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## Time-varying readmission diagnoses during 30 days after hospitalization for COPD exacerbation

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### Abstract

**Objective**—To investigate the longitudinal changes in **principal readmission diagnoses** within 30 days after hospitalization for acute exacerbation of COPD (AECOPD).

**Study setting**—Medicare claims data, 2010-2012.

**Study design**—Retrospective cohort study.

**Data collection methods**—We identified AECOPD hospitalizations aged ≥65 years, and examined the **principal** 30-day readmission diagnoses (respiratory-related, cardiac-related, and other conditions). We also constructed joinpoint regression models to test whether patients with each of the three major readmission conditions had a unique temporal pattern of readmission during the 30-day period.

**Principal findings**—Among 76,697 index hospitalizations with AECOPD, 14,090 (18.4%) were readmitted within 30 days. Respiratory-related conditions accounted for 55% of readmissions. The proportion of respiratory-related conditions as the readmission **diagnosis** decreased from post-discharge day 1 to day 8 (4.0% decrease), and then increased thereafter (13.2% increase;  $P=0.06$ ). Cardiac-related conditions had a similar non-linear trend with an inflection point at day 6 ( $P=0.02$ ), with a subsequent downward trend from day 22 ( $P=0.01$ ). By contrast, the other conditions increased from day 1 to day 6 (15.0% increase), and then significantly decreased (28.8% decrease;  $P=0.04$ ).

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**Conclusions**—The proportions of **principal discharge diagnosis of readmission** changed significantly at around post-discharge day 7. Our findings advance research into identification of the underlying mechanisms and development of targeted interventions to prevent readmissions.

### Keywords

COPD; 30-day readmission; age; hospitalization

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## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a major public health problem, affecting at least 12 million US adults.<sup>1,2</sup> Acute exacerbation of COPD (AECOPD) is responsible for 700,000 hospitalizations each year.<sup>3</sup> Of these, one in five result in readmission within 30 days.<sup>4</sup> To improve the quality of care and curb the healthcare burden of readmissions, the Affordable Care Act developed the Hospital Readmissions Reduction Program (HRRP) which penalizes hospitals for higher than expected 30-day readmission rate for the targeted conditions, including COPD.<sup>5</sup>

To develop effective strategies for reducing readmissions, it is important to understand why and when patients are readmitted after discharge.<sup>6</sup> However, only few studies have investigated the HRRP targeted conditions with regard to differences in 30-day readmission **diagnoses** between the early (e.g., the first 7 days) and late periods following hospital discharge.<sup>6,7,8</sup> Additionally, studies have demonstrated that patient care factors contribute to 30-day readmissions in a time-varying manner<sup>8,9</sup> – e.g., the effects of inpatient management on the readmission risk diminishes rapidly after discharge.<sup>9</sup> These studies suggest that 30-day readmission is not a homogeneous process and that it consists of different causes and time courses. Despite the clinical and policy relevance, no study has tested for the time-varying changes in the 30-day readmission **diagnoses** among the Medicare population, let alone patients hospitalized for AECOPD.

To address this knowledge gap, we analyzed the data of Medicare beneficiaries hospitalized for AECOPD to determine the **principal discharge diagnoses of 30-day readmission** and their different time courses following discharge. We hypothesized that the readmission **diagnoses** vary during the 30-day period and that their proportions change at around 7 days after discharge.

## METHODS

### Design and setting

We conducted a retrospective cohort study using a random sample of 5 million Medicare Beneficiaries from 2010 to 2012 Medicare Research Identifiable Files from the Centers for Medicare & Medicaid Services (CMS). Final action, fee-for-service, claims data, inpatient files were used to identify all Medicare beneficiaries who were hospitalized for AECOPD. To enable follow-up of specific patients, inpatient claims for individual patients were linked with the use of the Health Insurance Claim Number–Beneficiary Identification Code. The beneficiary identification code was then used to link beneficiary enrollment and

demographics information from the Master Beneficiary Summary File, and the Chronic Conditions File that includes 27 chronic condition data warehouse flags. The institutional review board of Massachusetts General Hospital approved this study (2013P002545).

