THE LANCET
Respiratory Medicine

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Clark TW, Beard KR, Brendish NJ, et al. Clinical impact of a routine, molecular, point-of-care, test-and-treat strategy for influenza in adults admitted to hospital (FluPOC): a multicentre, open-label, randomised controlled trial. *Lancet Respir Med* 2020; published online Dec 4. http://dx.doi.org/10.1016/S2213-2600(20)30469-0.

Supplementary appendix

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Definition of clinical outcome measures

Time to clinical improvement

The original chosen outcome measure of 'time to clinical stability' (definition given in the published protocol) was changed to 'time to clinical improvement' (TCCI), defined as the time to hospital discharge OR time to National Early Warning Score 2 (NEWS2) to drop to ≤2 and be maintained for at least 24 hours, in line with a new FDA proposed outcome measure for trials of influenza therapeutics.[1]

Hospital Recovery Scale

Hospital Recovery Scale (HRS) is a 6 category ordinal endpoint assessing a patient's clinical status. The scale provides 6 mutually exclusive conditions ordered from best to worst. The scale is currently being evaluated and used as an outcome measure in trials of influenza therapeutics.[2,3]

Score

1. Not hospitalised
2. Hospitalised in a non-critical care setting, not requiring supplementary oxygen
3. Hospitalised in a non-critical care setting, requiring supplementary oxygen
4. Admitted to the critical care unit not requiring mechanical ventilation
5. Admitted to the critical care unit requiring invasive mechanical ventilation
6. Death

HRS score is measured at various time points depending on the intervention being studied, usually between day 4 and 7.

***Table S1*. Influenza subtypes, viral co-detections and sample type in influenza-infected patients (ITTI population).**

Variable	mPOCT (n=100)	Control (n=102)
Influenza subtype*		
Influenza A	63 (63%)	78 (76%)
Influenza H3N2	40 (40%)	37 (36%)
Influenza H1N1	18 (18%)	30 (2%9)
Influenza A type unspecified	5 (5%)	11 (11%)
Influenza B	37 (37%)	26 (25%)
Non-influenza viruses		
Co-detection with other viruses	9 (9%)	8 (8%)
Influenza + HCoV	5 (5%)	4 (4%)
Influenza + Rhino/enterovirus	2 (2%)	2 (2%)
Influenza + RSV	2 (2%)	0 (0%)
Influenza + Adenovirus	0 (0%)	2 (2%)
Sample type		
NT swab obtained	100 (100%)	102 (100%)
Sputum obtained	13 (13%)	7 (7%)
Positive on NT swab	98 (98%)	102 (100%)
Positive on both sputum and NT swab	10 (10%)	6 (6%)
Positive on sputum only	2 (2%)	0 (0%)

All data are n (%). HCoV=human coronavirus, RSV=respiratory syncytial virus, NT=combined nose and throat swab. *2 patients in the control group had co-detection of influenza A and B.

***Table S2*. Antibiotic use and clinical outcomes in all patients (ITT population).**

Outcome	mPOCT (n=307)	Control (n=306)	Difference or Relative Risk (95% CI)	p value
Antibiotic given*	271 (88%)	278 (91%)	1·0 (0·9 to 1·0)	0·30
Median duration of antibiotics* (days)	6·4 (4·8 to 7·7)	6·3 (4·7 to 7·8)	-0·1 (-0·4 to 0·5)	0·92
Single dose only of antibiotics* given	20/271 (7%)	15/278 (5%)	1·4 (0·7 to 2·6)	0·34
Antibiotics* given for <24 hours	31/271 (11%)	19/278 (7%)	1·7 (1·0 to 2·9)	0·064
IV antibiotics given	196 (64%)	199 (65%)	1·0 (0·9 to 1·1)	0·76
Duration of IV antibiotics (days)	0·9 (0·0 to 2·8)	1·1 (0·0 to 2·8)	0·2 (0·0 to 0·3)	0·39
Single dose only of IV antibiotics given	64/196 (33%)	58/199 (29%)	1·1 (0·8 to 1·5)	0·45
IV antibiotics given for <24 hours	105/196 (54%)	92/199 (46%)	1·2 (1·0 to 1·4)	0·13
Length of stay (days)	3·1 (1·3 to 5·0)	3·0 (1·4 to 6·0)	-0·1 (-0·3 to 0·5)	0·65
Discharged within 24 hours of admission	58 (19%)	50 (16%)	1·2 (0·8 to 1·6)	0·41
Duration of supplementary O_2 (hours)	30·1 (8·5 to 61·1)	30·0 (11·0 to 92·0)	-0·1 (-4·0 to 9·0)	0·59
Time to clinical improvement† (hours)	9·7 (4·2 to 28·3)	12·1 (4·7 to 31·4)	2·4 (-1·0 to 4·1)	0·28

Data are n (%) or median (IQR). CI=confidence interval, IV=intravenous. *Relates to total antibiotic use including all intravenous and oral agents. †Time to clinical improvement is defined on page 3 of the supplementary appendices.

