xx / xx (xx)	xx (xx.x to xx.x)		
Missing	xx	xx			
Prior COVID-19 in the care home				xx (xx.x to xx.x)	0.xxx
Prior COVID-19 in the care home	xx / xx (xx)	xx / xx (xx)	xx (xx.x to xx.x)		
Missing	xx	xx			
No prior COVID-19 in the care home	xx / xx (xx)	xx / xx (xx)	xx (xx.x to xx.x)		
Missing	xx	xx			
Care home size				xx (xx.x to xx.x)	0.xxx
Small (≤30 residents)	xx / xx (xx)	xx / xx (xx)	xx (xx.x to xx.x)		
Missing	xx	xx			
Medium (>30 and ≤50 residents)	xx / xx (xx)	xx / xx (xx)	xx (xx.x to xx.x)		
Missing	xx	xx			
Large (>50 residents)	xx / xx (xx)	xx / xx (xx)	xx (xx.x to xx.x)		
Missing	xx	xx			
Care home has capacity to give Oxygen				xx (xx.x to xx.x)	0.xxx
Does have capacity	xx / xx (xx)	xx / xx (xx)	xx (xx.x to xx.x)		
Missing	xx	xx			
Does not have capacity	xx / xx (xx)	xx / xx (xx)	xx (xx.x to xx.x)		
Missing	xx	xx			
Age group				xx (xx.x to xx.x)	0.xxx
<80 years old	xx / xx (xx)	xx / xx (xx)	xx (xx.x to xx.x)		
Missing	xx	xx			
80-89 years old	xx / xx (xx)	xx / xx (xx)	xx (xx.x to xx.x)		
Missing	xx	xx			
≥ 90 years old	xx / xx (xx)	xx / xx (xx)	xx (xx.x to xx.x)		
Missing	xx	xx			
Sex				xx (xx.x to xx.x)	0.xxx
Female	xx / xx (xx)	xx / xx (xx)	xx (xx.x to xx.x)		
Missing	xx	xx			
Male	xx / xx (xx)	xx / xx (xx)	xx (xx.x to xx.x)		
Missing	xx	xx			
Resident vaccination status prior to randomisation				xx (xx.x to xx.x)	0.xxx
Fully vaccinated	xx / xx (xx)	xx / xx (xx)	xx (xx.x to xx.x)		
Missing	xx	xx			
Partially vaccinated	xx / xx (xx)	xx / xx (xx)	xx (xx.x to xx.x)		
Missing	xx	xx			
Not vaccinated	xx / xx (xx)	xx / xx (xx)	xx (xx.x to xx.x)		
Missing	xx	xx			

Data are n (%) unless otherwise indicated.

[1]Adjusted by all cluster-level minimisation factors and individual-level factors including age, sex, and vaccination status where technically possible.

Figure 13: Forest plot showing adjusted hazard ratio for all cause mortality according to subgroup

6 Supplementary analyses related to transmission

Table 24: Ordinal outcome and SARS-CoV-2 infection during the 60 days post-randomisation for all residents consenting

	Standard Care (n = *all consenting residents*)	Intervention (n = *all consenting residents*)	Adjusted effect (95% CI)	ICC
Ordinal outcome– most serious event experienced during the 60 days post-randomisation			*Adjusted common odds ratio*	
1) No SARS-CoV-2 infection	xx (xx)	xx (xx)	xx (xx.x to xx.x)	0.xxx
2) SARS-CoV-2 infection but remained in the care home	xx (xx)	xx (xx)		
3) Admission to hospital (all cause)	xx (xx)	xx (xx)		
4) Death (all cause)	xx (xx)	xx (xx)		
Missing	xx	xx		
SARS-CoV-2 infection			*Adjusted hazard ratio (95% CI)*	
No	xx (xx)	xx (xx)		
Yes	xx (xx)	xx (xx)	xx (xx.x to xx.x)	
Missing	xx	xx		

Data are n (%) unless otherwise indicated.
[1]Adjusted by all cluster-level minimisation factors and individual-level factors including age, sex, and vaccination status where technically possible.

7 Safety

7.1 Serious adverse events

Table 25: Summary of serious adverse events and reactions

	Standard care (n =)	Intervention (n =)
Any serious adverse event (SAE)	xx (%)	xx (%)
Total number of SAEs	xx	xx
Any serious adverse reaction (SAR, related to IMP not unexpected)	xx (%)	xx (%)
Total number of SSARs	xx	xx
Any Suspected Unexpected Serious Adverse Reaction (SUSAR)	xx (%)	xx (%)
Total number of SUSARs	xx	xx
Preferred term of SARs		
Preferred term 1	xx	xx
Preferred term 2	xx	xx
…..		
Preferred term of SUSARs		
Preferred term 1	xx	xx
Preferred term 2	xx	xx
…..		

7.2 Adverse events relevant to the intervention

Table 26: Summary of adverse events relevant to the intervention (as specified in relevant IMP protocol appendix)

Table only needed if reporting of other adverse events (in additions to SARs and SUSARs) if specified in protocol appendix for the IMP

	Standard Care (n = …)	Intervention (n = …)
Gastro-intestinal events		
Nausea	xx (%)	xx (%)
Any nausea reported		
Number of weeks nausea reported for each resident		
Mean[sd]	xx (xx)	xx (xx)
Median [25th, 75th centile]	xx (xx to xx)	xx (xx to xx)
Min, max	xx to xx	xx to xx
Missing	xx	xx
Worst severity of nausea for each resident (care home staff assessed)		
Mild	xx (%)	xx (%)
Moderate	xx (%)	xx (%)
Severe	xx (%)	xx (%)
Reported in:		
week 1	xx (%)	xx (%)
week 2	xx (%)	xx (%)
week 3	xx (%)	xx (%)
week 4	xx (%)	xx (%)
week 5	xx (%)	xx (%)
week 6	xx (%)	xx (%)
Repeat as above for each targeted adverse event collected		

7.3 Lists of SARs and SUSARs

Table 27: List of all SARs

Participant	Allocated group	Description (Preferred term)	Days from start of treatment to onset	Relationship to trial medication	Severity	Action taken	Outcome

Note – participant ID to be retracted if listing included in publication

Table 28: List of all SUSARs

Participant	Allocated group	Description (Preferred term)	Days from start of treatment to onset	Relationship to trial medication	Severity	Action taken	Outcome

Note – participant ID to be retracted if listing included in publication

8 Appendix

Table 29: PCR tests and results after positive lateral flow test for Covid-19

	Standard Care	Intervention
Positive lateral flow test	n = xx	n = xx
Confirmatory PCR test conducted on same day		
Yes	xx (xx)	xx (xx)
No corresponding PCR test in routine data/eCRF	xx (xx)	xx (xx)
SARS-CoV-2 status for outcomes		
Positive confirmed by PCR	xx (xx)	xx (xx)
Negative based on PCR	xx (xx)	xx (xx)
Positive based on no contradictory PCR	xx (xx)	xx (xx)

Table 30: Listing of protocol violations

Participant	Allocated group	Days from randomisation to violation	Violation type	Further details on violation

Note – participant ID to be retracted if listing included in publication