

SUPPLEMENTARY MATERIAL

Impact of Elexacaftor/Tezacaftor/Ivacaftor on Healthcare Resource Utilization and Associated Costs Among People With Cystic Fibrosis in the US: Retrospective Claims Analysis

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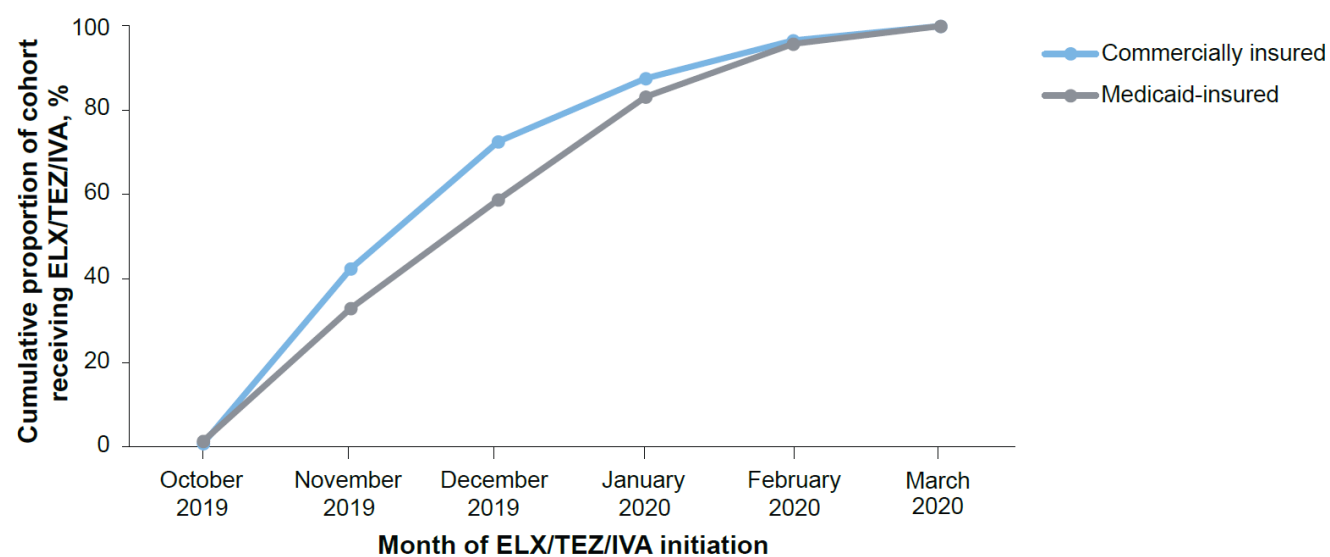
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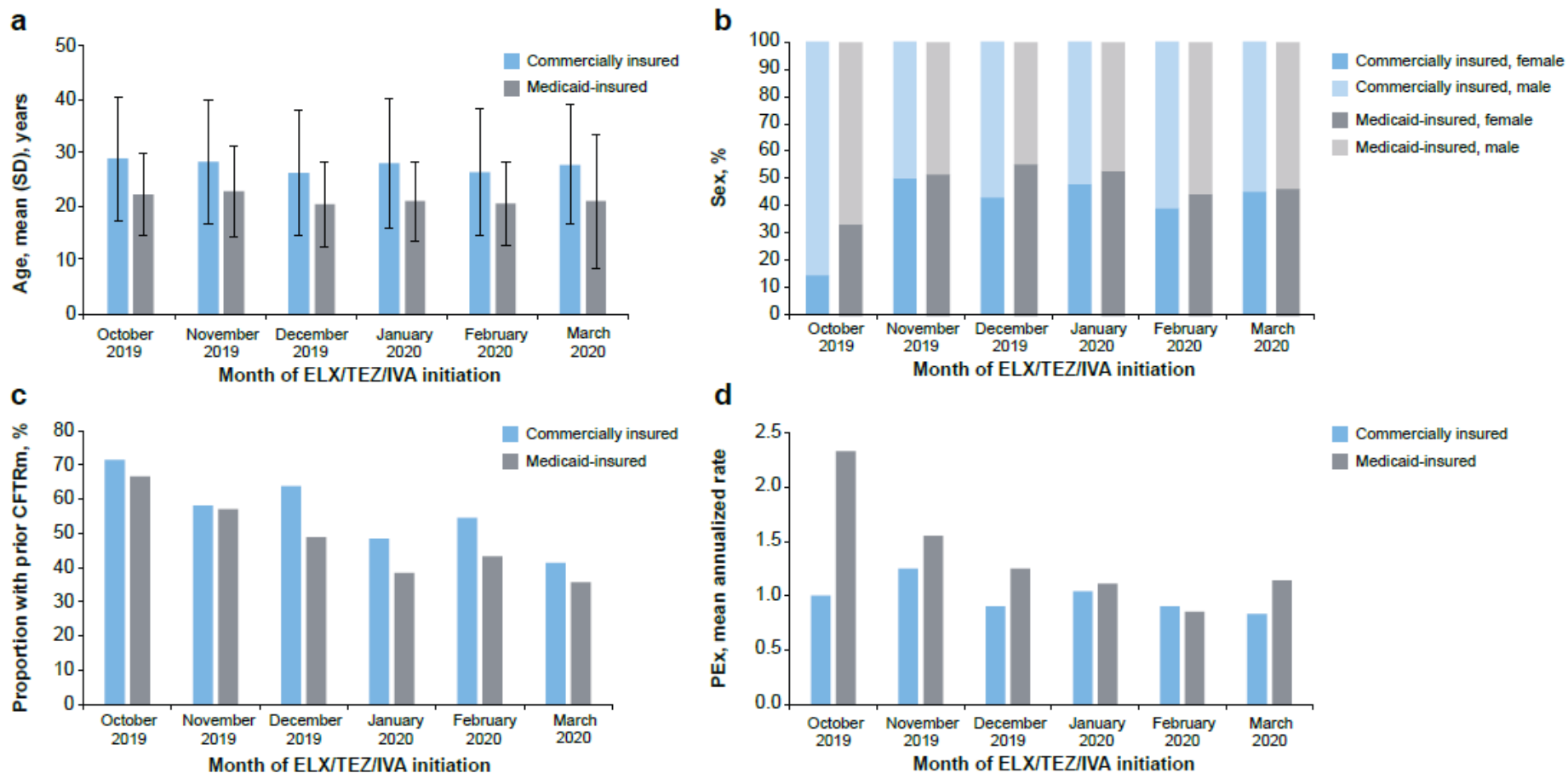
Figure S1. ELX/TEZ/IVA Initiation by Month During the Preindex Period

