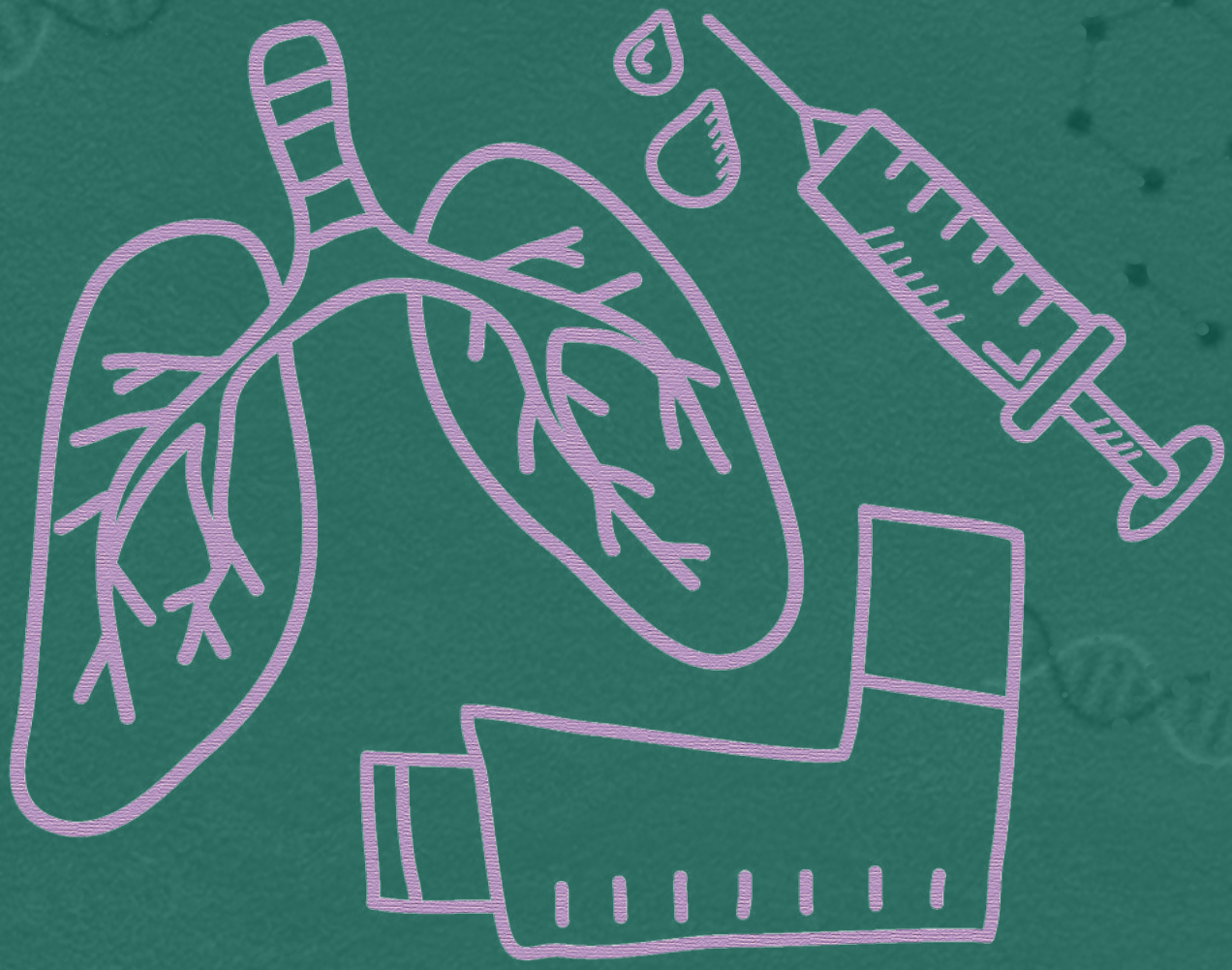
SERI SOCIAL & ECONOMIC RESEARCH INITIATIVE

Financing the Treatment of Severe Asthma:

A Case for Biologics Coverage by Private Insurance Providers



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Contents

EXECUTIVE SUMMARY

Severe asthma imposes a significant health and economic burden globally, with frequent exacerbations leading to increased hospitalisations, emergency treatments, and dependency on high-dose corticosteroids. Many patients remain inadequately controlled despite intensive therapy with inhaled corticosteroids (ICS) and systemic/oral corticosteroids (OCS).