***Table S3*. Adverse events in all patients (ITT population).**

Adverse event (AE)	mPOCT (n=307)	Control (n=306)	Relative Risk (95%CI)	p value
Patients with AEs	87 (28%)	92 (30%)	0·9 (0·7 to 1·2)	0·64
ICU or HDU admission	5 (2%)	9 (3%)	0·6 (0·2 to 1·6)	0·28
Death in hospital	3 (1%)	6 (2%)	0·5 (0·1 to 1·8)	0·31
Death within 30 days	3 (1%)	7 (2%)	0·4 (0·1 to 1·5)	0·20
Readmission within 30 days	33 (11%)	35 (12%)	0·9 (0·6 to 1·5)	0·77
Representation to hospital but without admission, within 30 days	7 (2%)	6 (2%)	1·2 (0·4 to 3·3)	0·79
Prolonged hospitalisation (>7 days)	53 (17%)	61 (20%)	0·9 (0·6 to 1·2)	0·41

All data are n (%) CI=confidence interval, ICU=intensive care unit, HDU=high dependency unit.

Figure S1. Details of subgroups in influenza-infected patients

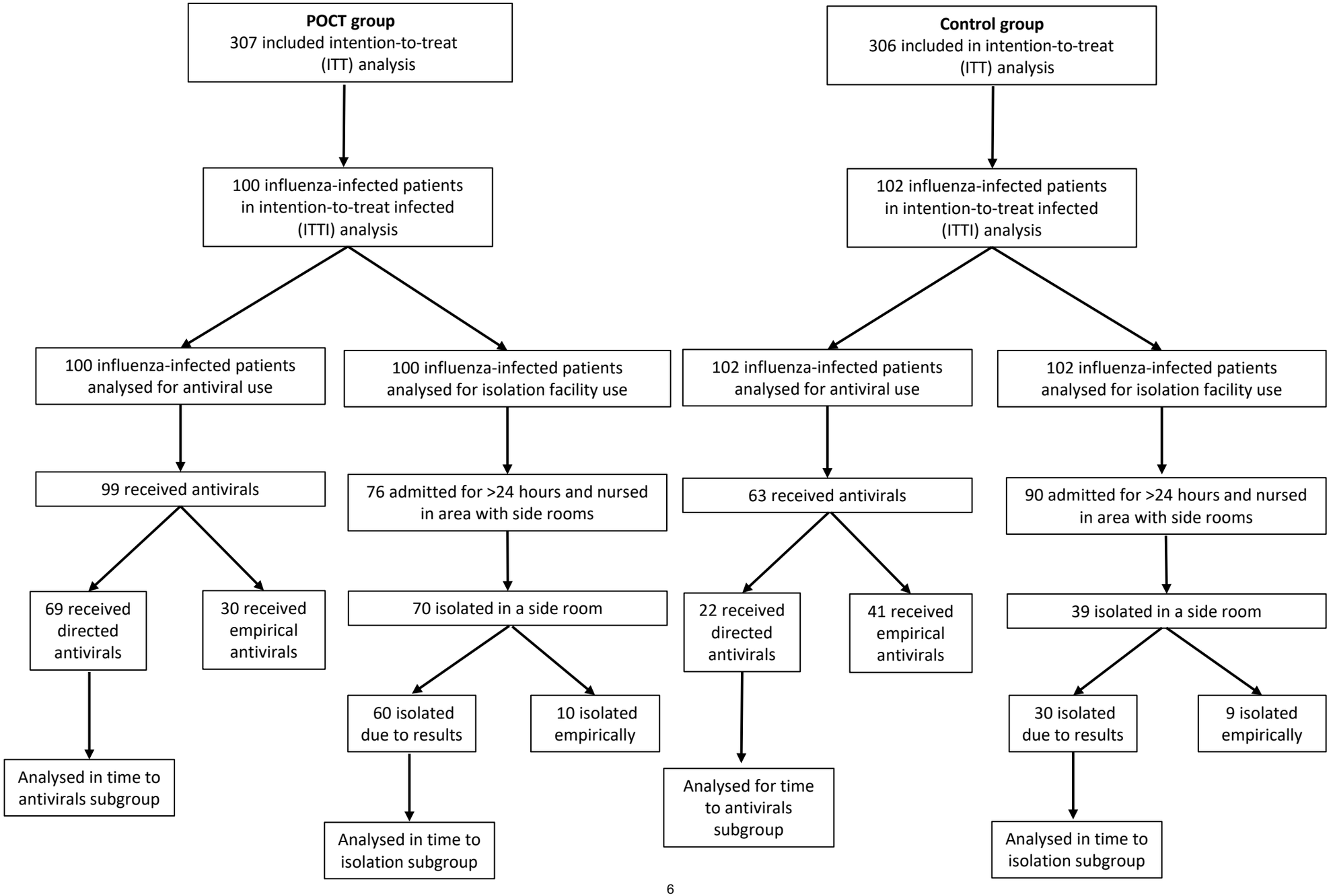
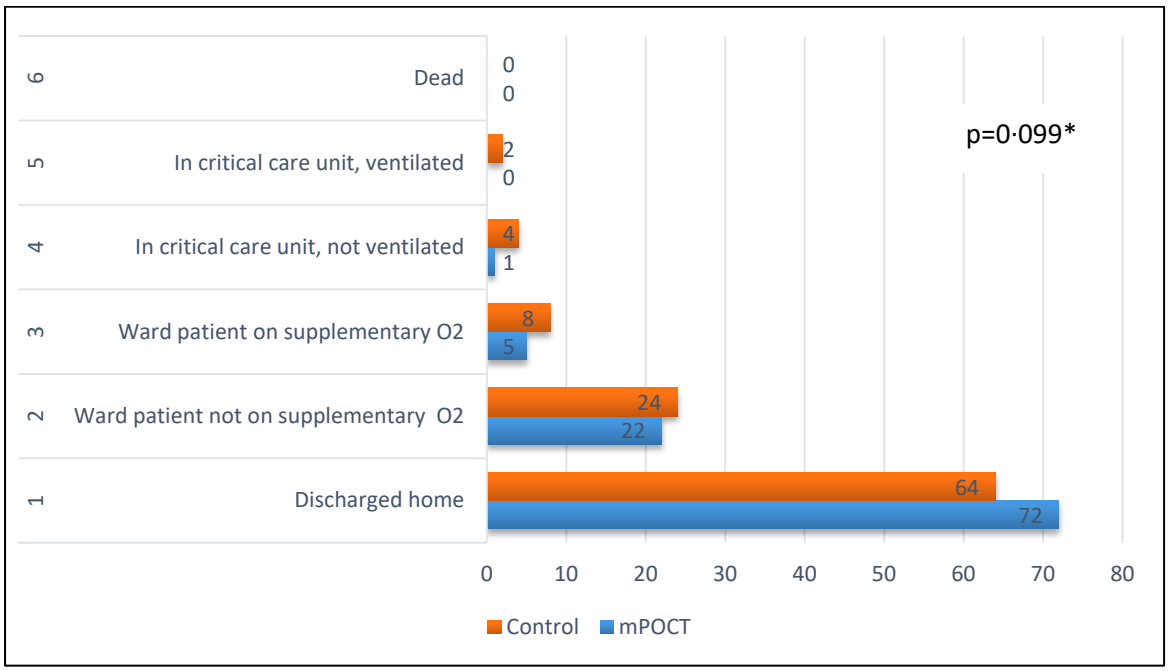
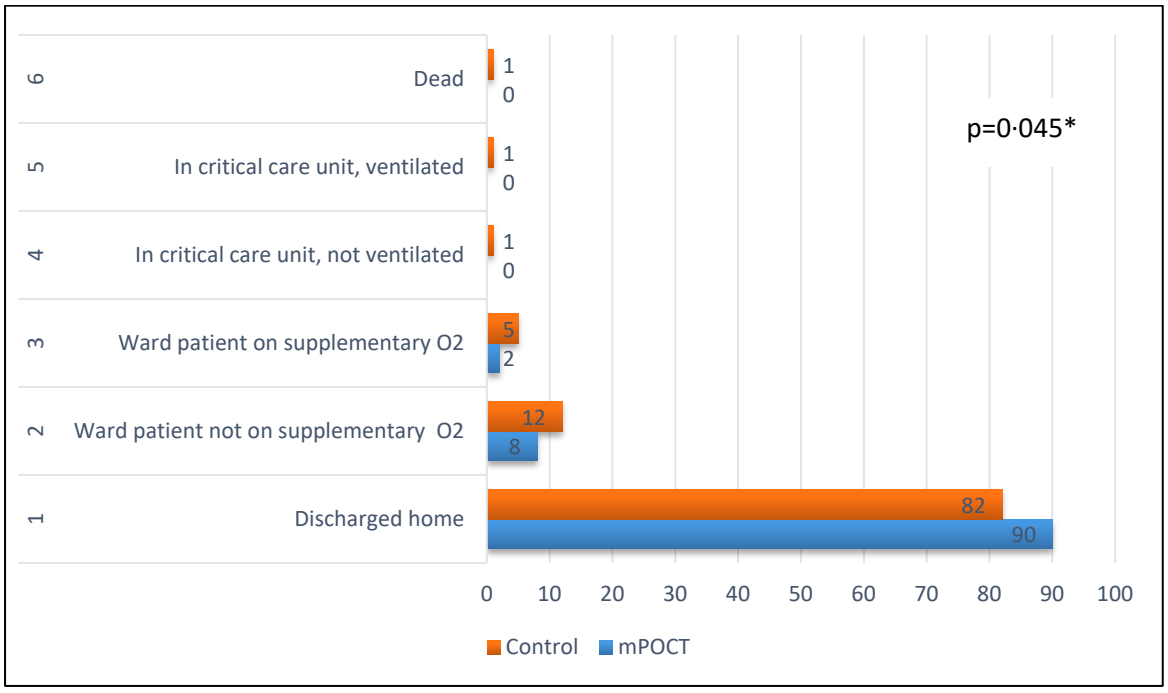