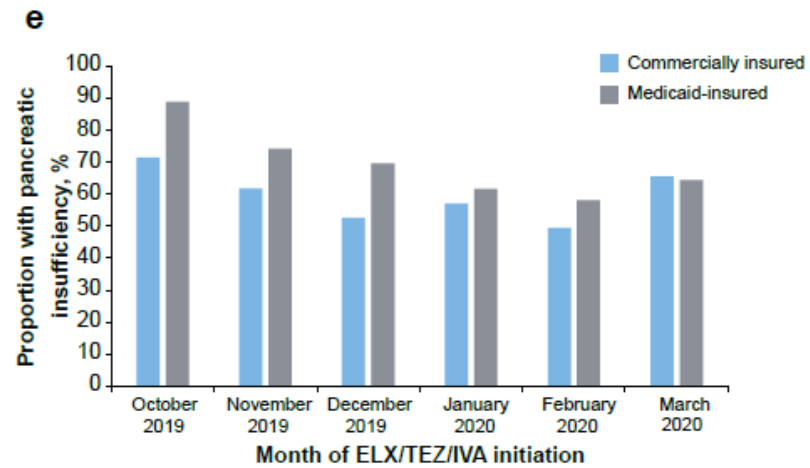


ELX/TEZ/IVA: elexacaftor/tezacaftor/ivacaftor.

Figure S2. Baseline Demographics and Characteristics by Month of ELX/TEZ/IVA Initiation

(a) Age; (b) sex, (c) prior CFTRm use; (d) PEx requiring hospitalizations or IV antibiotics; (e) pancreatic insufficiency.





CFTRm: cystic fibrosis transmembrane conductance regulator modulator; ELX/TEZ/IVA: elexacaftor/tezacaftor/ivacaftor; IV, intravenous; PEx: pulmonary exacerbation; SD, standard deviation.

Table S1. Use of Selected Non-CFTRm Outpatient Prescriptions

	Preindex period (6 months)	Prepandemic, postindex period (≤5 months)	Peripandemic, postindex period (≤9 months)
Commercially insured cohort (n = 851)			
Antibiotics^a			
Annualized mean (95% CI), n	8.00 (7.52, 8.44)	7.53 (6.95, 8.10)	5.28 (4.85, 5.75)
Change from preindex period, %	NA	-5.75 (-11.37, -0.39)	-33.93 (-40.44, -26.91)
Bronchodilators			
Annualized mean (95% CI), n	6.04 (5.58, 6.49)	5.52 (5.04, 6.01)	4.47 (4.03, 4.99)
Change from preindex period, %	NA	-8.51 (-14.81, 1.82)	-25.99 (-35.13, -15.34)
Antidiabetic agents^b			
Annualized mean (95% CI), n	1.40 (1.16, 1.68)	1.41 (1.12, 1.73)	1.11 (0.89, 1.35)
Change from preindex period, %	NA	0.22 (-15.23, 16.52)	-20.69 (-40.45, 5.59)
Antidepressants			
Annualized mean (95% CI), n	1.77 (1.50, 2.08)	1.85 (1.51, 2.20)	1.97 (1.63, 2.32)
Change from preindex period, %	NA	4.21 (-9.06, 18.88)	11.42 (-12.69, 41.47)
Antifungals			
Annualized mean (95% CI), n	0.14 (0.09, 0.20)	0.12 (0.05, 0.20)	0.10 (0.06, 0.14)
Change from preindex period, %	NA	-17.21 (-53.21, 24.56)	-31.55 (-62.65, 23.86)
Antihypertensives			
Annualized mean (95% CI), n	0.75 (0.57, 0.95)	0.75 (0.54, 1.00)	0.72 (0.54, 0.92)
Change from preindex period, %	NA	-0.12 (-24.46, 27.91)	-4.38 (-35.32, 40.44)
Anti-inflammatory agents			
Annualized mean (95% CI), n	1.92 (1.66, 2.16)	1.96 (1.66, 2.31)	1.59 (1.34, 1.85)
Change from preindex period, %	NA	2.38 (-9.51, 15.43)	-17.09 (-34.05, 1.03)
Appetite stimulants			
Annualized mean (95% CI), n	0.52 (0.39, 0.66)	0.53 (0.38, 0.69)	0.45 (0.31, 0.60)
Change from preindex period, %	NA	2.63 (-21.00, 25.74)	-12.76 (-44.10, 31.35)
Constipation treatments			
Annualized mean (95% CI), n	0.04 (0.02, 0.07)	0.03 (0.01, 0.06)	0.03 (0.02, 0.05)
Change from preindex period, %	NA	-28.70 (-80.58, 72.98)	-29.25 (-66.95, 56.61)
Digestive or pancreatic enzymes			
Annualized mean (95% CI), n	4.43 (4.16, 4.72)	4.47 (4.14, 4.79)	4.41 (4.13, 4.71)
Change from preindex period, %	NA	0.75 (-6.14, 7.41)	-0.55 (-9.24, 9.01)

