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PRIMUS: Prompt Initiation of Maintenance Therapy in the US

An Analysis of Triple Therapy Initiation Following a Disease Exacerbation Among Patients with Chronic Obstructive Pulmonary Disease

MAAZAP US-91735 Approved 08/24

PRIMUS Study Intent and Summary

Does prompt initiation of triple therapy following an exacerbation lower the odds of future exacerbations and reduce healthcare costs compared to delayed initiation?[1]

The PRIMUS study found that, among patients with COPD, prompt initiation of triple therapy following an exacerbation or COPD hospitalization (for severe exacerbation) was associated with decreased odds of future exacerbations and reduced healthcare costs[1,2]

1. Tkacz J, et al. *Int J Chron Obstruct Pulmon Dis.* 2022;17:329-342; 2. Evans KA, et al. Article and supplementary appendix. *J Manag Care Spec Pharm*. 2022;28(12):1366-1377.

PRIMUS examined the initiation of triple therapy specifically in the context of current treatment recommendations

PRIMUS: Exacerbation severity defined by treatment needed[2]

Moderate:
COPD-related office or ER visit associated with an **antibiotic or systemic corticosteroid prescription**

Severe:
Hospitalization visit with primary diagnosis for COPD

The GOLD Report defines a COPD exacerbation as an **event characterized by dyspnea and/or cough and sputum that worsen over <14 days**[1]

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for prevention, diagnosis and management of COPD: 2024 report. Accessed August 12, 2024. https://goldcopd.org/2024-gold-report/; 2. Tkacz J, et al. *Int J Chron Obstruct Pulmon Dis.* 2022;17:329-342.

PRIMUS examined whether the prompt initiation of triple therapy lowered the odds of future exacerbations and reduced healthcare costs, compared to delayed and very delayed initiation following an exacerbation

PRIMUS outcomes during the 12-month follow-up period

Occurrence of exacerbations[a]

Moderate or Severe
Moderate
Severe

Healthcare resource utilization and costs[a]

Total all-cause healthcare
COPD-related

[a]Adjusted for baseline patient characteristics, exacerbation history, and healthcare utilization.

Tkacz J, et al. *Int J Chron Obstruct Pulmon Dis.* 2022;17:329-342.

PRIMUS Study Overview[1]

Retrospective observational analysis of US healthcare claims data[a]

Study period: Between January 1, 2009 and March 31, 2020.

[a]Claims database was Merative (formerly IBM Watson Health) MarketScan® Commercial, Medicare Supplemental, and Multi-State Medicaid Research Databases.[1,2]

1. Tkacz J, et al. *Int J Chron Obstruct Pulmon Dis.* 2022;17:329-342; 2. Evans KA, et al. Article and supplementary appendix. *J Manag Care Spec Pharm*. 2022;28(12):1366-1377.

Data Sources and Methods[1]

Key inclusion criteria

- ≥40 years old on index exacerbation date
- ≥12 months of continuous enrollment (medical and pharmacy benefits) before (baseline) and after (follow-up) index exacerbation date
- ≥2 moderate or ≥1 severe exacerbation within the 12-month period preceding triple therapy initiation

Key exclusion criteria

- Triple therapy use during baseline

Triple therapy defined as:

- Open triple therapy with separate pharmacy claims for ICS, LAMA and LABA ≥14 consecutive and 30 total days of overlap during a 90-day period **or**
- Closed triple therapy (ICS+LABA+LAMA)[a]

Data sources (US health insurance claims):

Statistical analysis:

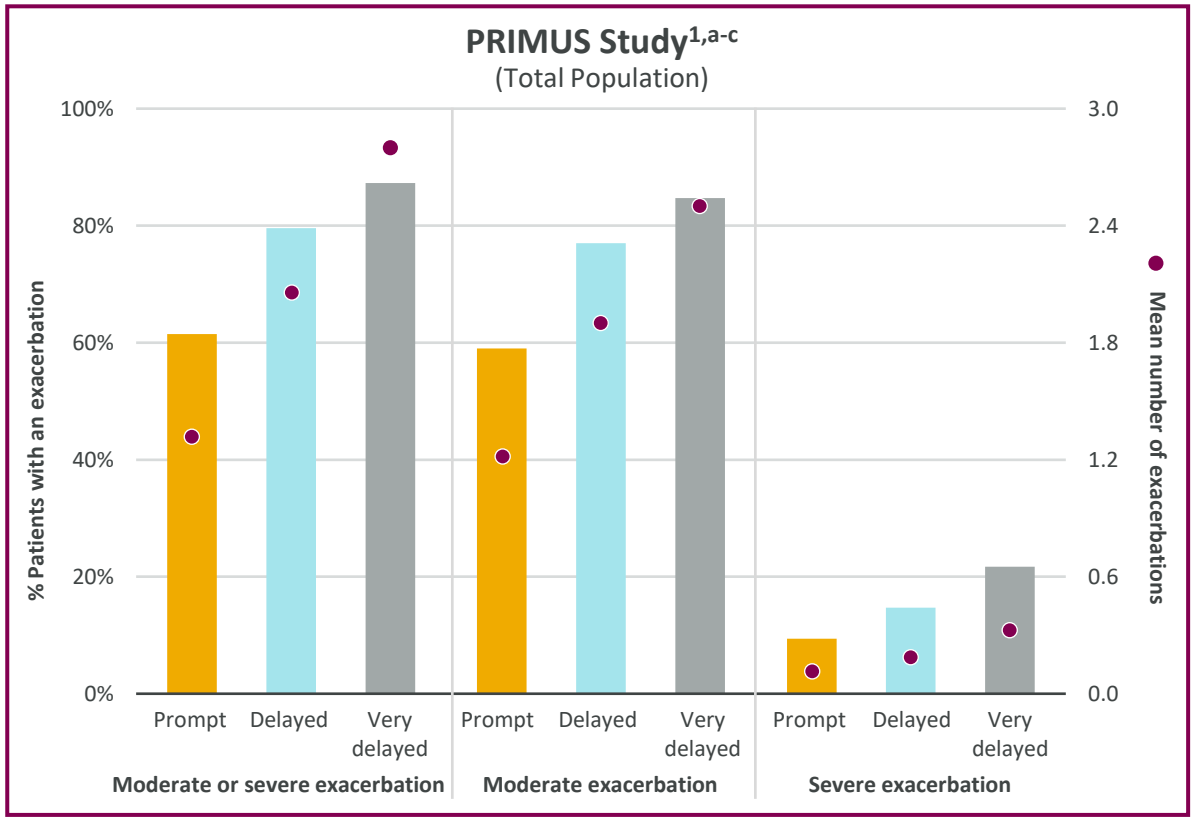
- Descriptive analyses
- Multivariable logistic regression for 30-day delay effect on odds of future events and negative binomial regression for change in number of exacerbations
- Generalized linear models to examine all-cause and COPD-related costs