Figure S2a. Hospital Recovery Scale score on day 4 of admission in influenza-infected patients.



*Difference between median scores

Figure S2b. Hospital Recovery Scale score on day 7 of admission in influenza-infected patients.



*Difference between median scores

Figure S3. Time-to-event curve for time to clinical improvement in influenza-infected patients.

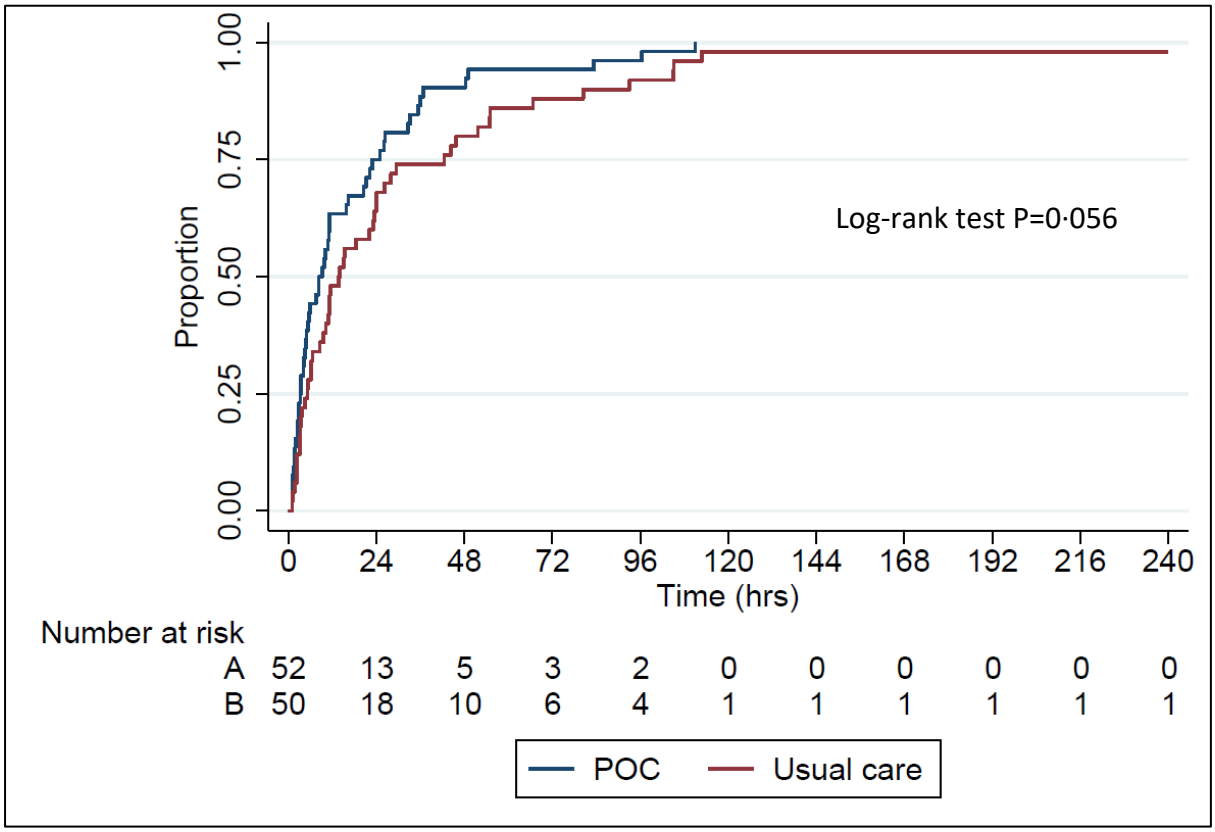


Figure S4. Time-to-event curve for time on supplementary oxygen in influenza-infected patients.