### Study population

Based on the CMS publicly-reported readmission measures,<sup>10</sup> we identified all hospitalizations made by patients (age ≥ 65 years) with a primary hospital discharge diagnosis of COPD using the *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* diagnostic codes (*ICD-9-CM* diagnosis codes 491.21, 491.22, 491.8, 491.9, 492.8, 493.20, 493.21, 493.22, and 496), or those with a primary diagnosis of respiratory failure (*ICD-9-CM* diagnosis codes 518.81, 518.82, 518.84, and 799.1) and secondary diagnosis of COPD (e-Table 1). We excluded patients who left the hospital against medical advice, those who were transferred to another acute care facility, those who died during the index hospitalization, those without continuous enrollment in Medicare fee-for-service for one year prior to the date of the index hospitalization, and those without at least 30 days post-discharge enrollment in Medicare fee-for-service. Transfers were identified as consecutive claims on the same day with different provider (hospital) numbers for the same beneficiary based on CMS methodology.<sup>10</sup> Additionally, according to the CMS recommendations,<sup>10</sup> we considered only the first readmission within 30 days of discharge as a readmission while we did not count additional readmissions within the 30-day period as 30-day readmissions or index hospitalizations. We considered subsequent hospitalizations occurring after 30 days from discharge as index hospitalizations if they met the inclusion criteria.

### Measurements

Medicare Master Beneficiary Summary Files included information on patient demographics (age, sex, race/ethnicity), quartiles for median household income, hospital admission and discharge dates, and enrollment status for Medicare beneficiaries. Median household income was determined by matching patients' home ZIP codes and year of enrollment to ZIP code-linked estimates of annual median household incomes.<sup>11</sup> Baseline health status was evaluated by the sum of the *Chronic Condition Data Warehouse (CCW)* defined chronic conditions that include 27 chronic condition indicator variables. These indicator variables have been developed from the claims data for chronic conditions that were deemed to be relevant to studies of Medicare-only beneficiaries.<sup>12</sup> From the 27 CCW chronic conditions, we excluded COPD and asthma for calculating comorbidities.

### Outcomes

The outcome was the primary discharge diagnosis at the readmission. A readmission was a hospital admission at any hospital for any reason occurring within 30 days of discharge from the index hospitalization for AECOPD.<sup>10</sup> First, the principal diagnoses (>14,000 *ICD-9-CM* diagnosis codes) were consolidated into 285 mutually exclusive diagnostic categories using the Agency for Healthcare Research Quality's Clinical Classifications Software (CCS),<sup>13</sup> as done previously.<sup>7,14,15</sup> Then, to make clinical interpretation more meaningful, and to address potential misclassifications, we further grouped the discharge diagnoses into 3 mutually-exclusive groups (e-Table 2): respiratory-related conditions (e.g., COPD, respiratory failure,

pneumonia; CCS 122-134), cardiac-related conditions (e.g., heart failure; CCS 96-108), and other conditions (e.g., sepsis).<sup>7</sup>

### Statistical analysis

To test whether patients with each of the three major readmission conditions (i.e., respiratory-related, cardiac-related, and other conditions) had a unique temporal pattern of readmission over 30-day period, we calculated the relative proportion of three conditions at each post-discharge day. Then, we constructed an **unadjusted** joinpoint regression model to investigate the change in the proportion of each condition during the 30-day period by using the Joinpoint Regression Program version 4.5.0.1 (Statistical Research and Applications Branch, National Cancer Institute).<sup>16</sup> This analysis compares models by starting with no joinpoints and subsequently testing whether 1 joinpoints needed to be entered into the model to best fit the data. If there is no joinpoint, it would suggest no significant changes over time. If there are one or more joinpoints, it would suggest significant changes in the outcome of interest. With the use of Bayesian information criterion method, we identified optimal number of joinpoints in the trend.<sup>17,18</sup> We also illustrated the change in the proportion of each grouped **readmission diagnosis** by using a LOWESS smoother with calculating 95% CI using a bootstrap method. In the sensitivity analysis, we stratified the analysis by age category (65-84 years vs. ≥85 years) according to a standard terminal age category in disease reporting in the US<sup>19</sup> and the previous literature.<sup>6,20,21</sup> We also used summary statistics to compare the proportion of each grouped **diagnosis** and five most frequent CCS-defined **principal discharge diagnoses** between age categories. As the temporal change was not examined between patients with different readmission **diagnoses** (i.e., no assumption of exchangeability was made), adjustment for covariates (e.g., demographics) was not conducted. We analyzed data using STATA 15.0 (StataCorp, College Station, TX) and R statistical software (version 3.4.0).