Biologics have emerged as **a transformative solution for patients with severe asthma who do not respond adequately to standard treatments with ICS and OCS.** These therapies significantly reduce exacerbations, improve patient quality of life, and lower the financial burden of severe asthma by decreasing the need for emergency care and hospitalisations. However, private insurance providers often do not cover biologics, limiting patient access to these life-changing treatments.

The key takeaways are as follows:

DEFINING THE ELIGIBLE PATIENT SUB-GROUP

International health agencies and regulatory bodies have developed clinical criteria to determine which patients would benefit most from biologics. These guidelines often consider factors such as persistent symptoms despite maximum standard therapy and frequent exacerbations requiring systemic corticosteroids. The report emphasises corticosteroid dependence and frequent exacerbations as primary criteria for biologic eligibility.

ADDRESSING MISCONCEPTIONS ABOUT ASTHMA ONSET

A major barrier to biologic coverage is the misconception that asthma is exclusively a childhood disease. Studies show that nearly half of middle-aged asthma patients developed the condition in adulthood, with adult-onset asthma often being more severe and less likely to enter remission. The misclassification of adult-onset asthma as childhood-onset results in unnecessary coverage denials, limiting access to effective treatments.

QUANTIFYING COST SAVINGS OF BIOLOGICS

Although biologic therapies involve higher upfront costs than standard treatments, their ability to reduce severe asthma exacerbations and dependence on OCS leads to long-term financial benefits by mitigating hospital admissions, emergency treatments and steroid-induced morbidity.

DEFINITION OF KEY TERMS

Terms	Definitions
SEVERE ASTHMA	A chronic respiratory condition characterised by frequent exacerbations, high dependency on inhaled corticosteroids (ICS) and systemic/oral corticosteroids (OCS), and poor symptom control despite standard treatment[1].
BIOLOGICS	Advanced targeted therapies that reduce asthma exacerbations, particularly in patients with severe, uncontrolled asthma[2].
INHALED CORTICOSTEROIDS (ICS)	Medications that reduce airway inflammation and help control asthma symptoms. High-dose ICS is commonly used for severe asthma management[3].
ORAL CORTICOSTERIOIDS (OCS)	Systemic steroids are used to manage severe asthma exacerbations but are associated with significant long-term side effects[4].
EXACERBATION	A worsening of asthma symptoms requiring additional treatment, such as emergency care, hospitalisation, or increased corticosteroid use[5].

[01] Global Initiative for Asthma, "Global Strategy for Asthma Management and Prevention."
[02] Ibid.
[03] World Health Organisation, "Asthma."
[04] Barry et al., "The Cost of Systemic Corticosteroid-Induced Morbidity in Severe Asthma: A Health Economic Analysis."
[05] Ivanova et al., "Effect of Asthma Exacerbations on Health Care Costs among Asthmatic Patients with Moderate and Severe Persistent Asthma."

INTRODUCTION

The Burden of Severe Asthma

Severe asthma is a condition characterised by a significant dependency on ICS and bronchodilators, often requiring frequent use of OCS to manage exacerbations[6]. Exacerbations, defined as asthma-related hospitalisations, emergency treatments or corticosteroid prescription[7], contribute a substantial health and economic burden. Globally, asthma is the 16th most common cause of years lived with disability and 28th most common cause of burden of disease as measured by disability-adjusted life years, with most asthma deaths occurring in low-middle income countries[8].

The economic impact of severe asthma is considerable, accounting for more than half of the treatment cost due to increased medication use, frequent outpatient and emergency room visits and hospitalisations[9].

With the increasing prevalence of asthma linked to urbanisation[10], **addressing the costs associated with the disease through appropriate and effective healthcare intervention would be imperative to mitigate the costs faced by patients and payers** such as private insurance providers.

