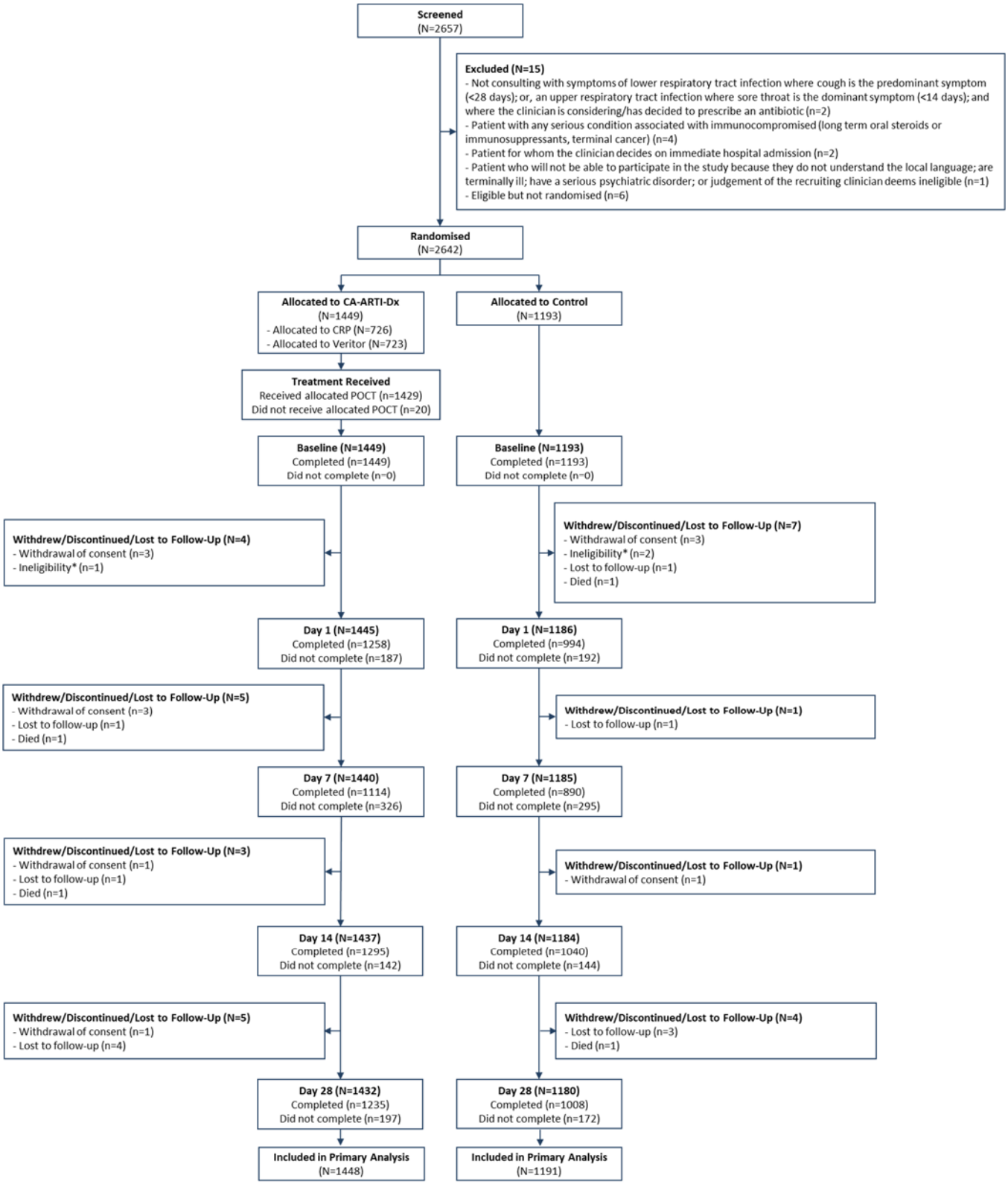

**Excluded from analysis population.*

FIGURE 1. PARTICIPANT FLOW DIAGRAM

3.2 BASELINE CHARACTERISTICS OF PARTICIPANTS

Baseline characteristics of the participants are provided in Table 1 split by if the participant was randomised to a CA-ARTI-Dx (CRP or Veritor) or to usual care, as well as overall. The baseline characteristics are also provided in Table 2 split by if the participant was randomised to CRP, or to Veritor (flu, GAS, or total), or to usual care and was eligible to receive CRP or Veritor.