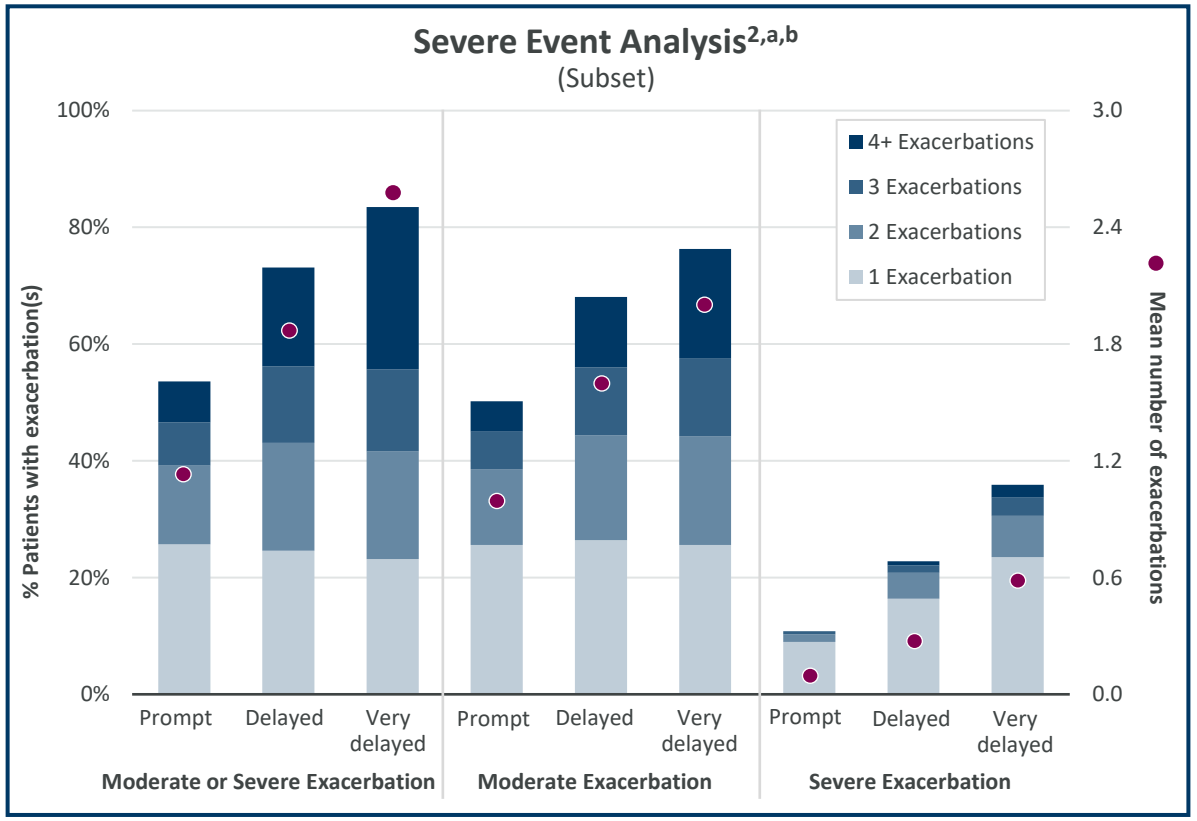
All models controlled for baseline patient characteristics, exacerbations, and healthcare utilization.

[a]Index treatment window (January 2010 to March 2019) and timing of closed triple therapy approval in the US (September 2017) resulted in only about 3% of the total study population and 1.7% of patients in the severe event analysis receiving closed triple therapy as their index treatment.[1,3]

1. Tkacz J, et al. *Int J Chron Obstruct Pulmon Dis.* 2022;17:329-342; 2. Evans KA, et al. Article and supplementary appendix. *J Manag Care Spec Pharm*. 2022;28(12):1366-1377; 3. Data on File, REF-174212, AstraZeneca Pharmaceuticals LP.

Triple therapy delay was associated with increased COPD exacerbations





Of those patients who had delayed or very delayed triple therapy initiation, **80% to ~90%** experienced another COPD exacerbation, compared to only ~60% of those who initiated triple therapy within 30 days of an exacerbation[1,c]

Consistent trends were observed among the subset of patients with a severe index exacerbation; however, patients who had delayed or very delayed triple therapy initiation were more than **2 and 3 times as likely** as prompt patients, respectively, to have a subsequent severe exacerbation[2,b]

