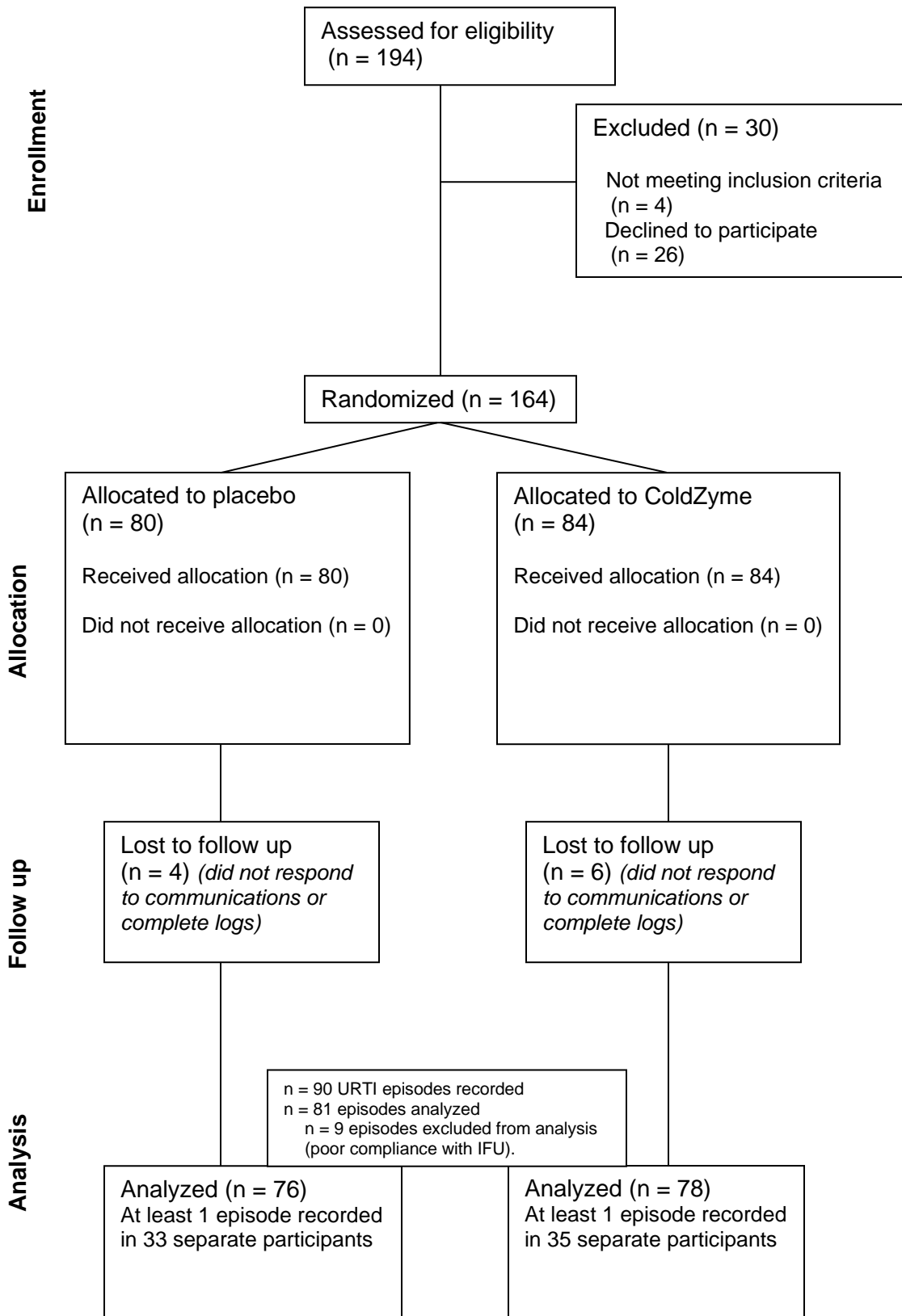


Participant flow



Baseline characteristics

Variable	Placebo (n = 76)	ColdZyme (n = 78)
Age (years) mean \pm SD	34 \pm 11	36 \pm 10
Sex (M/F)	54/22	48/30

Note: All results are shown with 1-tailed P values, due to the directional hypothesis.

Primary outcome measure

Variable	Placebo	ColdZyme	P
<u>URTI episode duration (days)</u>			0.015
Mean \pm SD	10.8 \pm 10.4	6.2 \pm 2.6	
Median (interquartile range)	7.0 (5 - 12)	5.5 (4 - 9)	

Secondary outcome measures

1. URTI parameters recorded using the Jackson common cold questionnaire

Symptom scores

Variable	Placebo	ColdZyme	P
<u>Jackson score (whole episode)</u>			0.032
Mean \pm SD	57.9 \pm 53.1	37.8 \pm 27.8	
Median (interquartile range)	38.0 (23 - 61)	28.0 (18 - 54)	
<u>Jackson score (mean per day)</u>			0.470
Mean \pm SD	5.7 \pm 2.4	5.7 \pm 2.4	
Median (interquartile range)	5.4 (4 - 7)	5.7 (4 - 7)	
<u>Jackson score (episode peak)</u>			0.199
Mean \pm SD	10.0 \pm 4.0	9.2 \pm 4.2	
Median (interquartile range)	9.0 (7 - 14)	9.0 (6 - 11)	

URTI episodes recorded in 44% of participants (68/154): Placebo 43% (33/76), ColdZyme 45% (35/78), with an average of 0.43 (range 0-3) episodes per person in Placebo and 0.62 (range 0-3) episodes per person in ColdZyme.

