Online Supplement

Original Research

Implementation of 2023 Canadian Thoracic Society Guidelines for Single-Inhaler Triple Therapy Could Reduce Exacerbation and Mortality Rates in COPD: PROMETHEUS Canada

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Supplementary Materials

Appendix A: References for baseline model patient characteristics

- **Prevalence:** https://health-infobase.canada.ca/ccdss/data-tool/Age?G=00&V=7&M=1
- **Incidence:** https://health-infobase.canada.ca/ccdss/data-tool/Age?G=00&V=7&M=1
- **Baseline GOLD Stage Distribution:** Leung C, Bourbeau J, Sin DD, et al. The Prevalence of Chronic Obstructive Pulmonary Disease (COPD) and the Heterogeneity of Risk Factors in the Canadian Population: Results from the Canadian Obstructive Lung Disease (COLD) Study. Int J Chron Obstruct Pulmon Dis. 2021;16:305-320.
- **Smoking Status:** NOVELTY provided by AstraZeneca; An Observational Study of Obstructive Lung Disease (NOVELTY) in Patients with a Diagnosis or Suspected Diagnosis of Asthma and/or COPD
- **FEV_1 Decline:** Barrecheguren, M, Pinto, L, Mostafavi-Pour-Manshadi, S-M, et al. Identification and definition of asthma–COPD overlap: The CanCOLD study. Respirology. 2020; 25: 836– 849. https://doi.org/10.1111/resp.13780
- **FEV_1 Decline from Smoking:** Oelsner EC, et. al. Lung function decline in former smokers and low-intensity current smokers: a secondary data analysis of the NHLBI Pooled Cohorts Study. Lancet Respir Med. 2020 Jan;8(1):34-44.
- **Asthma Comorbidity Rate:** Oostrik L. et al. Physical activity and symptom burden in COPD: the Canadian Obstructive Lung Disease study. Chronic Obstr Pulm Dis. 2023; 10(1): 89-101.
- **Smoking Cessation Rate:** Guanzhang, et al. Smoking and smoking cessation among people with chronic obstructive pulmonary disease (COPD), Canadian Journal of Respiratory, Critical Care, and Sleep Medicine, 2021; 5:4, 253-260.
- **Baseline Treatment Distribution:** Criner G, Martinez F, et. al. PROMETHEUS: Long-Term Exacerbation and Mortality Benefits of Implementing Single-Inhaler Triple Therapy in the US COPD Population. J Health Econ Outcomes Res. 2023 Jan 24;10(1):20-27.
- **[18] Treatment Transition:** Soler-Cataluña JJ, et. al. Impact of COPD Exacerbations and Burden of Disease in Spain: AVOIDEX Study," International Journal of Chronic Obstructive Pulmonary Disease, vol. 18, pp. 1103-1114, 2023.
- **Baseline Mortality Risk:** https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=3910000701
- **All-cause Mortality in Patients with COPD:** https://health-infobase.canada.ca/ccdss/data-tool/Age?G=00&V=7&M=1
- **Exacerbation Rates:** Criner G, Martinez F, et. al. PROMETHEUS: Long-Term Exacerbation and Mortality Benefits of Implementing Single-Inhaler Triple Therapy in the US COPD Population. J Health Econ Outcomes Res. 2023 Jan 24;10(1):20-27.
- **Cost:** Internal AZ data
- **RCTs**
    - Of note, the authors assumed SITT reduced moderate and severe exacerbations by 21% relative to therapy with no maintenance therapy or therapy with a single agent, 19% relative to therapy with two agents (i.e. LAMA–LABA or ICS–LABA), and 10% relative to multi-inhaler triple therapy. Additionally, the authors applied a 20% reduction in mortality for patients on SITT compared with those not on SITT based on data obtained from the following RCTs:
        - ETHOS: Rabe KF, Martinez FJ, et. al. Triple Inhaled Therapy at Two Glucocorticoid Doses in Moderate-to-Very-Severe COPD. N Engl J Med 2020;383(1):35-48.
        - IMPACT: Lipson DA, Barnhart F, et. al. Once-Daily Single-Inhaler Triple versus Dual Therapy in Patients with COPD. N Engl J Med 2018;378(18):1671-1680

Supplemental Table 1: Sensitivity analysis for the flagged population

				Severe Exacerbations		Moderate Exacerbations	
		Total Patient Years	Death counts	Counts	Cost, CA$	Counts	Cost, CA$
Status Quo	**Base Assumptions**	12.99M	1.25M	3.21M	50.12B	15.94M	9.27B
	10% Lower GOLD Stage	12.28M	1.18M	3.04M	47.45B	15.08M	8.77B
	10% Higher GOLD Stage	14.04M	1.36M	3.52M	54.92B	17.27M	10.04B
	10% Lower Exacerbation Rate	12.88M	1.17M	2.86M	44.76B	14.19M	8.26B
	10% Higher Exacerbation Rate	13.09M	1.32M	3.57M	55.62B	17.72M	10.30B
	COPD Population Growth -1%	12.45M	1.20M	3.08M	48.05B	15.28M	8.87B
	COPD Population Growth +1%	13.58M	1.29M	3.36M	52.43B	16.68M	9.72B
Increased SITT	**Base Assumptions**	14.02M	1.04M	3.05M	47.86B	13.13M	7.66B
	10% Lower GOLD Stage	13.25M	982.07K	2.88M	45.22B	12.42M	7.24B
	10% Higher GOLD Stage	15.17M	1.13M	3.33M	52.29B	14.23M	8.29B
	10% Lower Exacerbation Rate	13.81M	973.86K	2.70M	42.47B	11.61M	6.78B
	10% Higher Exacerbation Rate	14.21M	1.11M	3.41M	53.34B	14.67M	8.55B
	COPD Population Growth -1%	13.45M	1.01M	2.93M	45.93B	12.59M	7.33B
	COPD Population Growth +1%	14.63M	1.08M	3.18M	49.88B	13.71M	8.01B