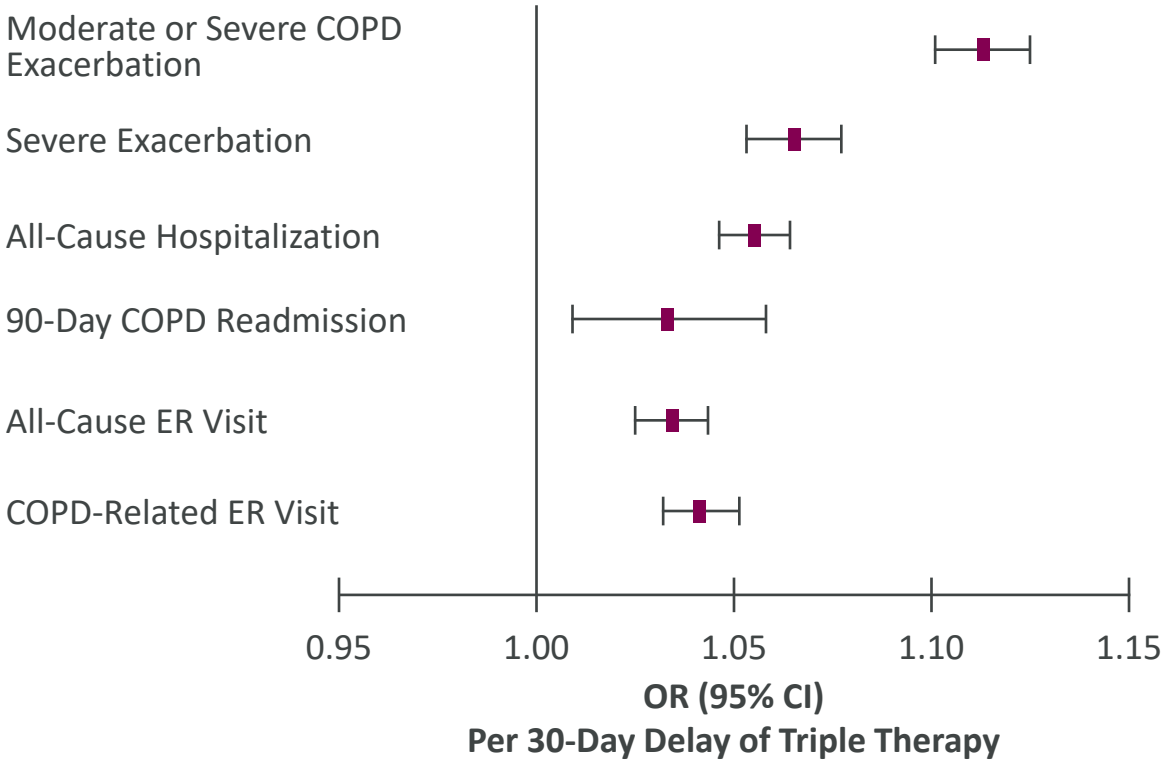
Prompt: ≤30 days post exacerbation; Delayed: 31-180 days post exacerbation; Very delayed: 181-365 days post exacerbation.

[a]Unadjusted analyses; [b]During 12-month follow-up period; [c]All comparisons between groups were statistically significant ($P<0.05$) for outcomes shown.

1.Tkacz J, et al. *Int J Chron Obstruct Pulmon Dis.* 2022;17:329-342; 2. Evans KA, et al. Article and supplementary appendix. *J Manag Care Spec Pharm*. 2022;28(12):1366-1377.

Each 30-day delay in initiating triple therapy was associated with an increase in the odds of another COPD exacerbation

Adjusted OR for HCRU and Exacerbations[a]



For the full study population, the mean time to triple therapy was 4 months, which equated to:

44%

GREATER ODDS OF A MODERATE OR SEVERE EXACERBATION

26%

GREATER ODDS OF A SEVERE EXACERBATION

compared with a patient who promptly received triple therapy <30 days after their exacerbation[b]

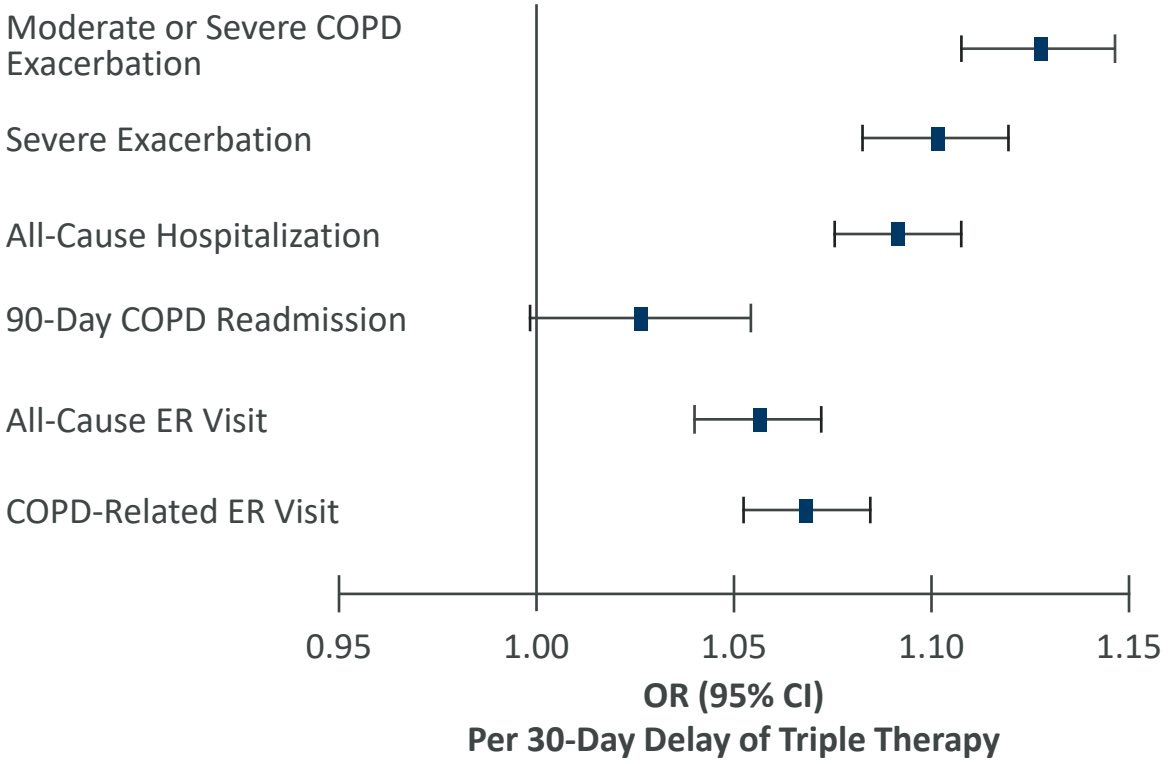
[a]During the 12-month follow-up period per 30-day delay of triple therapy, controlled for baseline patient characteristics, exacerbation history, and healthcare utilization; [b]11% and 6.5% increase, respectively, per 30-day delay of triple therapy.