2. URTI episodes with swab-confirmed pathogen detection

Swabs were returned and analyzed for 50 episodes (24 Placebo, 26 ColdZyme). No swabs were returned for 31 episodes (Jackson criteria were met but for those where swabs were not returned to the lab, qPCR pathogen detection could not be performed). The table below shows analysis for only all episodes from which swabs were received. At least one pathogen was detected in all cases where a swab was provided.

Variable	Placebo	ColdZyme	P
<u>URTI episode duration (days)</u>			0.003
Mean \pm SD	11.8 \pm 10.9	5.7 \pm 2.4	
Median (interquartile range)	7.0 (5 - 14)	5.0 (4 - 7)	
<u>Jackson score (whole episode)</u>			<0.001
Mean \pm SD	66.2 \pm 56.9	31.4 \pm 25.1	
Median (interquartile range)	46.5 (26 - 99)	21.0 (14 - 44)	
<u>Jackson score (mean per day)</u>			0.052
Mean \pm SD	6.0 \pm 2.3	5.0 \pm 2.1	
<u>Jackson score (episode peak)</u>			0.008
Mean \pm SD	10.6 \pm 3.9	8.1 \pm 4.2	
Median (interquartile range)	10.0 (7 - 14)	7.0 (5 - 10)	

3. Viral (and bacterial) load in pathogen-confirmed URTI episodes

Swabs were collected on days 1, 3, 5, and 7 of recorded episodes, and screened using the TrueMark™ Respiratory Panel 2.0 (ThermoFisher) on a QuantStudio 12K Flex Real-Time PCR System. Pathogens were normalised against RNase P using the Delta-Delta Ct method (to give relative quantification: Rq). Results are expressed as area under (AUC) Rq curve (days 1-7 inclusive).

Pathogen detection returned at least one positive in all swabs. In total 24 different pathogens were detected across samples (Adenovirus, H.influenzae, Rhinovirus, Epstein-Barr virus, Human herpesvirus 6, Influenza, Parainfluenza, Respiratory syncytial virus, Metapneumovirus, Measles, Mumps, Covid, MERS CoV, SARS CoV, SARS-CoV2 (Covid-19), Enterovirus, Bordetella, B.pertussis, K.pneumoniae, M.catarrhalis, M.pneumoniae, S.aureus, S.pneumoniae, P.jirovecii). Only H.influenzae (30 episodes: 14 Placebo, 16 ColdZyme) and Rhinovirus (50 episodes: 24 Placebo, 26 ColdZyme) were detected with sufficient frequency in each group to permit statistical comparisons on relative viral and bacterial loads.

Variable	Placebo	ColdZyme	P
H.influenzae bacterial load ×10⁻³ Rq (vs RNase P) AUC			0.080
Mean ± SD	351 ± 669	37 ± 84	
Median (interquartile range)	74 (0 - 404)	6 (0 - 19)	
Rhinovirus viral load ×10⁻³ Rq (vs RNase P) AUC			0.043
Mean ± SD	1427 ± 3141	337 ± 887	
Median (interquartile range)	129 (0 - 969)	2 (0 - 93)	

4. Training days affected by URTI episodes

Overall

Variable	Placebo	ColdZyme	P
Training days affected (total)			0.024
Mean \pm SD	7.2 \pm 9.5	3.5 \pm 3.2	
Median (interquartile range)	5.0 (3 - 9)	3.0 (1 - 6)	
Training days missed			0.004
Mean \pm SD	4.0 \pm 4.5	1.6 \pm 2.1	
Median (interquartile range)	3.0 (0 - 6)	1.0 (0 - 3)	
Training reduced (days)			0.310
Mean \pm SD	3.3 \pm 5.7	1.8 \pm 2.1	
Median (interquartile range)	2.0 (0 - 3)	1.0 (0 - 3)	

Only episodes with pathogen-confirmed swabs returned

Variable	Placebo	ColdZyme	P
Training days affected (total)			0.003
Mean \pm SD	8.5 \pm 10.6	3.0 \pm 3.2	
Median (interquartile range)	5.0 (3 - 9)	3.0 (0 - 5)	
Training days missed			0.007
Mean \pm SD	4.5 \pm 4.9	1.6 \pm 2.2	
Median (interquartile range)	3.0 (1 - 7)	0.0 (0 - 3)	
Training reduced (days)			0.042
Mean \pm SD	4.0 \pm 6.4	1.4 \pm 1.6	
Median (interquartile range)	2.0 (0 - 5)	0.5 (0 - 3)	