World Health Organization

Technical briefing for Appendix 3 of the Global Action Plan for Non-Communicable Diseases

Asthma and chronic obstructive pulmonary disease interventions

List of interventions

Number	Interventions
CR1	Acute treatment of asthma exacerbations with inhaled bronchodilators (salbutamol and ipratropium) and oral steroids
CR2	Acute treatment of chronic obstructive pulmonary disease (COPD) exacerbations with inhaled bronchodilator (salbutamol) and oral steroids
CR3	Long-term management of asthma with inhaled bronchodilator and low-dose beclomethasone
CR4	Long-term management of COPD with inhaled bronchodilators (salbutamol and ipratropium)

Identification of interventions

The interventions considered for analysis are drawn from the Package of Essential Non-Communicable Disease Interventions in low and middle income settings [1], as well as previous updates of the Appendix 3 interventions with WHO-CHOICE analysis [2]. For asthma treatment, WHO recommends a step wise approach, with each additional treatment step used when asthma symptoms remain uncontrolled at the previous treatment step. A total of four interventions are included:

For the 2022 update, interventions were redefined to reflect the latest PEN recommendations. Compared to the 2017 update, the patient management was divided into acute and long-term management of asthma and COPD and additional treatments such as oral steroids to control symptoms in the acute phase were added. One intervention was included to the 2022 update (i.e. long-term management of COPD with inhaled bronchodilators, CR4).

Methodological assumptions

- The impact of interventions was estimated with the OneHealth Tool [3].
- Methodology and data on changes in disability weights follows the 2017 appendix 3 update [4] and previously published CHOICE methodology for asthma and COPD [5].
- Country-specific asthma and COPD epidemiological parameters are derived from the Global Burden of Disease study for 2019 [6].
- The primary endpoint is the control of asthma or COPD –i.e. absence of asthma symptoms or stability of COPD symptoms

- Disability weights for asthma were taken from the GBD disability weight study for controlled, partially controlled, and uncontrolled [6]. Disability weighs were 0.015 for controlled, 0.036 for partially controlled and 0.133 for uncontrolled asthma.
- Disability weights for COPD were taken from the GBD disability weight study for mild, moderate and severe COPD [6]. Disability weights were 0.019 for mild, 0.225 for moderate and 0.407 for severe COPD.
- There are no studies or reports on the effect of asthma or COPD treatment on mortality, except for the use of low-dose inhaled corticosteroids for asthma in intervention CR3.

Table 1: Impact sizes used in WHO-CHOICE analysis

	Population (P), effect size of interventions (E) and outcomes (O)	**Comment on evidence and main changes to 2017 analysis**
CR1	**P:** Patients with acute exacerbation of asthma (uncontrolled asthma) **E:** 33.7% reduction in the DW for treatment of asthma with inhaled salbutamol, ipratropium and oral prednisolone (i.e. steroids) **O:** Health life years gained (HLY) through reduction in disability weight.	Added ipratropium and oral steroids. Addition of anticholinergic to SABA reduced risk of admission in children [9] and adults [10] as a proxy for severity. Early treatment with systemic steroids reduced admission rates [11].
CR2	**P:** Patients with acute exacerbation of COPD (uncontrolled COPD) **E:** 34% reduction in DW for treatment of COPD with ipratropium and oral prednisolone **O:** Health life years gained (HLY) through reduction in disability weight.	Added ipratropium and oral steroids. Systemic corticosteroids (e.g. oral prednisolone) reduces the risk of treatment failure, including hospital admission [12]. Increase in lung function (FEV1 and FVC) and improved dyspnoea from baseline with all regimes of inhaled SABA [13].
CR3	**P:** Patients with asthma receiving life-long treatment to keep symptoms controlled **E:** Treatment with inhaled salbutamol only (30% of patients in need), a combination of inhaled salbutamol and low-dose beclometasone (40% of patients) or inhaled salbutamol and high-dose beclometasone (30% of patients) • 7.98% reduction in the DW for treatment of asthma using low dose inhaled beclomethasone and short acting beta agonist. • 13.26% reduction in the DW for treatment of asthma using high dose inhaled beclomethasone and short acting beta agonist. • 50% reduction of death rate with one canister of inhaled corticosteroids every 2 months.	Additional treatment option (high-dose beclometasone). Changed distribution of population in need. Regular use of low-dose inhaled corticosteroids is associated with a decreased risk of death from asthma of 50%. The evidence is from a nested case-control study in Canada [7,8] Regular use of inhaled corticosteroids reduces risk of hospital admissions [14] and severe asthma [15].