The Role of Biologics in Severe Asthma Management

Innovative healthcare technologies, such as biologics, have been increasingly used for severe asthma patients who experience suboptimal outcomes from the standard of care (SOC) with ICS and OCS[11]. **Biologics** offer a promising opportunity to **reduce exacerbations, improve patient outcomes, and generate long-term cost savings by decreasing hospitalisations and emergency care needs.**

Objectives

The primary objectives of this report are:

- **IDENTIFYING THE ELIGIBLE PATIENT SUB-GROUP**
- **ADDRESSING MISCONCEPTIONS ABOUT ASTHMA ONSET**
- **QUANTIFYING COST SAVINGS OF BIOLOGICS**

[06] Ibrahim, Ismail, and Abdul Rani, "A Brief Review of Severe Asthma."
[07] Ivanova et al., "Effect of Asthma Exacerbations on Health Care Costs among Asthmatic Patients with Moderate and Severe Persistent Asthma."
[08] Ibrahim, Ismail, and Abdul Rani, "A Brief Review of Severe Asthma."
[09] Ivanova et al., "Effect of Asthma Exacerbations on Health Care Costs among Asthmatic Patients with Moderate and Severe Persistent Asthma."
[10] World Health Organisation, "Asthma."
[11] Jin, "Biological Treatments for Severe Asthma."

IDENTIFYING THE SUB-GROUP OF PATIENTS REQUIRING BIOLOGICS

To optimise biologics' benefits in treating severe asthma, it is crucial to define the sub-group of severe asthma patients most likely to benefit. Regulatory bodies such as the National Institute for Health and Care Excellence (NICE), which evaluates new health technologies of use in the UK National Health Service (NHS)[12] and Canada's Drug Agency have established eligibility criteria for biologic use in severe asthma patients.

Eligibility Criteria for Biologics

There are several ways in which this can be defined. For example, NICE has recommended that biologics such as tezepelumab, benralizumab, mepolizumab, reslizumab, omalizumab and dupilumab be used as an add-on therapy for treating severe asthma that is inadequately controlled in adults despite maintenance therapy with high-dose inhaled corticosteroids plus another drug with the following criteria[13,14,15,16,17,18]:

Biologic	Patient Criteria for Treatment
TEZEPELUMAB	Severe asthma who has: ■ Maintenance OCS ■ 3 or more exacerbations in the past year
BENRALIZUMAB	Severe eosinophilic asthma who has: ■ Blood eosinophil count ≥300 cells/μL ■ 4 or more exacerbations requiring systemic corticosteroids in the last 12 months or continuous oral corticosteroids for at least the equivalent of prednisolone 5 mg per day over the previous 6 months OR ■ Blood eosinophil count ≥400 cells/μL ■ 3 or more exacerbations requiring systemic corticosteroids in the last 12 months

[12] National Institute for Health and Care Excellence (NICE) "What We Do."
[13] National Institute for Health and Care Excellence (NICE) "Tezepelumab for Treating Severe Asthma: Technology Appraisal Guidance."
[14] National Institute for Health and Care Excellence (NICE) "Benralizumab for Treating Severe Eosinophilic Asthma: Technology Appraisal Guidance."
[15] National Institute for Health and Care Excellence (NICE) "Mepolizumab for Treating Severe Eosinophilic Asthma: Technology Appraisal Guidance."
[16] National Institute for Health and Care Excellence (NICE) "Reslizumab for Treating Severe Eosinophilic Asthma: Technology Appraisal Guidance."
[17] National Institute for Health and Care Excellence (NICE) "Omalizumab for Treating Severe Persistent Allergic Asthma: Technology Appraisal Guidance."
[18] National Institute for Health and Care Excellence (NICE) "Dupilumab for Treating Severe Asthma with Type 2 Inflammation: Technology Appraisal Guidance."

Biologic	Patient Criteria for Treatment
MEPOLIZUMAB	Severe refractory eosinophilic asthma who has: ■ Blood eosinophil count ≥300 cells/μL ■ 4 or more exacerbations requiring systemic corticosteroids in the last 12 months or continuous oral corticosteroids for at least the equivalent of prednisolone 5 mg per day over the previous 6 months OR ■ Blood eosinophil count ≥400 cells/μL ■ 3 or more exacerbations requiring systemic corticosteroids in the last 12 months
RESLIZUMAB	Severe eosinophilic asthma who has: ■ Blood eosinophil count ≥400 cells/μL ■ 3 or more exacerbations requiring systemic corticosteroids in the last 12 months
OMALIZUMAB	Severe persistent allergic asthma who has: ■ a positive skin test or in vitro reactivity to a perennial aeroallergen ■ reduced lung function ■ frequent daytime symptoms or night-time awakenings ■ Multiple documented severe exacerbations despite daily high-dose inhaled corticosteroids plus a long-acting inhaled beta2 agonista
DUPILUMAB	Severe asthma with type 2 inflammation who has: ■ Blood eosinophil count ≥150 cells/μL ■ 4 or more exacerbations requiring systemic corticosteroids in the last 12 months ■ fractional exhaled nitric oxide of 25 parts per billion or more ■ Not eligible for mepolizumab, reslizumab or benralizumab, or has asthma that has not responded adequately to these biological therapies

Canada's Drug agency has employed similar criteria with slight variations as shown in the following table[19]:

[19] Randall et al., "The Efficacy and Safety of Biologic Drugs to Treat Severe Asthma: Rapid Review."