TABLE 1. BASELINE CHARACTERISTICS SPLIT BY CA-ARTI-DX AND USUAL CARE, AS WELL AS OVERALL

	CA-ARTI-Dx (N=1448)	Usual Care (N=1191)	Overall (N=2639)
Age (years)			
Mean (SD)	45.2 (22.0)	43.9 (21.8)	44.6 (21.9)
[Range]	[1 to 100]	[1 to 98]	[1 to 100]
Missing	*0*	*0*	*0*
Age categories (stratification)*			
1-16 years, n(%)	142 (9.8%)	125 (10.5%)	267 (10.1%)
17-64 years, n(%)	994 (68.6%)	826 (69.4%)	1820 (69.0%)
65-79 years, n(%)	211 (14.6%)	163 (13.7%)	374 (14.2%)
80 or older, n(%)	101 (7.0%)	77 (6.5%)	178 (6.7%)
Missing	*0*	*0*	*0*
Age categories (EudraCT guidelines)			
Infants and toddlers (<24 months), n(%)	2 (0.1%)	4 (0.3%)	6 (0.2%)
Children (2-11 years), n(%)	96 (6.6%)	76 (6.4%)	172 (6.5%)
Adolescents (12-17 years), n(%)	58 (4.0%)	56 (4.7%)	114 (4.3%)
Adults (18-64 years), n(%)	980 (67.7%)	815 (68.4%)	1795 (68.0%)
Adults (65-84 years), n(%)	260 (18.0%)	205 (17.2%)	465 (17.6%)
Adults (85 years and over), n(%)	52 (3.6%)	35 (2.9%)	87 (3.3%)
Missing	*0*	*0*	*0*
Sex			
Male, n(%)	567 (39.2%)	431 (36.2%)	998 (37.8%)
Female, n(%)	881 (60.8%)	760 (63.8%)	1641 (62.2%)
Missing	*0*	*0*	*0*
Predominant symptom*			
Cough, n(%)	948 (65.5%)	696 (58.4%)	1644 (62.3%)
Sore throat, n(%)	500 (34.5%)	495 (41.6%)	995 (37.7%)
Missing	*0*	*0*	*0*
COVID-19 status*			
Positive, n(%)	80 (5.5%)	76 (6.4%)	156 (5.9%)
Negative/unknown, n(%)	1368 (94.5%)	1115 (93.6%)	2483 (94.1%)
Missing	*0*	*0*	*0*
Comorbidities*			
Yes, n(%)	550 (38.0%)	432 (36.3%)	982 (37.2%)
No, n(%)	898 (62.0%)	759 (63.7%)	1657 (62.8%)
Missing	*0*	*0*	*0*

	CA-ARTI-Dx (N=1448)	Usual Care (N=1191)	Overall (N=2639)
Setting*			
Primary care, n(%)	1326 (91.6%)	1105 (92.8%)	2431 (92.1%)
Long term care facility, n(%)	122 (8.4%)	86 (7.2%)	208 (7.9%)
Missing	*0*	*0*	*0*
Country			
Belgium, n(%)	64 (4.4%)	54 (4.5%)	118 (4.5%)
France, n(%)	13 (0.9%)	13 (1.1%)	26 (1.0%)
Georgia, n(%)	283 (19.5%)	215 (18.1%)	498 (18.9%)
Germany, n(%)	100 (6.9%)	80 (6.7%)	180 (6.8%)
Greece, n(%)	195 (13.5%)	155 (13.0%)	350 (13.3%)
Hungary, n(%)	109 (7.5%)	110 (9.2%)	219 (8.3%)
Ireland, n(%)	135 (9.3%)	92 (7.7%)	227 (8.6%)
Israel, n(%)	20 (1.4%)	10 (0.8%)	30 (1.1%)
Italy, n(%)	55 (3.8%)	47 (3.9%)	102 (3.9%)
Poland, n(%)	144 (9.9%)	127 (10.7%)	271 (10.3%)
Portugal, n(%)	31 (2.1%)	19 (1.6%)	50 (1.9%)
Spain, n(%)	44 (3.0%)	41 (3.4%)	85 (3.2%)
United Kingdom, n(%)	255 (17.6%)	228 (19.1%)	483 (18.3%)
Missing	*0*	*0*	*0*
Status of influenza season*			
Influenza season, n(%)	732 (50.6%)	473 (39.7%)	1205 (45.7%)
Not influenza season, n(%)	716 (49.4%)	718 (60.3%)	1434 (54.3%)
Missing	*0*	*0*	*0*
Relevant medical history†			
Cardiovascular disease, n(%)	263 (18.2%)	197 (16.5%)	460 (17.4%)
Diabetes, n(%)	114 (7.9%)	83 (7.0%)	197 (7.5%)
Chronic respiratory condition, n(%)	186 (12.8%)	148 (12.4%)	334 (12.7%)
Hepatic, hematologic, neurologic or neurodevelopment condition, n(%)	107 (7.4%)	62 (5.2%)	169 (6.4%)
Obesity, n(%)	189 (13.1%)	158 (13.3%)	347 (13.1%)
Missing	*0*	*0*	*0*
Flu vaccine in the last year			
Yes, n(%)	450 (31.1%)	345 (29.0%)	795 (30.1%)
No, n(%)	961 (66.4%)	822 (69.0%)	1783 (67.6%)
Unknown, n(%)	37 (2.6%)	24 (2.0%)	61 (2.3%)
Missing	*0*	*0*	*0*
Coronavirus vaccine in the last year			
Yes, n(%)	765 (52.8%)	591 (49.6%)	1356 (51.4%)
No, n(%)	650 (44.9%)	580 (48.7%)	1230 (46.6%)
Unknown, n(%)	33 (2.3%)	20 (1.7%)	53 (2.0%)
Missing	*0*	*0*	*0*