Immunosuppressants			
Annualized mean (95% CI), n	0.30 (0.16, 0.47)	0.21 (0.10, 0.36)	0.35 (0.20, 0.54)
Change from preindex period, %	NA	-31.74 (-62.74, 7.02)	14.62 (-42.62, 142.06)
Mucolytics^c			
Annualized mean (95% CI), n	5.04 (4.73, 5.35)	4.95 (4.58, 5.31)	4.27 (3.90, 4.61)
Change from preindex period, %	NA	-1.90 (-7.36, 4.03)	-15.26 (-23.80, -6.69)
Opioids			
Annualized mean (95% CI), n	0.39 (0.27, 0.52)	0.53 (0.36, 0.70)	0.35 (0.24, 0.50)
Change from preindex period, %	NA	33.85 (4.65, 73.18)	-10.12 (-45.78, 47.20)
Ursodeoxycholic acid			
Annualized mean (95% CI), n	0.74 (0.58, 0.90)	0.74 (0.57, 0.92)	0.65 (0.50, 0.81)
Change from preindex period, %	NA	0.27 (-16.28, 18.18)	-11.01 (-36.61, 21.11)
Vitamins			
Annualized mean (95% CI), n	0.90 (0.71, 1.09)	0.77 (0.58, 0.98)	0.70 (0.52, 0.91)
Change from preindex period, %	NA	-14.07 (-30.45, 2.91)	-21.99 (-46.08, 8.50)
Medicaid-insured cohort (n = 650)			
Antibiotics^a			
Annualized mean (95% CI), n	10.34 (9.55, 11.12)	9.82 (8.97, 10.71)	6.92 (6.40, 7.54)
Change from preindex period, %	NA	-4.97 (-11.21, 1.81)	-33.04 (-39.71, -25.15)
Bronchodilators			
Annualized mean (95% CI), n	9.33 (8.70, 9.98)	9.48 (8.70, 10.29)	7.65 (7.03, 8.27)
Change from preindex period, %	NA	1.58 (-4.69, 8.22)	-18.04 (-26.39, -8.97)
Antidiabetic agents^b			
Annualized mean (95% CI), n	2.00 (1.62, 2.37)	2.48 (1.94, 3.02)	1.70 (1.37, 2.01)
Change from preindex period, %	NA	23.97 (6.89, 40.42)	-14.69 (-34.46, 10.78)
Antidepressants			
Annualized mean (95% CI), n	2.44 (2.01, 2.87)	2.48 (2.03, 2.96)	2.29 (1.89, 2.69)
Change from preindex period, %	NA	1.46 (-10.63, 15.57)	-6.23 (-27.41, 18.99)
Antifungals			
Annualized mean (95% CI), n	0.19 (0.11, 0.31)	0.16 (0.08, 0.25)	0.10 (0.06, 0.14)
Change from preindex period, %	NA	-15.83 (-57.85, 50.11)	-50.27 (-74.23, -4.74)
Antihypertensives			
Annualized mean (95% CI), n	0.86 (0.63, 1.11)	0.88 (0.62, 1.18)	0.79 (0.59, 1.03)
Change from preindex period, %	NA	2.83 (-20.22, 27.42)	-7.09 (-36.33, 39.54)

Anti-inflammatory agents			
Annualized mean (95% CI), n	4.01 (3.56, 4.46)	3.62 (3.20, 4.09)	3.31 (2.95, 3.75)
Change from preindex period, %	NA	-9.66 (-18.59, -0.79)	-17.38 (-30.23, -1.92)
Appetite stimulants			
Annualized mean (95% CI), n	1.36 (1.09, 1.65)	1.51 (1.17, 1.88)	1.02 (0.80, 1.27)
Change from preindex period, %	NA	11.10 (-4.91, 28.71)	-25.22 (-45.30, 2.68)
Constipation treatments			
Annualized mean (95% CI), n	0.17 (0.09, 0.26)	0.24 (0.13, 0.37)	0.17 (0.07, 0.30)
Change from preindex period, %	NA	39.97 (-18.61, 155.65)	-0.67 (-57.92, 124.89)
Digestive or pancreatic enzymes			
Annualized mean (95% CI), n	6.18 (5.81, 6.56)	6.66 (6.25, 7.11)	6.17 (5.84, 6.54)
Change from preindex period, %	NA	7.81 (1.00, 15.12)	-0.12 (-7.92, 8.55)
Immunosuppressants			
Annualized mean (95% CI), n	0.18 (0.05, 0.34)	0.18 (0.04, 0.36)	0.27 (0.10, 0.46)
Change from preindex period, %	NA	1.11 (-60.79, 97.34)	55.91 (-50.16, 427.58)
Mucolytics^c			
Annualized mean (95% CI), n	5.83 (5.46, 6.21)	6.36 (5.94, 6.82)	5.43 (5.08, 5.78)
Change from preindex period, %	NA	9.18 (2.87, 15.77)	-6.83 (-14.71, 1.77)
Opioids			
Annualized mean (95% CI), n	0.62 (0.39, 0.89)	0.57 (0.36, 0.80)	0.36 (0.21, 0.55)
Change from preindex period, %	NA	-9.15 (-38.88, 31.90)	-41.73 (-69.36, 7.45)
Ursodeoxycholic acid			
Annualized mean (95% CI), n	1.12 (0.88, 1.37)	1.26 (0.99, 1.55)	1.14 (0.91, 1.38)
Change from preindex period, %	NA	12.10 (-3.03, 29.97)	1.88 (-25.00, 38.54)
Vitamins			
Annualized mean (95% CI), n	3.71 (3.25, 4.21)	3.49 (2.98, 4.07)	3.41 (2.93, 3.90)
Change from preindex period, %	NA	-5.95 (-16.37, 6.06)	-8.13 (-24.81, 10.18)

CFTRm: cystic fibrosis transmembrane conductance regulator modulator; CI: confidence interval ;NA: not applicable.

^a Includes acute and chronic use of inhaled, oral, injectable, intravenous, and other types of antibiotics.

^b Includes insulin agents (long-acting, short-acting, and other) and noninsulin agents.

^c Includes dornase alfa, acetylcysteine, hypertonic saline, and mannitol.