Biologic	Recommendation
TEZEPELUMAB	**Add-on maintenance treatment in adults and adolescents 12 years and older with severe asthma, only if:** ■ Asthma uncontrolled with high-dose ICS and 1 or more additional asthma controllers AND ■ Experienced 2 or more clinically significant asthma exacerbations in the past 12 months AND ■ A baseline assessment of asthma symptom control using a validated Asthma Control Questionnaire must be completed before initiation of tezepelumab treatment
BENRALIZUMAB	**Add-on maintenance treatment for adult patients with severe eosinophilic asthma if the following criteria are met:** **The patient is inadequately controlled with high-dose inhaled corticosteroids and 1 or more additional asthma controller(s) (eg, long-acting beta-agonists) if 1 of the following 2 clinical criteria is met:** ■ Blood eosinophil count of ≥ 300 cells/µL AND has experienced 2 or more clinically significant asthma exacerbations in the past 12 months OR ■ Blood eosinophil count of ≥ 150 cells/ µL AND is treated chronically with oral corticosteroids. **Benralizumab should not be prescribed to patients who smoke** **Benralizumab should not be used in combination with other biologics used to treat asthma.**

Biologic	Recommendation
MEPOLIZUMAB	**As an add-on maintenance treatment for adult patients with severe eosinophilic asthma, if the following criteria are met:** **01.** The patient must have a documented diagnosis of asthma **02.** The patient is inadequately controlled with high-dose inhaled corticosteroids, defined as greater or equal to 500 mcg of fluticasone propionate or equivalent daily, and 1 or more additional asthma controller(s) (eg, long-acting beta-agonists) **03.** The patient has 1 of the following: **3.1** Blood eosinophil count of ≥ 300 cells/μL AND has experienced 2 or more clinically significant asthma exacerbations in the past 12 months, OR **3.2** blood eosinophil count of ≥ 150 cells/μL AND is receiving maintenance treatment with oral corticosteroids
OMALIZUMAB	**For adults and adolescents (12 years of age and older) with moderate to severe persistent asthma who have a positive skin test or in vitro reactivity to a perennial aeroallergen, if the following clinical criterion is met:** Inability to use, intolerance to, or inadequate response to an inhaled corticosteroid long-acting beta-agonist combination, and at least 1 other reimbursed alternative asthma treatment
DUPILUMAB	Add-on maintenance treatment in patients aged 6 years and older with severe asthma with a type 2/eosinophilic phenotype or oral corticosteroid–dependent asthma

The common denominator across these criteria would be the continued use of ICS and OCS but with persistent exacerbations.

Furthermore, discussions with a respiratory physician and member of the expert committee for the Health Technology Assessment Report on Biologics for severe asthma[20] confirmed that an important criterion in considering a severe asthma patient for biologics is their ineffective response to the continued use of ICS and OCS[21].

This was also presented at the National TB and Lung Diseases Conference per the Global Initiative for Asthma (GINA) recommendations for the use of add-on biologic therapies in patients with severe asthma[22].

It is recommended that eligibility for biologic treatment in severe asthma patients be determined based on corticosteroid use, as reducing corticosteroid dependence also lowers the risk of steroid-related comorbidities.

ADDRESSING MISCONCEPTIONS ON ADULT ONSET ASTHMA AND CHILDHOOD ONSET ASTHMA

A critical issue affecting insurance coverage for biologics is the misclassification of asthma as exclusively being a childhood-onset condition. Addressing misconceptions on adult-onset and childhood-onset asthma is pivotal in ensuring severe asthma patients receive the necessary coverage for biologics.

This issue was also highlighted by a respiratory physician, whereby patients struggle to obtain coverage for biologics, from either their private insurance providers or other third-party payers[23], in treating their severe asthma. This is due to the misconception that asthma is exclusively a childhood disease, leading to the misclassification of severe asthma as childhood-onset, despite being diagnosed in adulthood.

Asthma is mistakenly considered a childhood disease[24] but global longitudinal studies, such as in the United States and Tasmania, found that approximately half of the middle-aged patients with asthma have had onset in adulthood rather than childhood[25,26].