Tkacz J, et al. *Int J Chron Obstruct Pulmon Dis.* 2022;17:329-342.

Following a COPD hospitalization,[a] each 30-day delay in initiating triple therapy was associated with a relatively greater increase in the odds of a future exacerbation[1,2]

Severe Event Analysis Subset

Adjusted OR for HCRU and Exacerbations[1,b]



Among patients hospitalized for a COPD exacerbation, the mean time to triple therapy was ~3.5 months, which approximated to:

53%

GREATER ODDS OF A MODERATE OR SEVERE EXACERBATION

40%

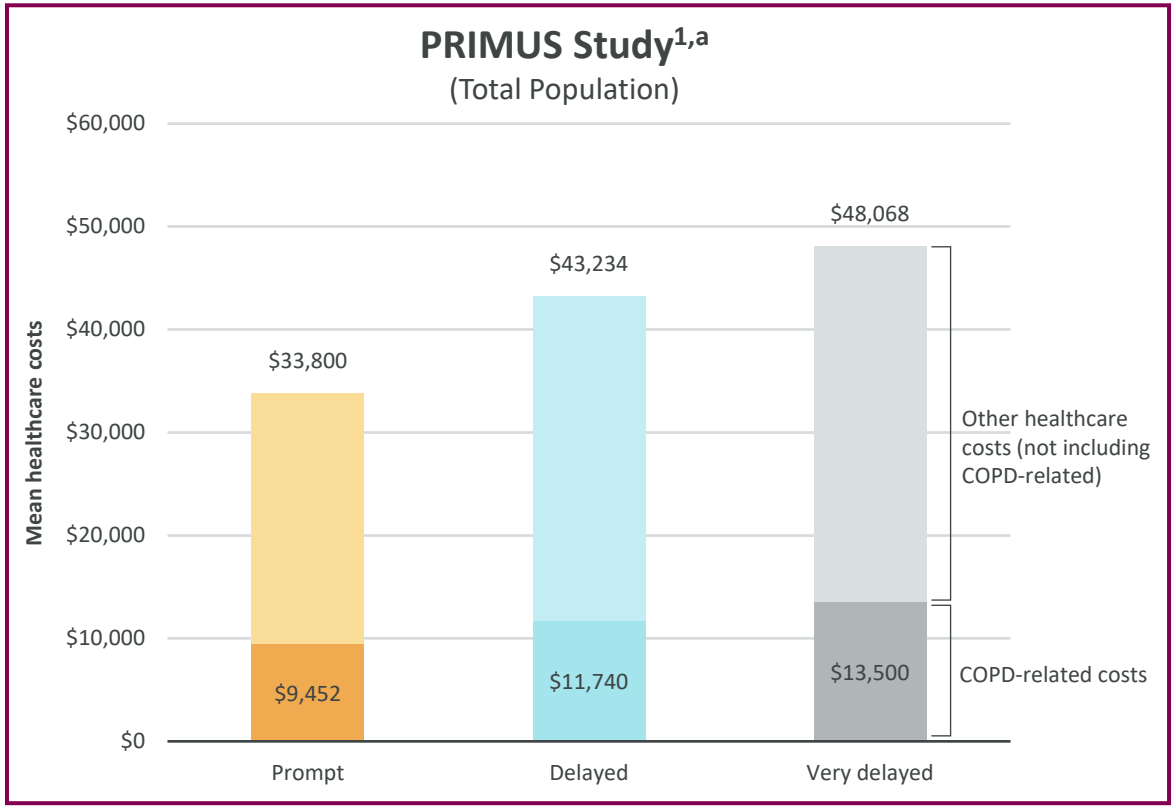
GREATER ODDS OF A SEVERE EXACERBATION

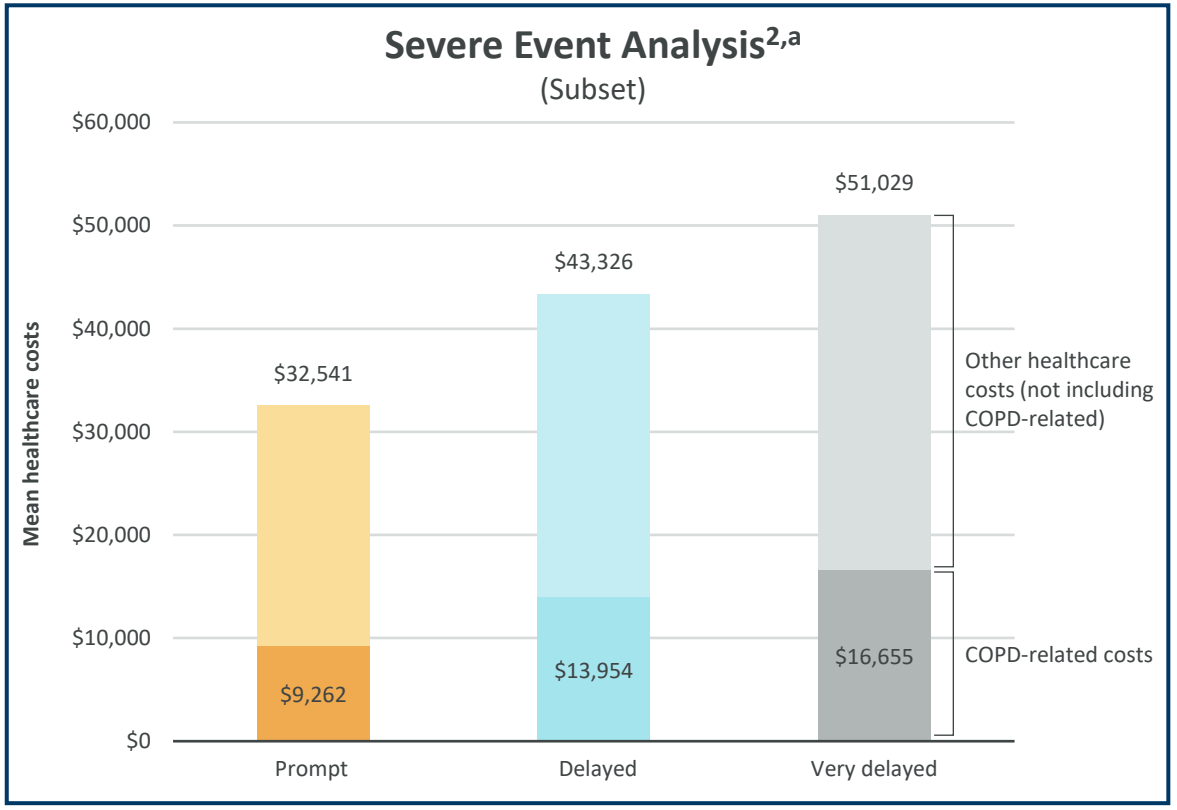
compared with a patient who promptly received triple therapy <30 days after their severe index exacerbation[1,c]

[a]Hospitalization for a severe COPD exacerbation; [b]During the 12-month follow-up period per 30-day delay of triple therapy, controlled for baseline patient characteristics, exacerbation history, and healthcare utilization; [c]13% and 10% increase, respectively, per 30-day delay of triple therapy.