## RESULTS

### Baseline Characteristics

From 2010 to 2012, we identified 118,198 hospitalizations for AECOPD. Of these, 76,697 (65%) were determined as index hospitalizations at risk for 30-day readmissions (53,486 unique patients), based on the CMS-defined methodology. The index hospitalizations were made by patients with the median age of 76 years (IQR, 71-83 years); 60% were female, 85% were non-Hispanic white, and 73% had ≥5 comorbidities (Table 1).

### 30-day Readmission Diagnosis

The crude 30-day readmission rate within 30 days after hospitalization for AECOPD was 18.4%. Overall, respiratory-related conditions accounted for 54.7% of readmission **diagnoses**, cardiac-related conditions for 14.4%, and other conditions for 30.9% (eTable 3). By *CCS* category, COPD (30.0%) was the most frequent **readmission diagnosis**, followed by pneumonia (9.4%), respiratory failure (8.5%), heart failure (6.4%), and sepsis (4.6%). Among the other conditions, overall, septicemia was the most common readmission diagnosis (16% of the other conditions), followed by renal failure (6%), fluid and electrolyte disorders (5%), and gastrointestinal hemorrhage (5%). Compared to patients aged 65-84

years, those aged  $\geq 85$  years were more likely to be readmitted with cardiac-related or other conditions (both  $P < 0.001$ ).

### Time-varying readmission diagnoses during the 30-day period

Figure 1 illustrates the changes in the proportion of respiratory-related, cardiac-related, and other conditions by day as the 30-day readmission **diagnosis**. For example, overall, the proportion of respiratory-related conditions decreased immediately after discharge, and the downward trend changed to an upward trend around one week after discharge; the other conditions had a different pattern. Specifically, the joinpoint model demonstrated that the proportion of respiratory-related conditions initially decreased by 4.0% until day 8 (0.5% decrease per day; Table 2) and then increased by 13.2% until day 30 (0.6% increase per day), reflecting an inflection point at day 8 ( $P = 0.06$ ). Likewise, the proportion of cardiac-related conditions decreased by 18.6% until day 6 (3.1% decrease per day), increased by 20.8% until day 22 (1.3% increase per day), and then again decreased by 16.8% (2.1% decrease per day), with significant inflection points at days 6 and 22 (both  $P < 0.05$ ). By contrast, the proportion of other conditions increased by 15.0% until day 6 (2.5% increase per day), and then decreased by 28.8% (1.2% decrease per day), reflecting a significant inflection point at day 6 ( $P = 0.04$ ).

Stratification by age category showed similar non-linear patterns of the proportion of 30-day readmission **diagnoses** during the 30-day period – with a potentially greater magnitude of changes in the older group (Figure 1). Although statistical power was limited in this subgroup analysis, the joinpoint models demonstrated that the proportion of the other conditions had an earlier inflection point (day 3) in patients aged 65–84 years while that had late inflection points (days 12 and 16) in patients aged  $\geq 85$  years (Table 2).

## DISCUSSION

In nationally-representative data from 76,697 Medicare beneficiaries hospitalized for AECOPD, we found time-varying **30-day principal readmission diagnoses**. Specifically, the proportions of respiratory- and cardiac-related conditions had a nadir in the early phase (day 7) of the 30-day period and increased thereafter, while the other conditions had a different pattern. Compared to patients (aged 65–84 years), older patients (aged  $\geq 85$  years) were more likely to be readmitted with cardiac-related or other conditions, and appeared to have more pronounced changes in the **readmission diagnoses**.