Moreover, distinguishing between adult and childhood-onset asthma helps to determine which patients require biologics, as adult-onset asthma progresses differently from childhood-onset asthma. Childhood-onset asthma is mainly mild and remission is common[27] whereas adult-onset asthma is more severe and remission is uncommon[28].

[20] Maharita AR, Baihaqi M., Khairil Idham I., Anna Sani, Izzuna MMG. "Biologics in Severe Asthma: Health Technology Assessment."
[21] Omar, Discussion on Treating Severe Asthma Patients with Biologics.
[22] Omar, "National TB & Lung Diseases Conference: Latest Update on Severe Asthma Management."
[23] Omar, Discussion on Treating Severe Asthma Patients with Biologics.
[24] Trivedi and Denton, "Asthma in Children and Adults-What Are the Differences and What Can They Tell Us About Asthma?"
[25] Sood et al., "Adult-Onset Asthma Becomes the Dominant Phenotype among Women by Age 40 Years. the Longitudinal CARDIA Study."
[26] Tan et al., "Clinical and Functional Differences between Early-Onset and Late-Onset Adult Asthma: A Population-Based Tasmanian Longitudinal Health Study."
[27] Bronnimann and Burrows, "A Prospective Study of the Natural History of Asthma. Remission and Relapse Rates."
[28] Maestrelli, "Natural History of Adult-Onset Asthma: Insights from Model of Occupational Asthma."

The misconception that asthma is only a childhood-onset disease prevents adequate coverage for adult-onset asthma patients, who are more likely to have severe asthma requiring biologic treatment. Innovative therapies such as biologics must be examined, specifically for their ability to reduce patients' exacerbations and generate potential cost savings. Given the significant burden of severe asthma and the challenges in obtaining treatment coverage, patients must understand such benefits.

COST SAVINGS OF BIOLOGICS

Decision-Making Context

Biologics do not always meet the criteria for standard cost-effectiveness, particularly from a public-payer perspective. There have been mixed results in various territories in terms of their cost-effectiveness.[29,30] From the Ministry of Health's (MOH) perspective in Malaysia, it has been proven to positively impact quality-adjusted life years but at a cost that exceeds Malaysians' willingness to pay[31]. Nevertheless, there are other perspectives to consider, such as third-party payers, namely private insurance providers who can provide alternative funding and coverage for severe asthma patients with biologics. Cost savings achieved by reducing exacerbations and OCS dependence would be a key area of focus.

Methodology

An Excel-based cost-minimisation model was developed to compare the reduction in exacerbation costs and OCS dependence costs achieved through biologics versus standard of care (SOC). Similar methods were employed in a cost comparison of benralizumab, mepolizumab, and dupilumab in patients with severe asthma from a US third-party-payer perspective[32]. The key difference is that this report is concerned with comparing exacerbation costs and OCS dependence costs of severe asthma patients on biologics versus SOC rather than comparing the costs and cost-offsets between biologics. A third-party-payer perspective is taken as this report aims to demonstrate the cost savings that biologics would give if private insurance companies in Malaysia provided adequate coverage. Perspective, as defined by the Pharmacoeconomic guidelines for Malaysia, is adopted for deciding on the types of costs and health benefits to include, which is determined by the context of the study, persons or institutions affected by the outcome of interest, and those that bear the costs of the healthcare intervention[33]. Hence, the cost-savings of biologics in reducing severe asthma exacerbations and OCS dependence are the outcome of interest.

A cost comparison between biologics and SOC in terms of cost savings from exacerbation reductions and OCS dependence reduction is conducted to illustrate why biologics coverage will provide healthcare cost savings in the medium to long term.

[29] McQueen et al., "Cost-Effectiveness of Biological Asthma Treatments: A Systematic Review and Recommendations for Future Economic Evaluations."
[30] Alves, Rufo, and Crispim, "Economic Evaluation of Biological Treatments in Patients with Severe Asthma: A Systematic Review."
[31] Maharita AR, Baihaqi M., Khairil Idham I., Anna Sani, Izzuna MMG, "Biologics in Severe Asthma: Health Technology Assessment."
[32] Ministry of Health Malaysia, "Pharmacoeconomic Guidelines for Malaysia."
[33] Xu et al., "A Cost Comparison of Benralizumab, Mepolizumab, and Dupilumab in Patients with Severe Asthma- A US Third-Party Payer Perspective."