1. Evans KA, et al. Article and supplementary appendix. *J Manag Care Spec Pharm*. 2022;28(12):1366-1377; 2. Tkacz J, et al. *Int J Chron Obstruct Pulmon Dis.* 2022;17:329-342.

Triple therapy delay was associated with increased COPD-related costs





Patients who had delayed or very delayed triple therapy initiation incurred **28% and 42% greater total healthcare costs**, respectively, compared to those who received prompt triple therapy[b]

Patients who had delayed or very delayed triple therapy initiation following a severe COPD exacerbation incurred **33% and 57% greater mean total healthcare costs**, respectively, compared to those who received prompt triple therapy[b]

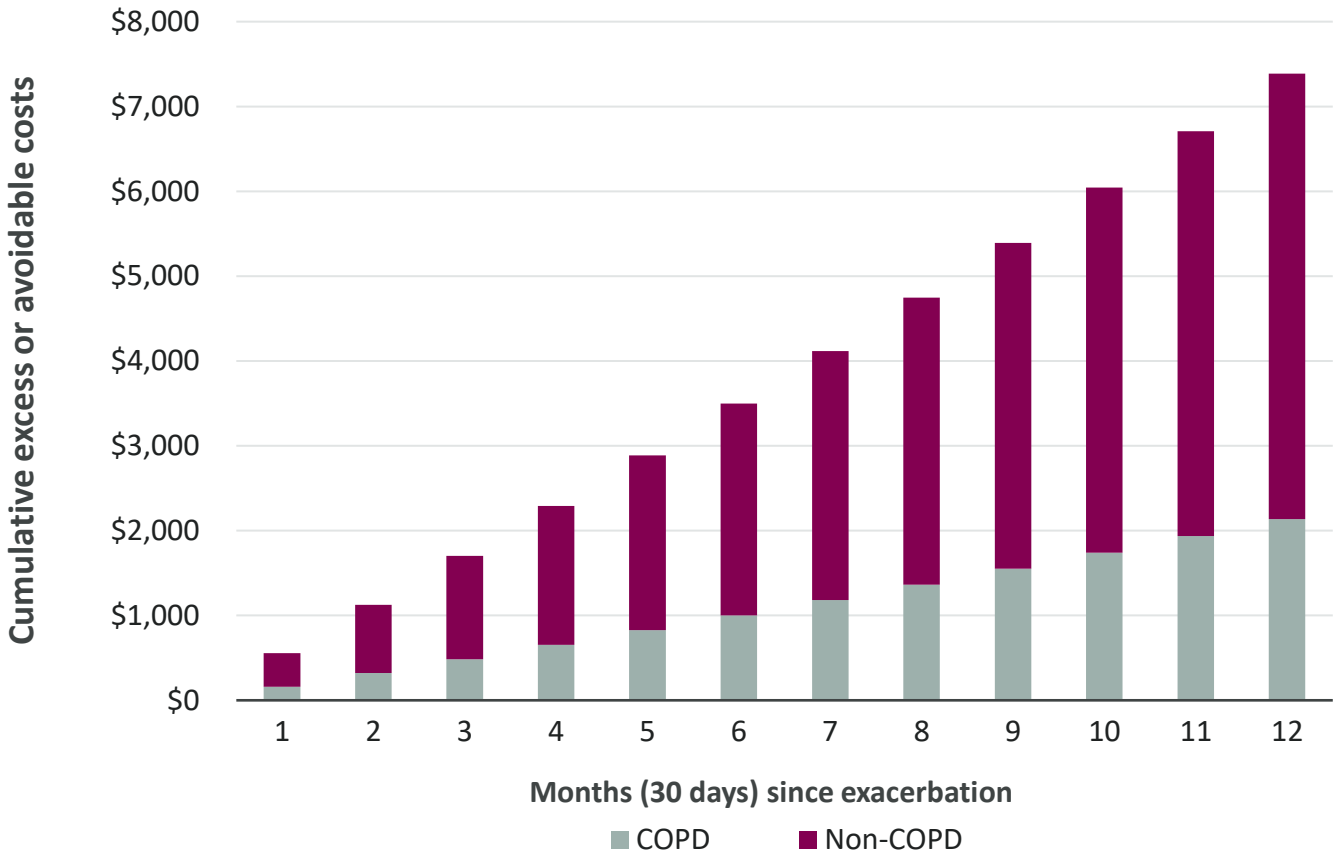
Prompt: ≤30 days post exacerbation; Delayed: 31-180 days post exacerbation; Very delayed: 181-365 days post exacerbation.