Consistent with our findings, a prior study using the 2006–2010 Medicare data reported that, after hospitalization for COPD, respiratory-related conditions accounted for approximately 50% of 30-day readmissions and that COPD was the leading **diagnosis**.<sup>7</sup> In this previous study, the proportion of COPD as the readmission diagnosis was 25% in the early phase and 30% in the late phase of 30-day period following discharge.<sup>7</sup> Additionally, in patients with the three other HRRP conditions (heart failure, myocardial infarction, and pneumonia), another study using Medicare data also demonstrated the differences in the proportion of readmissions for recurrent heart failure and pneumonia between different time periods (0–3 days, 4–7 days, 8–15 days, and 16–30 days).<sup>6</sup> Our study corroborates these prior studies, and extends them by demonstrating, for the first time, significant changes in the proportion of

three major **readmission diagnoses** (i.e., respiratory-related, cardiac-related, and other conditions) with unique inflection points after being hospitalized for AECOPD.

The underlying mechanisms of the time-varying **readmission diagnoses** are likely multifactorial. First, the timing of the changes (e.g., the nadir of the respiratory-related conditions at post-discharge day 8) corresponds to the timing of recovery from AECOPD – a function of acute illness severity and AECOPD management. A prospective cohort study reported that the median time to recover from AECOPD is 7 days and that peak expiratory flow improves by day 6 from the onset.<sup>22</sup> Additionally, the subsequent increase in the respiratory conditions for readmission might be attributable to the diminished in-hospital treatment effects and to the transitions in care from hospital-level to community-level care.<sup>9,23</sup> Indeed, a prior study using state-level administrative datasets reported that the contribution of hospital care to readmission risks declines after discharge, reaching a nadir at post-discharge day 7.<sup>9</sup> Furthermore, in contrast to the intensified treatment for AECOPD and related respiratory conditions (e.g., pneumonia) during hospitalization, it is possible that comorbid conditions other than AECOPD (e.g., diabetes) are undermanaged during the hospitalization at discharge.<sup>24</sup> Moreover, the literature has also shown that hospitalized patients (particularly older individuals) acquire vulnerability to myriad conditions that lead to a readmission – post-hospital syndrome.<sup>25,26</sup> These mechanisms may explain, at least partially, the observed increase in the readmissions for other conditions in the early phase of 30-day period.

In conjunction with the previous literature,<sup>6–8,22,23,27,28</sup> our findings suggest that, while readmission is one of the easy-to-measure metrics, its underlying mechanisms are complex (e.g., patient's clinical factors, quality of inpatient, transitional, and outpatient care, social support, transportation, health literacy and behavior). The quality of care during the index hospitalizations is solely a beginning part of readmission processes and its contribution rapidly diminishes after discharge. In contrast, the relative importance of other factors (e.g., chronic illness severity, outpatient care, social- and community-level factors) increases over time. In this context, this hypothesis generating study facilitates future investigations. To reduce readmissions and improve outcomes in patients with COPD, future studies should examine which of these readmissions are potentially preventable, identify their underlying mechanisms, and develop targeted preventive interventions based on the time-periods (e.g., 0-7 and 8-30 day periods). Indeed, studies have shown that well-executed communication among hospital providers, patients, and receiving providers at hospital discharge lowers readmissions in patients with chronic conditions, including COPD.<sup>23,24,28–30</sup>

### Potential Limitations

Our study has several potential limitations. First, because this study is based on the claims data, misclassification of hospitalizations is possible. Nevertheless, we identified hospitalizations for COPD according to the CMS definitions<sup>11</sup> which have a high specificity and positive predictive value (both 90%).<sup>31</sup> Furthermore, Medicare data are considered accurate, are rigorously tested, and widely used to investigate readmissions.<sup>32,33</sup> Second, the Medicare data do not contain some useful clinical and sociodemographic information which precluded us from evaluating the contribution of chronic severity of COPD and patient post-

discharge environment. Therefore, our study does not completely address the complexity of mechanisms underlying readmissions (e.g., poor social support networks). **Third, the current study used unadjusted joinpoint regression models because the temporal change was not compared between patients with different readmission diagnoses (i.e., no assumption of exchangeability was made). Yet, our findings might have been confounded by time-varying factors (e.g., comorbidities, socioeconomic status) even in a relatively short period (i.e., 30-day period after hospital discharge).** Finally, the study population comprised Medicare beneficiaries with age  $\geq 65$  years, and, therefore, our inference may be not generalizable to younger individuals with COPD. Regardless, our study population accounts for 70% of hospitalizations for AECOPD,<sup>4</sup> and is the one on which recent national improvement efforts have focused.<sup>5</sup>