To generate quantitative estimates of the cost savings of biologics, exacerbation reduction data from clinical trial studies of biologics such as tezepelumab, benralizumab, mepolizumab, and dupilumab[34,35], and exacerbation costs data from a real-world study on the economic burden of severe asthma treatment[36] were utilised. OCS dependence costs data were used from a health economic analysis estimating the additional healthcare costs of steroid-induced morbidity[37].

The level of exacerbation used was two per year because various studies indicate that this is the minimum number of exacerbations severe asthma patients experience[38,39,40]. This scenario was chosen for the base-case results to be prudent, even though the number of exacerbations is likely to exceed twice a year[41,42]. The exacerbation costs data from Mexico were adapted into a Malaysian context by converting these costs into a common currency using purchasing power parity (PPP), a method that's utilised to enhance generalisability in economic evaluations[43]. As the OCS dependence costs data were expressed in 2013 Great British Pounds, these costs were converted using PPP as well.

These methods were adapted to generalise OCS dependence cost and exacerbation costs, including hospitalisation and emergency treatments. The generalised costs were adjusted for inflation using OpenDOSM's inflation data provided by the Department of Statistics Malaysia[44].

Sensitivity Analyses

Sensitivity analyses assess the confidence level associated with an economic evaluation's output. They are performed by varying key inputs to evaluate and record the output number. Sensitivity analyses are an important part of the evaluation process and give decision-makers valuable information about the robustness of their decisions based on the findings of an economic evaluation.

A one-way sensitivity analysis (OWSA) was conducted to explore the uncertainty in the cost savings of biologics from exacerbation reduction and OCS dependence reduction. OWSA involves varying inputs one at a time to evaluate the effect of a certain input parameter on the results[45,46]. The lower and upper bounds for parameters such as exacerbation rate reduction and OCS dependence rate reduction, which were +/- 10% of the base, are used to observe the impact on the marginal cost difference between SOC and biologics for annual exacerbations costs and OCS dependence costs. The lower and upper bounds for parameters such as the cost of exacerbations and OCS dependence were utilised from studies

[34] Xu et al., "A Cost Comparison of Benralizumab, Mepolizumab, and Dupilumab in Patients with Severe Asthma- A US Third-Party Payer Perspective."
[35] Habash et al., "Cost-Effectiveness of Tezepelumab in Canada for Severe Asthma."
[36] López-Tiro et al., "Economic Burden of Severe Asthma Treatment: A Real-Life Study."
[37] Barry et al., "The Cost of Systemic Corticosteroid-Induced Morbidity in Severe Asthma: A Health Economic Analysis."
[38] Ibrahim, Ismail, and Abdul Rani, "A Brief Review of Severe Asthma."
[39] Christian Jacob, Jennifer S. Haas, Benno Bechtel, Peter Kardos and Sebastian Braun, "Assessing Asthma Severity Based on Claims Data: A Systematic Review."
[40] Global Initiative for Asthma, "Global Strategy for Asthma Management and Prevention."
[41] Ibid.
[42] Omar, "National TB & Lung Diseases Conference: Latest Update on Severe Asthma Management."
[43] Sculpher et al., "Generalisability in Economic Evaluation Studies in Healthcare: A Review and Case Studies."
[44] Department of Statistics Malaysia, "Monthly CPI Inflation by Division (2-Digit)"
[45] York Health Economics Consortium, "Sensitivity Analysis."
[46] York Health Economics Consortium, "Univariate/One Way Sensitivity Analysis."

such as the cost of exacerbations and OCS dependence were utilised from studies that observed the management of asthma-related event costs in a Malaysian Suburban Hospital[47] and analysed the health economic impact and cost of systemic corticosteroid-induced morbidity[48].

A probabilistic sensitivity analysis (PSA) was conducted around the model base case by running a multivariate simulation with 10,000 iterations, assuming various distributional characteristics of each model input variable and characterising uncertainty in the model results. PSAs produce outputs based on the distribution of input parameters[49]. This was repeated in 10,000 iterations and graphed to illustrate the level of confidence that each biologic is cost-saving in terms of annual exacerbation costs and OCS dependence costs compared to SOC.

[47] Yong and Shafie, "How Much Does Management of an Asthma-Related Event Cost in a Malaysian Suburban Hospital?"
[48] Barry et al., "The Cost of Systemic Corticosteroid-Induced Morbidity in Severe Asthma: A Health Economic Analysis."
[49] York Health Economics Consortium, "Probabilistic/Stochastic Sensitivity Analysis."