Table S2. Costs of Selected Non-CFTRm Outpatient Prescriptions in US Dollars

	Preindex period (6 months)	Prepandemic, postindex period (≤5 months)	Peripandemic, postindex period (≤9 months)
Commercially insured cohort (n = 851)			
Antibiotics^a			
Annualized mean (95% CI), n	18,325 (16,469, 20,387)	18,521 (16,280, 20,889)	12,992 (11,263, 14,660)
Change from preindex period, %	NA	1.07 (−8.90, 10.95)	−29.10 (−40.20, −16.14)
Bronchodilators			
Annualized mean (95% CI), n	1184 (1066, 1305)	1130 (988, 1,269)	895 (769, 1020)
Change from preindex period, %	NA	−4.58 (−13.82, 4.71)	−24.44 (−36.57, −10.95)
Antidiabetic agents^b			
Annualized mean (95% CI), n	891 (713, 1081)	833 (659, 1029)	695 (553, 850)
Change from preindex period, %	NA	−6.52 (−22.40, 12.46)	−22.03 (−41.46, 6.20)
Antidepressants			
Annualized mean (95% CI), n	42 (25, 72)	35 (24, 51)	42 (27, 62)
Change from preindex period, %	NA	−17.02 (−51.12, 33.69)	0.46 (−50.18, 96.33)
Antifungals			
Annualized mean (95% CI), n	4 (3, 6)	2 (1, 4)	2 (1, 3)
Change from preindex period, %	NA	−43.63 (−68.72, −12.45)	−45.38 (−72.52, 2.23)
Antihypertensives			
Annualized mean (95% CI), n	22 (9, 44)	17 (8, 29)	20 (10, 34)
Change from preindex period, %	NA	−21.93 (−47.34, 45.00)	−10.50 (−68.28, 156.22)
Anti-inflammatory agents			
Annualized mean (95% CI), n	331 (269, 395)	317 (249, 392)	250 (193, 311)
Change from preindex period, %	NA	−4.25 (−20.66, 12.88)	−24.72 (−44.70, 3.31)
Appetite stimulants			
Annualized mean (95% CI), n	26 (16, 39)	25 (12, 45)	24 (11, 43)
Change from preindex period, %	NA	−5.42 (−48.04, 40.79)	−7.82 (−63.70, 93.48)
Constipation treatments			
Annualized mean (95% CI), n	8 (1, 17)	1 (0, 3)	8 (2, 17)
Change from preindex period, %	NA	−83.31 (−98.79, 63.28)	7.84 (−77.00, 871.99)
Digestive or pancreatic enzymes			
Annualized mean (95% CI), n	25,834 (24,201, 27,433)	28,455 (26,202, 30,943)	27,841 (25,912, 29,689)
Change from preindex period, %	NA	10.15 (1.45, 18.82)	7.77 (−1.32, 18.28)

Immunosuppressants			
Annualized mean (95% CI), n	657 (282, 1102)	645 (184, 1263)	761 (307, 1303)
Change from preindex period, %	NA	-1.88 (-53.82, 43.87)	15.83 (-57.69, 206.88)
Mucolytics^c			
Annualized mean (95% CI), n	26,186 (24,478, 27,780)	25,967 (23,873, 28,063)	21,861 (19,915, 23,696)
Change from preindex period, %	NA	-0.83 (-7.20, 6.13)	-16.52 (-24.87, -7.20)
Opioids			
Annualized mean (95% CI), n	16 (6, 31)	15 (5, 29)	12 (2, 32)
Change from preindex period, %	NA	-5.40 (-32.50, 37.91)	-20.77 (-87.41, 249.84)
Ursodeoxycholic acid			
Annualized mean (95% CI), n	179 (139, 223)	187 (135, 245)	145 (109, 181)
Change from preindex period, %	NA	4.45 (-15.77, 28.78)	-18.71 (-42.67, 13.98)
Vitamins			
Annualized mean (95% CI), n	461 (317, 639)	371 (218, 542)	291 (179, 426)
Change from preindex period, %	NA	-19.43 (-49.40, 17.44)	-36.87 (-67.00, 9.95)
Medicaid-insured cohort (n = 650)^d			
Antibiotics^a			
Annualized mean (95% CI), n	16,420 (14,186, 18,888)	22,204 (17,459, 28,094)	13,082 (10,716, 15,498)
Change from preindex period, %	NA	35.25 (8.23, 70.84)	-20.33 (-37.68, 0.32)
Bronchodilators			
Annualized mean (95% CI), n	1248 (1063, 1451)	1424 (1164, 1689)	1098 (912, 1297)
Change from preindex period, %	NA	14.12 (1.01, 27.40)	-12.00 (-30.22, 12.15)
Antidiabetic agents^b			
Annualized mean (95% CI), n	867 (623, 1115)	1041 (749, 1344)	877 (649, 1104)
Change from preindex period, %	NA	20.16 (0.78, 42.43)	1.26 (-62.45, 47.63)
Antidepressants			
Annualized mean (95% CI), n	23 (14, 35)	21 (14, 29)	25 (17, 35)
Change from preindex period, %	NA	-9.37 (-38.59, 28.09)	9.60 (-40.46, 105.32)
Antifungals			
Annualized mean (95% CI), n	159 (2, 448)	66 (1, 177)	2 (1, 3)
Change from preindex period, %	NA	-58.52 (-81.14, 84.65)	-98.67, (-99.58, -17.68)
Antihypertensives			
Annualized mean (95% CI), n	9 (5, 15)	13 (5, 22)	13 (7, 20)
Change from preindex period, %	NA	33.19 (-20.46, 92.14)	34.18 (-33.88, 172.17)