## CONCLUSIONS

Based on the nationally-representative 30-day readmission data of 76,697 Medicare beneficiaries hospitalized for AECOPD, we found time-varying **principal readmission diagnoses**, with important changes occurring at around post-discharge day 7. The respiratory- and cardiac-related conditions had their peak at the late phase while the other conditions had their peak at the early phase of the 30-day period following discharge. Additionally, older patients (aged  $\geq 85$  years) were more likely to be readmitted with cardiac-related or other conditions, and appeared to have more pronounced longitudinal changes in their readmission **diagnoses**. These findings lend additional support to the concept that the underlying mechanisms of 30-day readmissions are complex. For clinicians, the observed heterogeneity in **readmission diagnoses** underscore the importance of continued efforts to improve in-hospital and post-discharge care for COPD and comorbidities. For researchers and policymakers, our findings advance research into identification of the complex underlying mechanisms and development of targeted interventions to prevent readmissions.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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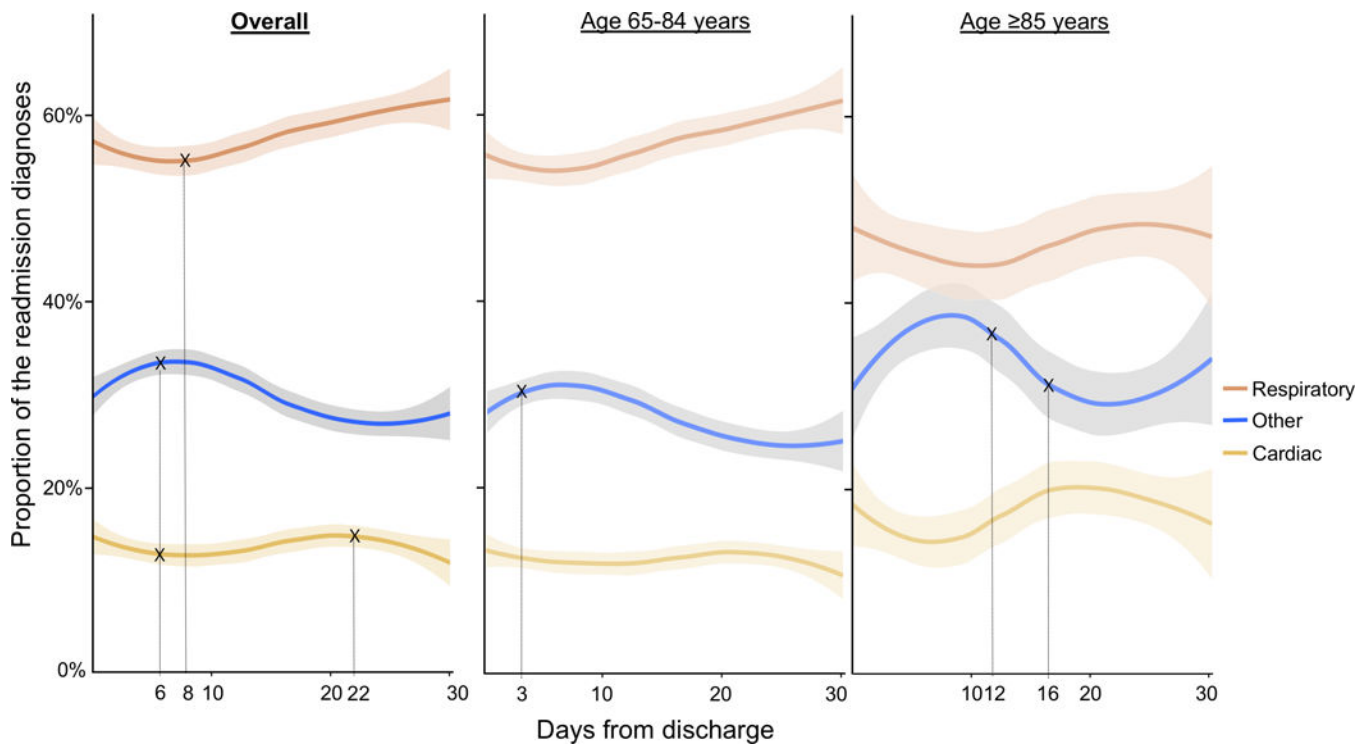
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**Figure 1. Changes in the proportion of the three grouped 30-day readmission diagnoses, overall and stratified by age group**