[a]Unadjusted analyses among Commercial/Medicare patients, all comparisons between groups were statistically significant ($P<0.05$) for outcomes shown; [b]During 12-month follow-up period.

1. Tkacz J, et al. *Int J Chron Obstruct Pulmon Dis.* 2022;17:329-342; 2. Evans KA, et al. Article and supplementary appendix. *J Manag Care Spec Pharm*. 2022;28(12):1366-1377.

Every 30-day delay in initiating triple therapy resulted in excess healthcare costs[1]

Estimated effect of every 30-day delay in initiating therapy[2,a]



Initiating triple therapy 6 months late incurred **$3,497** greater total healthcare costs per patient.

For every 30-day delay in triple therapy initiation, costs increased by an average:

$616 & **$178**

PER PATIENT PER MONTH FOR ALL-CAUSE HEALTHCARE COSTS

PER PATIENT PER MONTH FOR COPD-RELATED COSTS

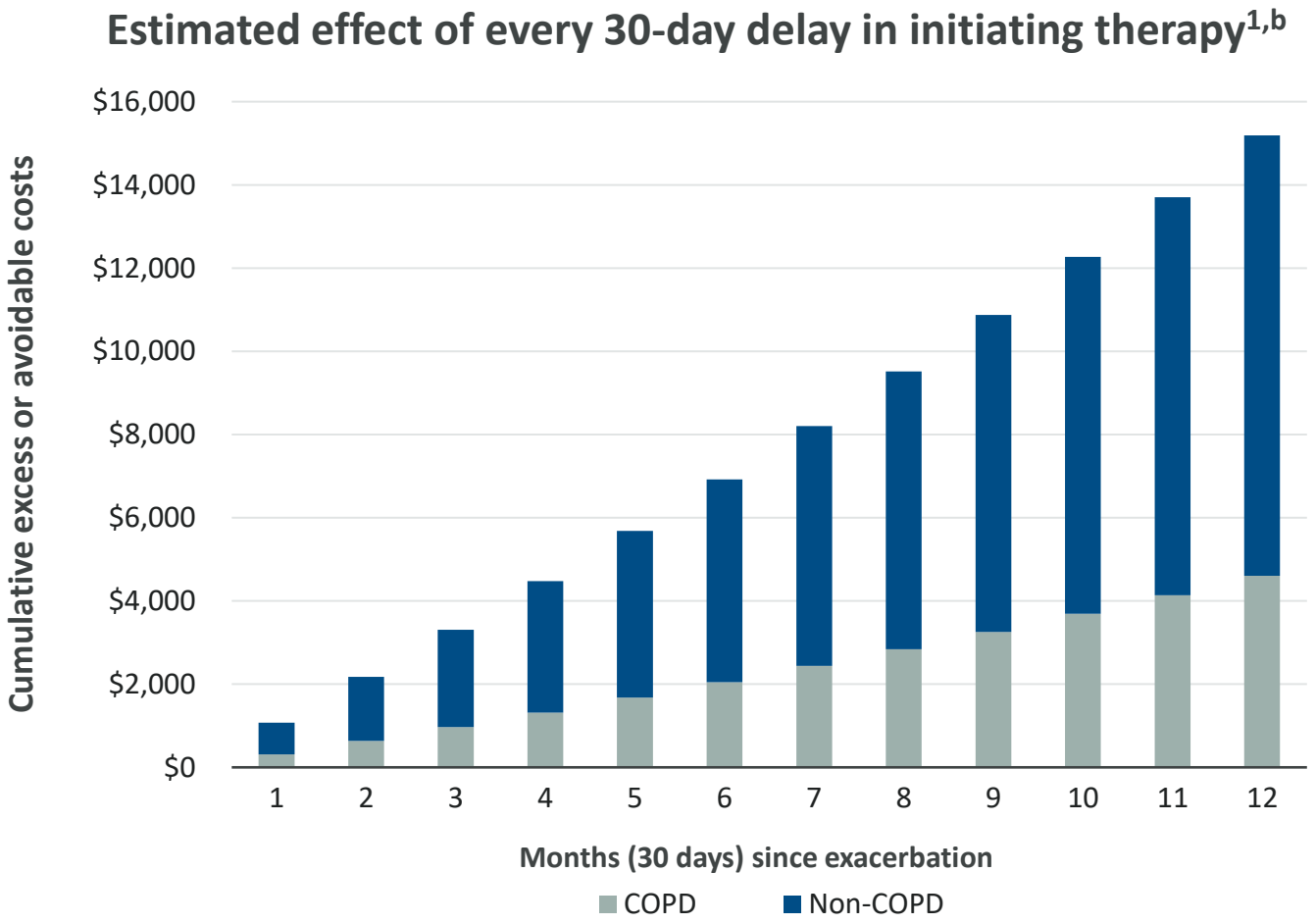
compared to a patient who received triple therapy <30 days after their initial exacerbation

[a]During the 12-month follow-up period, controlled for baseline patient characteristics, exacerbation history, and healthcare utilization.