Anti-inflammatory agents			
Annualized mean (95% CI), n	383 (283, 487)	345 (246, 453)	266 (195, 349)
Change from preindex period, %	NA	-9.72 (-25.85, 8.63)	-30.46 (54.49, 3.13)
Appetite stimulants			
Annualized mean (95% CI), n	41 (26, 60)	43 (25, 64)	22 (15, 29)
Change from preindex period, %	NA	3.98 (-19.62, 31.59)	-47.97 (-68.61, -11.77)
Constipation treatments			
Annualized mean (95% CI), n	1 (0, 3)	1 (0, 2)	1 (0, 2)
Change from preindex period, %	NA	-36.35 (-87.02, 137.18)	-50.35 (-97.52, 299.89)
Digestive or pancreatic enzymes			
Annualized mean (95% CI), n	22,498 (20,422, 24,584)	28,307 (25,059, 31,322)	26,138 (23,923, 28,606)
Change from preindex period, %	NA	25.82 (14.51, 37.38)	16.18 (2.79, 31.83)
Immunosuppressants			
Annualized mean (95% CI), n	107 (12, 263)	21 (1, 52)	91 (18, 186)
Change from preindex period, %	NA	-79.89 (-99.54, 103.02)	-14.64, -86.68, 805.21)
Mucolytics^c			
Annualized mean (95% CI), n	20,428 (18,496, 22,455)	24,462 (21,957, 27,163)	19,446 (17,367, 21,579)
Change from preindex period, %	NA	19.75 (10.68, 29.82)	-4.81 (-17.79, 8.64)
Opioids			
Annualized mean (95% CI), n	15 (5, 30)	12 (2, 24)	22 (2, 59)
Change from preindex period, %	NA	-22.34 (-58.56, 4.11)	43.62 (-89.22, 660.22)
Ursodeoxycholic acid			
Annualized mean (95% CI), n	117 (83, 159)	133 (92, 181)	116 (73, 171)
Change from preindex period, %	NA	13.30 (-20.74, 63.89)	-0.83, -42.11, 62.18)
Vitamins			
Annualized mean (95% CI), n	503 (286, 755)	559 (270, 896)	471 (231, 725)
Change from preindex period, %	NA	11.05 (-34.23, 78.65)	-6.27 (-57.07, 91.44)

CFTRm: cystic fibrosis transmembrane conductance regulator modulator; CI: confidence interval; NA: not applicable.

^a Includes acute and chronic use of inhaled, oral, injectable, intravenous, and other types of antibiotics.

^b Includes insulin agents (long-acting, short-acting, and other) and noninsulin agents.

^c Includes dornase alfa, acetylcysteine, hypertonic saline, and mannitol.

^d People with indemnity plans only.

Table S3. Pulmonary Exacerbations Stratified by Age

	Preindex period	Prepandemic, postindex period	Preindex period	Prepandemic, postindex period	Preindex period	Prepandemic, postindex period	Preindex period	Prepandemic, postindex period
Commercially insured cohort								
	12-17 years (n = 183)		18-26 years (n = 282)		27-34 years (n = 170)		≥35 years (n = 216)	
Any PEx								
Annualized mean (95% CI), n	1.95 (1.69, 2.24)	1.35 (1.01, 1.69)	2.22 (1.95, 2.51)	1.32 (1.04, 1.61)	2.37 (1.98, 2.78)	1.63 (1.29, 2.03)	1.94 (1.67, 2.24)	1.34 (1.05, 1.65)
Change from preindex period, %	NA	-31.02 (-47.89, -13.64)	NA	-40.48 (-52.27, -26.80)	NA	-31.28 (-46.19, -12.29)	NA	-30.75 (-45.08, -16.26)
PEX requiring hospitalization or IV antibiotics								
Annualized mean (95% CI), n	0.67 (0.48, 0.86)	0.25 (0.10, 0.44)	0.84 (0.67, 1.03)	0.39 (0.25, 0.54)	0.98 (0.73, 1.24)	0.39 (0.22, 0.61)	0.85 (0.65, 1.07)	0.37 (0.20, 0.55)
Change from preindex period, %	NA	-62.55 (-83.59, -36.62)	NA	-53.48 (-68.89, -34.34)	NA	-59.58 (-77.86, -34.19)	NA	-57.00 (-74.99, -38.35)
Medicaid-insured cohort								
	12-17 years (n = 248)		18-26 years (n = 247)		27-34 years (n = 112)		≥35 years (n = 43)	
Any PEx								
Annualized mean (95% CI), n	2.26 (1.96, 2.54)	1.38 (1.07, 1.71)	2.68 (2.34, 3.02)	1.28 (0.98, 1.56)	2.98 (2.51, 3.49)	2.10 (1.61, 2.63)	2.08 (1.53, 2.74)	1.73 (0.85, 2.76)
Change from preindex period, %	NA	-39.10 (-52.32, -24.50)	NA	-52.33 (-62.73, -40.47)	NA	-29.57 (-44.95, -10.74)	NA	-17.24 (-55.31, 24.46)
PEX requiring hospitalization or IV antibiotics								
Annualized mean (95% CI), n	0.90 (0.69, 1.10)	0.26 (0.12, 0.43)	1.40 (1.16, 1.67)	0.57 (0.35, 0.79)	1.79 (1.38, 2.21)	1.12 (0.72, 1.55)	0.93 (0.51, 1.42)	0.97 (0.25, 1.77)

Change from preindex period, %	NA	-70.99 (-85.24, -51.83)	NA	-59.17 (-74.86, -40.33)	NA	-37.23 (-56.35, -11.37)	NA	4.75 (-69.07, 83.81)
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CI: confidence interval; IV: intravenous; NA: not applicable; PEx: pulmonary exacerbation.