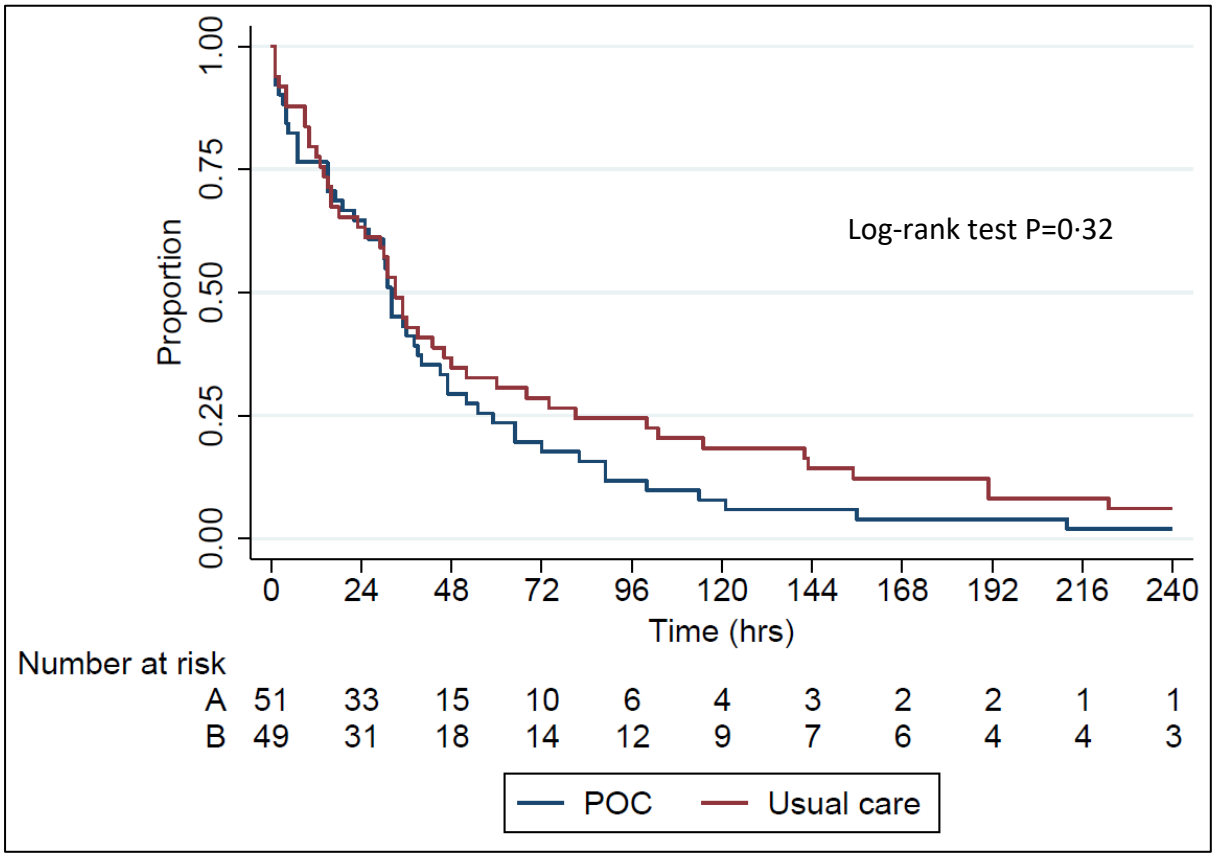
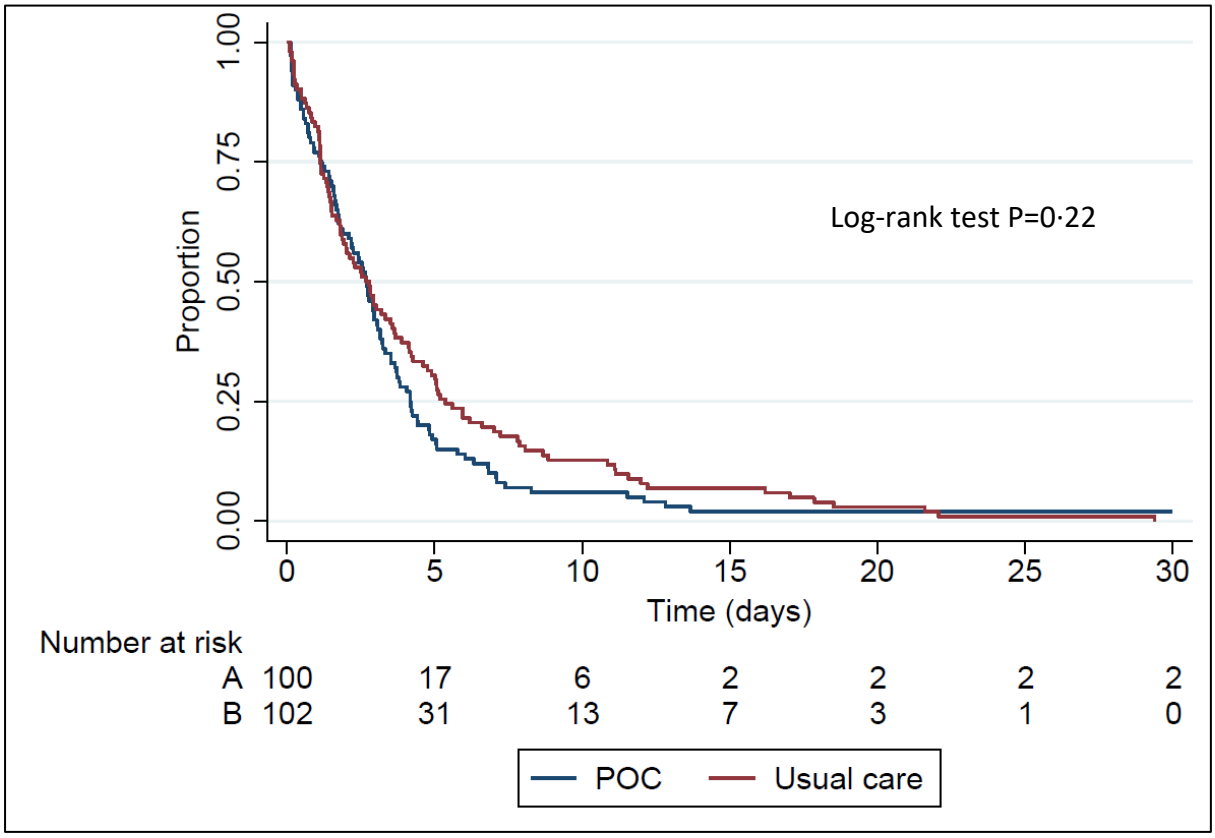


Figure S5. Time-to-event curve for time to discharge in influenza infected-patients.



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1. ClinicalTrials.gov Identifier: NCT03684044. Study to Assess Efficacy and Safety of Baloxavir Marboxil In Combination With Standard-of-Care Neuraminidase Inhibitor In Hospitalized Participants With Severe Influenza. https://clinicaltrials.gov/ct2/show/NCT03684044. Accessed Dec 2019.

2. ClinicalTrials.gov Identifier: NCT03376321. A Study to Evaluate the Efficacy and Safety of Pimodivir in Combination With the Standard-of-Care Treatment in Adolescent, Adult, and Elderly Hospitalized Participants With Influenza A Infection.

https://clinicaltrials.gov/ct2/show/NCT03376321. Accessed December 2019.

3. King JC, Beigel JH, Ison MG, et al. Clinical Development of Therapeutic Agents for Hospitalized Patients With Influenza: Challenges and Innovations. Open Forum Infect Dis 2019;6:ofz137.