1. Tkacz J, et al. *Int J Chron Obstruct Pulmon Dis.* 2022;17:329-342; 2. Data on File, US-64758, AstraZeneca Pharmaceuticals LP.

Excess healthcare costs per 30-day delay in triple therapy initiation were twice as high among the subset of patients with a severe COPD exacerbation[1,2,a]

Severe Event Analysis Subset



Initiating triple therapy 6 months late incurred **$6,924** greater total healthcare costs per patient.

For every 30-day delay in triple therapy initiation, costs increased by an average:

$1,266 & **$383**

PER PATIENT PER MONTH FOR ALL-CAUSE HEALTHCARE COSTS

PER PATIENT PER MONTH FOR COPD-RELATED COSTS

compared to a patient who received triple therapy <30 days after their severe index exacerbation[1]

[a]Compared to the total population of PRIMUS study; [b]During the 12-month follow-up period, controlled for baseline patient characteristics, exacerbation history, and healthcare utilization.

1. Evans KA, et al. Article and supplementary appendix. *J Manag Care Spec Pharm*. 2022;28(12):1366-1377; 2. Tkacz J, et al. *Int J Chron Obstruct Pulmon Dis.* 2022;17:329-342.

Every 30-day delay in initiating triple therapy resulted in greater likelihood of future COPD exacerbations and costs

Compared to a patient who received triple therapy <30 days after their initial exacerbation, each 30-day delay[a] was associated with:

		PRIMUS[1] (Total Population)	Severe Event Analysis[2] (Subset)
Exacerbations:	**Increased odds of a moderate or severe event**	**11%**	**13%**
	Increased odds of a severe event	**7%**	**10%**
Healthcare Costs:	**Increased all-cause costs**	**1.8%**	**3%**
	Increased COPD-related costs	**2.1%**	**4%**

[a]Adjusted for patient characteristics and baseline exacerbation history.

1. Tkacz J, et al. *Int J Chron Obstruct Pulmon Dis.* 2022;17:329-342; 2. Evans KA, et al. Article and supplementary appendix. *J Manag Care Spec Pharm*. 2022;28(12):1366-1377.

PRIMUS Study Limitations

Study limitations included:

- Multivariate regression analysis was used to control for baseline patient demographics and clinical characteristics[1]
- Disease status, study outcomes, and covariates are subject to potential misclassification, due to coding limitations[1]
- The study was limited to patients with commercial, Medicare, or Medicaid insurance. Medications received as samples, inpatient medications, or medications paid with cash were not captured[1]
- The index treatment window (January 2010 to March 2019) and the timing of closed triple therapy approval in the US (September 2017) resulted in 3% of the total study population and 1.7% of patients in the severe event analysis receiving closed triple therapy as their index treatment, thus, limiting the ability to compare outcomes between open vs closed triple therapy initiators[1,2]

1. Tkacz J, et al. *Int J Chron Obstruct Pulmon Dis.* 2022;17:329-342; 2. Data on File, REF-174212, AstraZeneca Pharmaceuticals LP.

Summary[1,2]

Prompt initiation of triple therapy following an exacerbation or COPD hospitalization[a] was associated with **decreased odds of future exacerbations and reduced healthcare costs**

Every 30-day delay in initiating triple therapy resulted in **greater odds of future COPD exacerbations and costs** compared to a patient who received triple therapy <30 days after their initial exacerbation or COPD hospitalization[a]

Among the subset of **patients hospitalized for a COPD exacerbation**, delayed triple therapy initiation was associated with relatively greater burden, including **higher odds of a future severe exacerbation and greater healthcare costs**[b]

[a]Hospitalization for a severe COPD exacerbation; [b]Compared to the total population of PRIMUS study.

1. Tkacz J, et al. *Int J Chron Obstruct Pulmon Dis.* 2022;17:329-342; 2. Evans KA, et al. Article and supplementary appendix. *J Manag Care Spec Pharm*. 2022;28(12):1366-1377.

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Back-up slides

PRIMUS Study: Demographic Characteristics

	All Patients (N=24,770)	Prompt[a] (N=7,577)	Delayed[b] (N=9,676)	Very Delayed[c] (N=7,517)
Age, mean (SD)	62.0 (11.0)	62.5 (11.1)	62.0 (11.1)	61.4 (10.9)
Male, n (%)	9626 (38.9%)	3,117 (41.1%)	3,810 (39.4%)	2,699 (35.9%)
Payer category, n (%)				
Commercial	7,652 (30.9%)	2,665 (35.2%)	2,996 (31.0%)	1,991 (26.5%)
Medicare Supplemental	8,064 (32.6%)	2,595 (34.3%)	3,141 (32.5%)	2,328 (31.0%)
Medicaid	9,054 (36.6%)	2,317 (30.6%)	3,539 (36.6%)	3,198 (42.5%)
Urban residence, n (%)	18,819 (76.0%)	5,937 (78.4%)	7,332 (75.8%)	5,550 (73.8%)
Index year, n (%)				
2010–2014	14,107 (57.0%)	4,256 (56.2%)	5,335 (55.1%)	4,516 (60.1%)
2015–2019	10,663 (43.1%)	3,321 (43.8%)	4,341 (44.9%)	3,001 (39.9%)

[a]Triple therapy within 30 days after or on the index exacerbation date; [b]Triple therapy between 31 and 180 days after index exacerbation; [c]Triple therapy between 181 and 365 days after index exacerbation.

Tkacz J, et al. *Int J Chron Obstruct Pulmon Dis.* 2022;17:329-342.