Table S4. All-Cause Healthcare Resource Utilization Stratified by Age^a

	Preindex period	Postindex, prepandemic period	Preindex period	Postindex, prepandemic period	Preindex period	Postindex, prepandemic period	Preindex period	Postindex, prepandemic period
Commercially insured cohort								
	12-17 years (n = 183)		18-26 years (n = 282)		27-34 years (n = 170)		≥35 years (n = 216)	
Hospitalizations								
Annualized mean (95% CI), n	0.71 (0.52, 0.91)	0.27 (0.12, 0.47)	0.85 (0.66, 1.07)	0.41 (0.25, 0.59)	0.85 (0.59, 1.15)	0.32 (0.11, 0.57)	0.56 (0.39, 0.74)	0.24 (0.10, 0.40)
Change from preindex period, %	NA	-61.34 (-81.43, -38.16)	NA	-51.98 (-69.36, -27.57)	NA	-62.76 (-85.89, -29.52)	NA	-56.10 (-81.03, -22.79)
Hospitalization days								
Annualized mean (95% CI), n	6.54 (4.69, 8.48)	1.97 (0.65, 3.80)	8.38 (5.99, 11.07)	286 (1.66, 4.33)	8.16 (5.27, 11.53)	2.84 (0.79, 5.86)	5.19 (3.19, 7.72)	2.13 (0.77, 3.85)
Change from preindex period, %	NA	-69.82 (-90.03, -42.56)	NA	-65.84 (-79.85, -46.75)	NA	-65.23 (-90.07, -27.08)	NA	-58.84 (-85.73, -18.71)
Outpatient visits								
Annualized mean (95% CI), n	19.98 (17.84, 22.15)	20.90 (18.23, 24.22)	20.49 (17.94, 23.33)	20.82 (17.83, 24.32)	27.50 (21.71, 33.81)	25.17 (19.85, 31.47)	26.33 (23.36, 29.64)	23.36 (20.52, 26.56)
Change from preindex period, %	NA	4.61 (-7.88, 19.83)	NA	1.59 (-6.91, 10.84)	NA	-8.47 (-17.97, 1.89)	NA	-11.31 (-20.98, -0.99)
Medicaid-insured cohort								
	12-17 years (n = 248)		18-26 years (n = 247)		27-34 years (n = 112)		≥35 years (n = 43)	
Hospitalizations								
Annualized mean (95% CI), n	1.01 (0.78, 1.25)	0.36 (0.19, 0.57)	1.65 (1.36, 1.95)	0.55 (0.31, 0.80)	2.09 (1.57, 2.64)	1.12 (0.72, 1.54)	1.12 (0.65, 1.67)	1.41 (0.49, 2.51)

Change from preindex period, %	NA	-64.33 (-81.00, -42.17)	NA	-66.41 (-80.16, -50.67)	NA	-46.35 (-63.17, -25.91)	NA	26.74 (-46.40, 102.81)
Hospitalization days								
Annualized mean (95% CI), n	12.79 (9.78, 15.96)	3.42 (1.44, 5.98)	20.91 (16.21, 26.26)	5.86 (2.59, 10.13)	23.57 (17.57, 30.09)	11.53 (6.93, 16.15)	13.95 (6.67, 22.26)	13.93 (5.30, 24.90)
Change from preindex period, %	NA	-73.29 (-88.01, -55.00)	NA	-71.96 (-87.01, -53.84)	NA	-51.06 (-68.35, -29.67)	NA	-0.17 (-56.86, 72.57)
Outpatient visits								
Annualized mean (95% CI), n	25.42 (21.24, 30.13)	25.72 (21.23, 31.19)	27.35 (22.84, 32.38)	27.28 (22.40, 32.99)	20.85 (18.04, 24.05)	19.94 (17.51, 22.37)	23.19 (18.08, 28.99)	23.05 (18.90, 27.41)
Change from preindex period, %	NA	1.15 (-10.07, 12.03)	NA	-0.23 (-12.80, 13.93)	NA	-4.35 (-15.62, 8.01)	NA	-0.59 (-18.92, 20.10)

CI: confidence interval; NA: not applicable.

^a All outcomes were evaluated across the entire cohort, irrespective of individual patient healthcare experiences (eg, people with no hospitalizations contributed 0 hospitalization days to that period).

Table S5. All-Cause Healthcare Costs in US Dollars Stratified by Age^{a,b}

	Preindex period	Prepandemic, postindex period	Preindex period	Prepandemic, postindex period	Preindex period	Prepandemic, postindex period	Preindex period	Prepandemic , postindex period
Commercially insured cohort								
	12-17 years (n = 183)		18-26 years (n = 282)		27-34 years (n = 170)		≥35 years (n = 216)	
Hospitalizations								
Annualized mean (95% CI), n	39,617 (27,135, 53,012)	13,800 (3658, 26,949)	39,670 (26,899, 55,746)	15,363 (8044, 24,649)	31,400 (20,202, 43,806)	9584 (2932, 18,575)	23,591 (13,095, 36,231)	14,826 (3063, 34,172)
Cost difference from preindex period, \$	NA	-25,817	NA	-24,307	NA	-21,816	NA	-8,765
Change from preindex period, %	NA	-65.17 (-90.21, -28.38)	NA	-61.27 (-77.05, -40.84)	NA	-69.48 (-90.27, -39.54)	NA	-37.15 (-86.28, 74.02)
PEX (all types)								
Annualized mean (95% CI), n	31,813 (20,535, 44,533)	12,773 (2838, 25,701)	30,635 (20,689, 40,517)	12,645 (6496, 21,441)	23,365 (14,622, 33,394)	3372 (1102, 6338)	18,176 (9284, 30,134)	4036 (1071, 7991)
Cost difference from preindex period, \$	NA	-19,040	NA	-17,990	NA	-19,993	NA	-14,140
Change from preindex period, %	NA	-59.85 (-90.72, -12.01)	NA	-58.72 (-78.82, -32.39)	NA	-85.57 (-95.52, -68.33)	NA	-77.80 (-93.75, -47.38)
Medicaid-insured cohort^c								
	12-17 years		18-26 years		27-34 years		≥35 years	

	(n = 248)		(n = 247)		(n = 112)		(n = 43)	
Hospitalizations								
Annualized mean (95% CI), n	40,156 (20,854, 64,986)	8418 (1068, 23,363)	46,041 (32,215, 64,184)	13,822 (4445, 25,425)	38,146 (24,180, 56,506)	21,262 (8124, 39,185)	79,413 (2352, 228,705)	7,805 (0, 20,082)
Cost difference from preindex period, \$	NA	−31,738	NA	−32,219	NA	−16,884	NA	−71,608
Change from preindex period, %	NA	−79.04 (−96.94, −47.20)	NA	−69.98 (−88.89, −43.06)	NA	−44.26 (−78.62, 18.98)	NA	−90.17 (−100.00, 233.41)
PEX (all types)								
Annualized mean (95% CI), n	33,855 (17,199, 53,225)	8011 (838, 22,605)	41,167 (28,323, 58,257)	12,733 (3564, 24,447)	32,774 (20,013, 51,400)	19,893 (7176, 36,829)	77,449 (916, 226,172)	5,242 (9, 12,704)
Cost difference from preindex period, \$	NA	−25,844	NA	−28,434	NA	−12,881	NA	−72,207
Change from preindex period, %	NA	−76.34 (−97.15, −41.94)	NA	−69.07 (−90.49, −38.05)	NA	−39.30 (−77.90, 33.39)	NA	−93.23 (−99.99, 259.45)

CFTRm: cystic fibrosis transmembrane conductance regulator modulator; CI: confidence interval; ELX/TEZ/IVA: ellexacaftor/tezacaftor/ivacaftor; NA: not applicable; PEX: pulmonary exacerbation.