Overall, there was a non-linear U-shaped change in the proportion of respiratory-related conditions (red) as the readmission diagnosis with an inflection point at day 8 after discharge. The proportion of cardiac-related conditions (yellow) had a similar non-linear pattern with inflection points at day 6 and day 22. By contrast, the proportion of the other conditions (blue) had a different pattern with an inflection point at day 6. Compared to patients aged 65-84 years, those aged ≥85 years appeared to have a greater magnitude of changes, with delayed inflection points for the other conditions (at days 3 and 12). Marks (x) indicate the inflection points.

**Table 1**

Characteristics of index hospitalizations for acute exacerbation of chronic obstructive pulmonary disease, 2010-2012

Variables	Overall (n=76,697)
<b>Age (year), median (IQR)</b>	76 (71-83)
<b>Age category</b>	
65-84 years	62,257 (81)
85 years	14,440 (19)
<b>Sex</b>	
Male	30,987 (40)
Female	45,710 (60)
<b>Race/ethnicity</b>	
Non-Hispanic white	65,257 (85)
Non-Hispanic black	6,536 (9)
Hispanics	3,303 (4)
Other/unknown	1,601 (2)
<b>Median household income</b>	
1st quartile (lowest)	17,299 (23)
2nd quartile	17,860 (24)
3rd quartile	18,380 (25)
4th quartile (highest)	21,485 (29)
<b>Number of comorbidities *</b>	
0-1	3,754 (5)
2-4	17,325 (23)
5	55,618 (73)
<b>Discharge year</b>	
2010	27,037 (35)
2011	27,046 (35)
2012	22,614 (29)
<b>Geographic region</b>	
Northeast	13,908 (18)
Midwest	19,586 (26)
South	34,056 (44)
West	9,007 (12)
Guam, Puerto Rico and Virgin Islands	140 (0.18)

Data were shown as n (%) unless otherwise specified.

Abbreviation: IQR, interquartile range

\* Comorbidities were based on 27 chronic conditions (excluding chronic obstructive pulmonary disease) defined by the Centers for Medicare & Medicaid Services.

**Table 2**  
Changes in the proportion of grouped 30-day readmission diagnoses by using joinpoint regression analysis

Conditions as the readmission diagnosis	Trend 1			Change between trends 1 and 2			Trend 2			Change between trends 2 and 3			Trend 3	
	Total change, %	Change by day, %	Day of the change	P value for the trend change	Total change, %	Change by day, %	Day of the change	P value for the change	Total change, %	Change by day, %	Day of the change	P value for the change	Total change, %	Change by day, %
<b>Overall (n=14,090)</b>														
Respiratory-related	-4.0%	-0.5%	Day 8	0.06	13.2%	0.6%	-		20.8%	1.3%	Day 22	0.01	-16.8%	-2.1%
Cardiac-related	-18.6%	-3.1%	Day 6	0.02	20.8%	1.3%	Day 22	0.01	20.8%	1.3%	Day 22	0.01	-16.8%	-2.1%
Other	15.0%	2.5%	Day 6	0.04	-28.8%	-1.2%	-		-28.8%	-1.2%	-		-16.8%	-2.1%
<b>Age category</b>														
<b>Age 65-84 years (n=11,463)</b>														
Respiratory-related	15.0%	0.5%	-											
Cardiac-related	3.0%	0.1%	-											
Other	29.1%	9.7%	Day 3	0.29	-29.7%	-1.1%	-		-29.7%	-1.1%	-		-16.8%	-2.1%
<b>Age 85 years (n=2,627)</b>														
Respiratory-related	21.0%	0.7%	-											
Cardiac-related	6.0%	0.2%	-											
Other	21.6%	1.8%	Day 12	0.18	-32.0%	-8.0%	Day 16	0.21	-32.0%	-8.0%	Day 16	0.21	14.0%	1.0%