PRIMUS Study: Clinical Characteristics

	All Patients (N=24,770)	Prompt[a] (N=7,577)	Delayed[b] (N=9,676)	Very Delayed[c] (N=7,517)
Comorbid conditions, n (%)				
Cardiovascular disease	13,673 (55.2%)	3,941 (52.0%)	5,294 (54.7%)	4,438 (59.0%)
Asthma	7,792 (31.5%)	2,027 (26.8%)	3,072 (31.7%)	2,693 (35.8%)
Acute bronchitis or bronchiolitis	7,434 (30.0%)	1,967 (26.0%)	2,952 (30.5%)	2,515 (33.5%)
Chronic cough	6,985 (28.2%)	1,943 (25.6%)	2,716 (28.1%)	2,326 (30.9%)
Pneumonia	5,158 (20.8%)	1,360 (17.9%)	1,919 (19.8%)	1,879 (25.0%)
Oxygen therapy, n (%)	6,622 (26.7%)	1,233 (16.3%)	2,500 (25.8%)	2,889 (38.4%)
Any dual therapy,[d] n (%)	14,137 (57.1%)	3,831 (50.6%)	5,619 (58.1%)	4,687 (62.4%)
Monotherapy only,[e] n (%)	9,016 (36.4%)	2,930 (38.7%)	3,571 (36.9%)	2,515 (33.5%)
No maintenance treatment, n (%)	1,617 (6.5%)	816 (10.8%)	486 (5.0%)	315 (4.2%)
Index exacerbation type, n (%)				
Moderate	17,998 (72.7%)	4,609 (60.8%)	7,678 (79.4%)	5,711 (76.0%)
Severe	6,772 (27.3%)	2,968 (39.2%)	1,998 (20.6%)	1,806 (24.0%)

[a]Triple therapy within 30 days after or on the index exacerbation date; [b]Triple therapy between 31 and 180 days after index exacerbation; [c]Triple therapy between 181 and 365 days after index exacerbation; [d]Any claims for an ICS/LABA, LAMA/LABA, or SABA/SAMA combination medication; [e]No claims for dual therapy and any claims for an ICS, LABA, LAMA, SABA, SAMA, oral or injectable corticosteroid, methylxanthine, mucolytic agent, or PDE-4 inhibitor.

Tkacz J, et al. *Int J Chron Obstruct Pulmon Dis.* 2022;17:329-342.

Severe Event Analysis: Demographic Characteristics

Severe Event Analysis Subset

	All Patients (N=6,772)	Prompt[a] (N=2,968)	Delayed[b] (N=1,998)	Very Delayed[c] (N=1,806)
Age, mean (SD)	63.7 (11.3)	64.1 (11.1)	63.8 (11.6)	62.7 (11.2)
Male, n (%)	2,695 (39.8%)	1,223 (41.2%)	791 (39.6%)	681 (37.7%)
Payer category, n (%)				
Commercial	2,161 (31.9%)	1,077 (36.3%)	625 (31.3%)	459 (25.4%)
Medicare Supplemental	2,573 (38.0%)	1,191 (40.1%)	753 (37.7%)	629 (34.8%)
Medicaid	2,038 (30.1%)	700 (23.6%)	620 (31.0%)	718 (39.8%)
Urban residence, n (%)	5,401 (79.8%)	2,415 (81.4%)	1,601 (80.1%)	1,385 (76.7%)
Index year, n (%)				
2010–2014	4,281 (63.2%)	1,895 (63.8%)	1,195 (59.8%)	1,191 (65.9%)
2015–2019	2,491 (36.8%)	1,073 (36.2%)	803 (40.2%)	615 (34.1%)

[a]Triple therapy within 30 days after or on the index exacerbation date; [b]Triple therapy between 31 and 180 days after index exacerbation; [c]Triple therapy between 181 and 365 days after index exacerbation.

Evans KA, et al. Article and supplementary appendix. *J Manag Care Spec Pharm*. 2022;28(12):1366-1377.

Severe Event Analysis: Clinical Characteristics

Severe Event Analysis Subset

	All Patients (N=6,772)	Prompt[a] (N=2,968)	Delayed[b] (N=1,998)	Very Delayed[c] (N=1,806)
Any long-acting maintenance therapy, n (%)	3,781 (55.8)	1,422 (47.9)	1,156 (57.9)	1,203 (66.6)
ICS	593 (8.8%)	197 (6.6%)	190 (9.5%)	206 (11.4%)
LABA	126 (1.9%)	37 (1.2%)	39 (2.0%)	50 (2.8%)
LAMA	1,324 (19.6%)	524 (17.7%)	412 (20.6%)	388 (21.5%)
LAMA/LABA	73 (1.1%)	31 (1.0%)	25 (1.3%)	17 (0.9%)
ICS/LABA	2,339 (34.5%)	877 (29.5%)	682 (34.2%)	780 (43.2%)
Any short-acting medication, n (%)	5,168 (76.3%)	2,099 (70.7%)	1,542 (77.2%)	1,527 (84.6%)
No long or short-acting medications, n (%)	1,252 (18.5%)	710 (23.9%)	330 (16.5%)	212 (11.7%)
Oxygen therapy, n (%)	1,317 (19.4%)	364 (12.3%)	401 (20.1%)	552 (30.6%)
Any COPD-related primary care visit, n (%)				
Commercial/Medicare	1,227 (25.9%)	497 (21.9%)	381 (27.6%)	349 (32.1%)
Medicaid	791 (38.8%)	238 (34.0%)	254 (41.0%)	299 (41.6%)
Any COPD-related pulmonologist visit, n (%)				
Commercial/Medicare	529 (11.2%)	171 (7.5%)	172 (12.5%)	186 (17.1%)
Medicaid	54 (2.6%)	12 (1.7%)	16 (2.6%)	26 (3.6%)

[a]Triple therapy within 30 days after or on the index exacerbation date; [b]Triple therapy between 31 and 180 days after index exacerbation; [c]Triple therapy between 181 and 365 days after index exacerbation.

Evans KA, et al. Article and supplementary appendix. *J Manag Care Spec Pharm*. 2022;28(12):1366-1377.