^a Excludes costs for CFTRm.

^b All outcomes were evaluated across the entire cohort, irrespective of individual patient healthcare experiences (eg, people with no hospitalizations contributed \$0 in hospitalization costs to that period).

^c People with indemnity plans only.

Table S6. Pulmonary Exacerbations Stratified by Prior CFTRm Use

	Preindex period (6 months)	Prepandemic, postindex period (≤5 months)	Preindex period (6 months)	Prepandemic, postindex period (≤5 months)
Commercially insured cohort				
	No prior CFTRm use (n = 361)		Prior CFTRm use (n = 490)	
Any PEx				
Annualized mean (95% CI), n	2.21 (1.98, 2.48)	1.38 (1.16, 1.63)	2.05 (1.86, 2.23)	1.41 (1.19, 1.60)
Change from preindex period, %	NA	-37.85 (-48.53, -25.55)	NA	-31.44 (-41.18, -21.95)
PEx requiring hospitalization or IV antibiotics				
Annualized mean (95% CI), n	0.84 (0.69, 0.99)	0.32 (0.22, 0.46)	0.83 (0.71, 0.97)	0.38 (0.27, 0.48)
Change from preindex period, %	NA	-61.53 (-74.56, -44.81)	NA	-54.42 (-66.79, -40.16)
Medicaid-insured cohort				
	No prior CFTRm use (n = 339)		Prior CFTRm use (n = 311)	
Any PEx				
Annualized mean (95% CI), n	2.45 (2.18, 2.72)	1.49 (1.20, 1.79)	2.62 (2.34, 2.90)	1.51 (1.25, 1.79)
Change from preindex period, %	NA	-39.20 (-51.18, -27.48)	NA	-42.20 (-51.39, -31.21)
PEx requiring hospitalization or IV antibiotics				
Annualized mean (95% CI), n	1.20 (1.00, 1.41)	0.61 (0.42, 0.81)	1.30 (1.09, 1.51)	0.58 (0.40, 0.77)
Change from preindex period, %	NA	-49.19 (-64.07, -31.53)	NA	-54.98 (-67.90, -39.88)

CFTRm: cystic fibrosis transmembrane conductance regulator modulator; CI: confidence interval; IV: intravenous; NA: not applicable;
PEx: pulmonary exacerbation.

Table S7. All-Cause Healthcare Resource Utilization Stratified by Prior CFTRm Use

	Preindex period (6 months)	Prepandemic, postindex period (≤months)	Preindex period (6 months)	Prepandemic, postindex period (≤5 months)
Commercially insured cohort				
	No prior CFTRm use (n = 361)		Prior CFTRm use (n = 490)	
Hospitalizations				
Annualized mean (95% CI), n	0.77 (0.60, 0.96)	0.36 (0.21, 0.53)	0.73 (0.60, 0.87)	0.29 (0.19, 0.38)
Change from preindex period, %	NA	-53.24 (-73.08, -27.91)	NA	-60.22 (-71.79, -46.14)
Hospitalization days				
Annualized mean (95% CI), n	7.34 (5.50, 9.36)	3.04 (1.61, 4.84)	6.98 (5.34, 8.68)	2.09 (1.29, 2.94)
Change from preindex period, %	NA	-58.62 (-78.04, -31.71)	NA	-70.09 (-79.85, -56.03)
Outpatient visits				
Annualized mean (95% CI), n	24.05 (21.10, 27.26)	21.85 (19.11, 24.78)	22.72 (20.54, 24.88)	22.84 (20.44, 25.62)
Change from preindex period, %	NA	-9.17 (-15.30, -2.86)	NA	0.52 (-6.85, 9.62)
Medicaid-insured cohort				
	No prior CFTRm use (n = 339)		Prior CFTRm use (n = 311)	
Hospitalizations				
Annualized mean (95% CI), n	1.46 (1.22, 1.72)	0.70 (0.46, 0.95)	1.43 (1.18, 1.67)	0.61 (0.43, 0.80)
Change from preindex period, %	NA	-52.46 (-66.52, -35.00)	NA	-57.17 (69.83, -43.58)
Hospitalization days				
Annualized mean (95% CI), n	18.77 (15.01, 23.24)	7.22 (4.17, 10.88)	16.77 (13.71, 19.72)	6.07 (3.86, 8.29)
Change from preindex period, %	NA	-61.55 (-76.26, -44.67)	NA	-63.78 (-76.00, -50.14)
Outpatient visits				
Annualized mean (95% CI), n	26.58 (22.92, 31.10)	28.30 (23.57, 33.69)	23.77 (21.05, 26.96)	21.98 (19.63, 24.60)
Change from preindex period, %	NA	6.49 (-5.49, 19.09)	NA	-7.53 (-15.02, 0.64)

CFTRm: cystic fibrosis transmembrane conductance regulator; CI: confidence interval; NA: not applicable.