	O: Health life years gained (HLY) through mortality averted and reduction in disability weight.	
CR4	**P:** Patients with COPD receiving life-long treatment to keep symptoms controlled **I:** Treatment with inhaled salbutamol and ipratropium • 15% reduction in the DW for treatment of COPD with inhaled salbutamol. • 17% reduction in the DW for treatment of COPD with inhaled ipratropium. **O:** Health life years gained (HLY) through reduction in disability weight.	New intervention Inhaled salbutamol has shown to lead to improvement in quality of life (daily breathlessness score) [16]. Ipratropium bromide vs SABA for stable COPD: small benefits to lung function, quality of life and requirement for oral steroids [17].

DW = disability weight

Table 2: Costing assumptions used in WHO-CHOICE analysis

- Data on quantities obtained from PEN protocol, literature and expert opinion [1].
- Data on prices for drugs and supplies obtained from UNICEF and MSH price indicator (median seller price) [18,19]
- Unit costs for the visits were obtained from the WHO-CHOICE price database [20].

	Major costing assumptions	**Comments**

CR1	• Visits:
	  ○ 1 outpatient visit for acute exacerbation (all patients: mild/moderate/severe)
	  ○ 3 inpatient bed-days for acute exacerbation (25% of patients presenting to the health facility[1])
	• Drugs:
	  ○ Mod-severe: salbutamol 10 puffs (100 microg/puff) every 20 min for 1 hour, then every 6 hours for 3 days (total = 150 puffs) (50% of patients presenting to health facility)
	  ○ Mod-severe: ipratropium 8 puffs (20 microg/puff) every 20 min for 1 hour, then stop (total = 24 puffs) (50% of patients presenting to health facility)
	  ○ Mild: salbutamol 5 puffs every 6 hours for 3 days (total = 60 puffs) (50% of patients presenting to health facility)
	  ○ All: Prednisolone 50mg per day for 5 days
	• Supplies: Spacer to use with meter-dose inhaler
		Salbutamol dose and frequency depend on severity of episode
		
		Ipratropium for all but mild attacks to speed recovery and prevent admission – not needed once stabilised

[1] From Griffiths and Kirkland: 25% admission rate among those treated with SABA alone [9,10]

CR2	• Visits:
	  ○ 1 outpatient visit for acute exacerbation
	  ○ 4 inpatient bed-days for acute exacerbation (25% of patients presenting to the health facility)
	• Drugs:
	  ○ Salbutamol 4 puffs (100 microg/puff) every 20 minutes for 1 hour, then 2 puffs every 6 hours for 5 days) (total=52 puffs)
	  ○ Prednisolone 50mg per day for 5 days
	• Supplies: Spacer to use with meter-dose inhaler
		From Walters 2014 [12] ~25% patients need intensified treatment/ admission without corticosteroids

CR3	• Visits:
	  ○ 2 follow-up outpatient visits per year
	• Drugs:
	  ○ Salbutamol as needed: on average 1 puff (100µg) per day for 365 days +
	  ○ Beclometasone: on average 200µg per day for 365 days (low-dose) (2 puffs per day).
	  ○ Beclomethasone: on average 400µg per day for 365 days (high-dose) (4 puffs per day).
	• Supplies: None
		Salbutamol: 1 puff per day equates to 1-2 inhalers per year (3 or more 200-dose canisters/years is considered over-use) [21]
		
		Dose of ICS will vary – some may need higher dose, but some will only use as needed with SABA

CR4	• Visits:
	  ○ 2 follow-up outpatient visits per year
	• Drugs:
	  ○ Salbutamol as needed: on average 1 puff (100 microg) per day for 365 days (all COPD patients)
	  ○ Salbutamol 800 µg per day (2 puffs 4x/day) for 365 days + (for 25% of patients with COPD)
	  ○ Ipratropium 120µg per day (2 puffs 3x/day) for 365 days (for 5% of patients with COPD))
	• Supplies: None
		Dose from Sestini 2010 [16]: salbutamol 200microg 4x/day (similar to PEN 2020 [1])
		
		From ATS statement – dyspnea affects 25% patients seeking care in ambulatory settings
		
		Ipratropium not generally recommended but can be trialled for symptomatic benefit in individual patients [17].

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