	CA-ARTI-Dx (N=1448)	Usual Care (N=1191)	Overall (N=2639)
Coronavirus vaccine dose at baseline			
Not vaccinated, n(%)	683 (47.2%)	600 (50.4%)	1283 (48.6%)
1st dose, n(%)	20 (1.4%)	14 (1.2%)	34 (1.3%)
2nd dose, n(%)	188 (13.0%)	144 (12.1%)	332 (12.6%)
3rd dose, n(%)	557 (38.5%)	433 (36.4%)	990 (37.5%)
Missing	*0*	*0*	*0*
Coronavirus vaccine manufacturer details†			
N (Vaccinated)	**765**	**591**	**1356**
Moderna, n(%)	112 (14.6%)	89 (15.1%)	201 (14.8%)
Oxford AstraZeneca, n(%)	101 (13.2%)	75 (12.7%)	176 (13.0%)
Pfizer/BioNTech, n(%)	636 (83.1%)	502 (84.9%)	1138 (83.9%)
Janssen, n(%)	13 (1.7%)	7 (1.2%)	20 (1.5%)
Other, n(%)	44 (5.8%)	37 (6.3%)	81 (6.0%)
Unknown, n(%)	18 (2.4%)	8 (1.4%)	26 (1.9%)
Missing	*0*	*0*	*0*
Pneumococcal vaccination in last five years			
Yes, n(%)	191 (13.2%)	151 (12.7%)	342 (13.0%)
No, n(%)	1189 (82.1%)	983 (82.5%)	2172 (82.3%)
Unknown, n(%)	68 (4.7%)	57 (4.8%)	125 (4.7%)
Missing	*0*	*0*	*0*
Medical history of antibiotic allergy/intolerance			
Yes, n(%)	99 (6.8%)	97 (8.1%)	196 (7.4%)
No, n(%)	1273 (87.9%)	1043 (87.6%)	2316 (87.8%)
Unknown, n(%)	76 (5.2%)	51 (4.3%)	127 (4.8%)
Missing	*0*	*0*	*0*
Smoking			
Yes, n(%)	273 (18.9%)	213 (17.9%)	486 (18.4%)
No, n(%)	1161 (80.2%)	966 (81.1%)	2127 (80.6%)
Unknown, n(%)	14 (1.0%)	12 (1.0%)	26 (1.0%)
Missing	*0*	*0*	*0*
Signs and symptoms†			
Ear pain, n(%)	141 (9.7%)	130 (10.9%)	271 (10.3%)
Rhinitis, n(%)	574 (39.6%)	489 (41.1%)	1063 (40.3%)
Sore throat or difficulty swallowing, n(%)	870 (60.1%)	770 (64.7%)	1640 (62.1%)
Cough, n(%)	1173 (81.0%)	908 (76.2%)	2081 (78.9%)
General symptoms, n(%)	1065 (73.5%)	899 (75.5%)	1964 (74.4%)
Missing	*0*	*0*	*0*
Suspected etiology			
Viral, n(%)	631 (43.6%)	507 (42.6%)	1138 (43.1%)
Bacterial, n(%)	423 (29.2%)	340 (28.5%)	763 (28.9%)
Not clear, n(%)	394 (27.2%)	344 (28.9%)	738 (28.0%)
Missing	*0*	*0*	*0*