Table S8. All-Cause Healthcare Costs in US Dollars Stratified by Prior CFTRm Use^a

	Preindex period (6 months)	Prepandemic, postindex period (≤5 months)	Preindex period (6 months)	Prepandemic, postindex period (≤5 months)
Commercially insured cohort				
	No prior CFTRm use (n = 361)		Prior CFTRm use (n = 490)	
Hospitalizations				
Annualized mean (95% CI), n	34,682 (25,222, 45,948)	18,598 (8507, 33,014)	33,368 (24,456, 42,789)	10,301 (5862, 15,696)
Cost difference from preindex period, \$	NA	-16,084	NA	-23,067
Change from preindex period, %	NA	-46.38 (-74.08, 3.99)	NA	-69.13 (-81.11, -54.96)
PEx (all types)				
Annualized mean (95% CI), n	27,775 (19,290, 37,785)	7758 (2965, 14,887)	25,167 (18,320, 31,645)	9111 (4788, 14,265)
Cost difference from preindex period, \$	NA	-20,017	NA	-16,056
Change from preindex period, %	NA	-72.07 (-88.80, -46.99)	NA	-63.80 (-80.11, -43.79)
Medicaid-insured cohort ^b				
	No prior CFTRm use (n = 207)		Prior CFTRm use (n = 179)	
Hospitalizations				
Annualized mean (95% CI), n	40,919 (27,339, 58,854)	13,107 (5520, 22,330)	48,364 (28,663, 74,959)	13,568 (5108, 24,926)
Cost difference from preindex period, \$	NA	-27,812	NA	-34,796
Change from preindex period, %	NA	-67.97 (-87.01, -38.08)	NA	-71.95 (-88.91, -44.98)
PEx (all types)				
Annualized mean (95% CI), n	34,036 (22,994, 48,564)	12,063 (4880, 21,435)	44,924 (24,952, 71,754)	12,583 (4058, 23,625)
Cost difference from preindex period, \$	NA	-21,973	NA	-32,341
Change from preindex period, %	NA	-64.56 (-86.63, -29.25)	NA	-71.99 (-90.10, -43.48)

CFTRm: cystic fibrosis transmembrane conductance regulator modulator; CI: confidence interval; ELX/TEZ/IVA: ellexacaftor/tezacaftor/ivacaftor; IV: intravenous; NA: not applicable; PEx: pulmonary exacerbation.

^a Excludes costs for CFTRm.

^b People with indemnity plans only.

Table S9. Sensitivity Analysis: Pulmonary Exacerbations Adjusted for Seasonality

	Preindex period (5 months)	Prepandemic, postindex period (≤5 months)
Commercially insured cohort (n = 628)^a		
Any PEx		
Annualized mean (95% CI), n	1.99 (1.76, 2.22)	1.36 (1.19, 1.54)
Change from preindex period, %	NA	-31.72 (-41.20, -21.11)
PEx requiring hospitalization or IV antibiotics		
Annualized mean (95% CI), n	0.72 (0.58, 0.85)	0.33 (0.25, 0.43)
Change from preindex period, %	NA	-53.57 (-66.00, -38.74)
Medicaid-insured cohort (n = 507)^a		
Any PEx		
Annualized mean (95% CI), n	2.76 (2.48, 3.05)	1.46 (1.24, 1.69)
Change from preindex period, %	NA	-46.95 (-55.85, -37.13)
PEx requiring hospitalization or IV antibiotics		
Annualized mean (95% CI), n	1.38 (1.15, 1.60)	0.58 (0.43, 0.73)
Change from preindex period, %	NA	-58.33 (-69.51, -45.13)

CI: confidence interval; IV: intravenous; NA: not applicable; PEx: pulmonary exacerbation.

^a People with continuous health plan enrollment during the seasonality-adjusted preindex period.

Table S10. Sensitivity Analysis: All-Cause Healthcare Resource Utilization Adjusted for Seasonality

	Preindex period (5 months)	Prepandemic, postindex period (≤5 months)
Commercially insured cohort (n = 851)		
Hospitalizations		
Annualized mean (95% CI), n	0.84 (0.67, 1.01)	0.33 (0.24, 0.43)
Change from preindex period, %	NA	-60.77 (-72.35, -47.63)
Hospitalization days		
Annualized mean (95% CI), n	8.35 (6.37, 10.58)	2.55 (1.66, 3.54)
Change from preindex period, %	NA	-69.52 (-81.18, -55.27)
Outpatient visits		
Annualized mean (95% CI), n	31.25 (27.93, 34.81)	30.55 (27.18, 33.73)
Change from preindex period, %	NA	-2.26 (-12.90, 10.30)
Medicaid-insured cohort (n = 650)		
Hospitalizations		
Annualized mean (95% CI), n	1.68 (1.42, 1.94)	0.67 (0.50, 0.85)
Change from preindex period, %	NA	-60.32 (-70.67, -47.82)
Hospitalization days		
Annualized mean (95% CI), n	19.46 (16.05, 22.85)	6.44 (4.27, 8.97)
Change from preindex period, %	NA	-66.89 (-78.11, -52.82)
Outpatient visits		
Annualized mean (95% CI), n	37.64 (32.53, 43.39)	36.64 (32.10, 41.53)
Change from preindex period, %	NA	-2.66 (-14.40, 9.47)

CI: confidence interval; NA: not applicable.

Table S11. Sensitivity Analysis: All-Cause Healthcare Costs in US Dollars Adjusted for Seasonality^a

	Preindex period (5 months)	Prepandemic, postindex period (≤5 months)
Commercially insured cohort (n = 851)		
Hospitalizations		
Annualized mean (95% CI), \$	45,100 (32,389, 61,163)	11,766 (7655, 16,542)
Cost difference from preindex period, \$	NA	-33,334
Change from preindex period, %	NA	-73.91 (-84.17, -59.54)
PEx (all types)		
Annualized mean (95% CI), \$	28,843 (20,067, 39,864)	8101 (4774, 12,279)
Cost difference from preindex period, \$	NA	-20,741
Change from preindex period, %	NA	-71.91 (-84.58, -54.75)
Medicaid-insured cohort (n = 386)^b		
Hospitalizations		
Annualized mean (95% CI), \$	53,079 (35,716, 72,432)	14,570 (7005, 25,346)
Cost difference from preindex period, \$	NA	-38,509
Change from preindex period, %	NA	-72.55 (-87.35, -49.49)
PEx (all types)		
Annualized mean (95% CI), \$	44,752 (28,852, 63,278)	13,341 (6075, 23,720)
Cost difference from preindex period, \$	NA	-31,411
Change from preindex period, %	NA	-70.19 (-87.60, -41.27)

CFTRm: cystic fibrosis transmembrane conductance regulator modulator; CI: confidence interval; NA; not applicable; PEx: pulmonary exacerbation.

^a Excludes costs for CFTRm.

^b People with indemnity plans only.