	CA-ARTI-Dx (N=1448)	Usual Care (N=1191)	Overall (N=2639)
Antibiotic prescribing likelihood			
Low likelihood, n(%)	755 (52.1%)	619 (52.0%)	1374 (52.1%)
Medium likelihood, n(%)	412 (28.5%)	340 (28.5%)	752 (28.5%)
High likelihood, n(%)	281 (19.4%)	232 (19.5%)	513 (19.4%)
Missing	*0*	*0*	*0*

*NB Percentages have been computed with the number of participants with the response available as the denominator. *Stratification factors. †Not mutually exclusive.*

TABLE 9. SUMMARY STATISTICS, ADJUSTED TREATMENT EFFECTS, AND P-VALUES FOR THE PRIMARY ANALYSES COMPARING PARTICIPANTS RANDOMISED TO A CA-ARTI-DX (CRP OR VERITOR) AGAINST PARTICIPANTS RANDOMISED TO USUAL CARE

	CA-ARTI-Dx (N=1448)	Usual Care (N=1191)	Treatment Effect [95% CI]*	P-value†
Antibiotic prescription‡				
Adjusted risk difference			-1.30% [-4.86% to 2.26%]	0.4742
Yes, n(%)	662 (45.7%)	561 (47.1%)		
No, n(%)	786 (54.3%)	629 (52.9%)		
Missing	*0*	*1*		
Returned to usual activities				
Yes, n(%)	1314 (95.7%)	1066 (96.2%)		
No, n(%)	59 (4.3%)	42 (3.8%)		
Missing	*75*	*83*		
Time (days) to return to usual activities§				
Adjusted hazard ratio			1.00 [0.92 to ∞]	<0.0001
Median (IQR)	4.0 (2.0 to 8.0)	4.0 (2.0 to 7.0)		
Missing	*82*	*87*		

**CA-ARTI-Dx versus Usual Care. †Level of statistical significance (two-sided) = 0.05 for the antibiotic prescription outcome; level of statistical significance (one-sided) = 0.025 for the days to return to usual activities non-inferiority outcome. ‡Logit-binomial generalised linear mixed model adjusted for intervention arm, baseline SARS-CoV-2 status, predominant symptom at baseline, influenza season, age, comorbidities, an interaction between predominant symptom and influenza season, and setting as fixed effects, and site as a random effect. A risk difference less than 0 indicates improvement in favour of CA-ARTI-Dx. §Mixed effects Cox proportional hazards regression model adjusted for intervention arm, baseline SARS-CoV-2 status, predominant symptom at baseline, influenza season, age, comorbidities, an interaction between predominant symptom and influenza season, and setting as fixed effects, and site as a random effect. 11 participants (7 in the CA-ARTI-Dx arm and 4 in the usual care arm) had a time to return to usual activities of 0 and were not included in the model. Non-inferiority margin = 0.80. P-value indicates non-inferiority of CA-ARTI-Dx in days to return to usual activities. A lower limit of the 95% confidence interval above 0.80 indicates non-inferiority of CA-ARTI-Dx.*

TABLE 19. FREQUENCY AND PERCENTAGE OF SERIOUS ADVERSE EVENTS

	Received CRP (N=717)	Received Veritor (N=712)	Received Usual Care (N=1210)	Overall (N=2639)
Experienced a serious adverse event				
Yes, n(%)	12 (1.7%)	14 (2.0%)	16 (1.3%)	42 (1.6%)
No, n(%)	705 (98.3%)	698 (98.0%)	1194 (98.7%)	2597 (98.4%)
Number of serious adverse events				
0, n(%)	705 (98.3%)	698 (98.0%)	1194 (98.7%)	2597 (98.4%)
1, n(%)	12 (1.7%)	14 (2.0%)	16 (1.3%)	42 (1.6%)
>1, n(%)*	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Severity of serious adverse event				
N (Number of SAEs)	**12**	**14**	**16**	**42**
Mild, n(%)	2 (16.7%)	1 (7.1%)	4 (25.0%)	7 (16.7%)
Moderate, n(%)	9 (75.0%)	10 (71.4%)	7 (43.8%)	26 (61.9%)
Severe, n(%)	1 (8.3%)	3 (21.4%)	5 (31.3%)	9 (21.4%)
Causality of serious adverse event				
N (Number of SAEs)	**12**	**14**	**16**	**42**
Not related, n(%)	9 (75.0%)	14 (100.0%)	16 (100.0%)	39 (92.9%)
Possibly related, n(%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Probably related, n(%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Definitely related, n(%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unknown, n(%)	3 (25.0%)	0 (0.0%)	0 (0.0%)	3 (7.1%)

**No participants reported experiencing more than one serious adverse event during the trial.*