Findings

FINDINGS

Base Case Results

Figure 1.1
Comparison of Exacerbation Costs

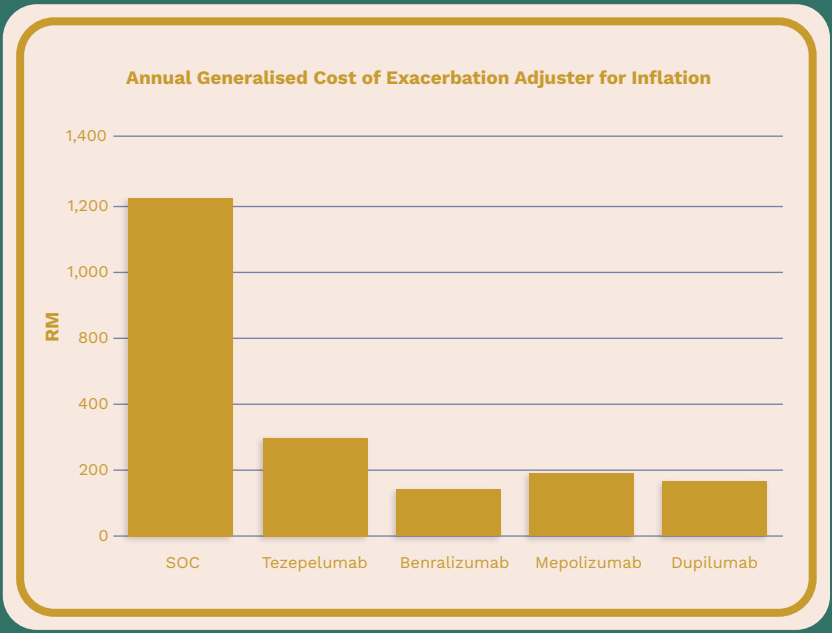


Figure 1.1 compares the exacerbation costs between SOC and various biologics, demonstrating that the biologics presented provide cost savings with lower exacerbation costs (refer to Appendix A and B for details on the calculation of generalised costs). The results in Figure 1.1 show that SOC incurs a higher exacerbation cost per year than all biologics used in the cost comparison. The annual exacerbation costs for SOC are RM1,223 compared to RM355, RM168, RM227 and RM198 for Tezepelumab, Benralizumab, Mepolizumab and Dupilumab, respectively. **The exacerbation costs for severe asthma patients on biologics are less than half the exacerbation costs for patients on SOC.**

Figure 1.2
Annual Cost Savings of Biologics in Exacerbation Reduction

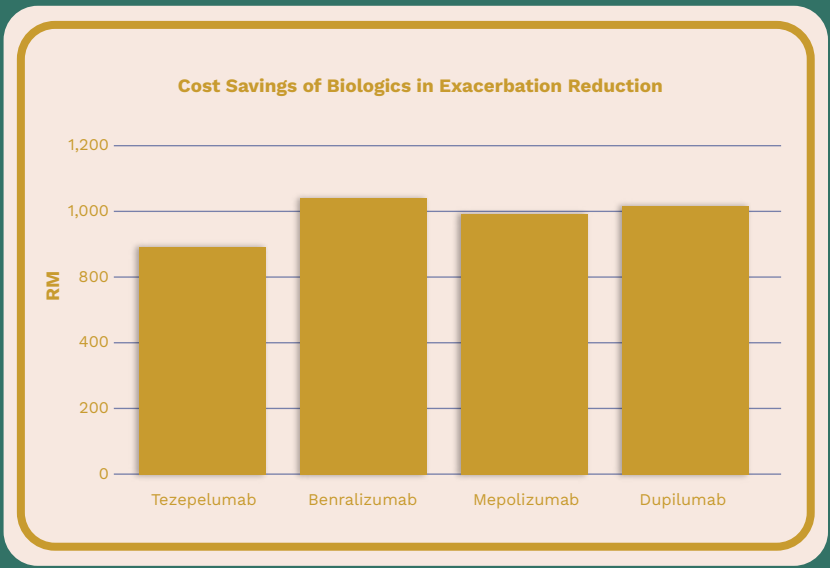


Figure 1.2 presents the base-case results of the expected annual cost savings through each biologic's exacerbation reduction (refer to Appendix C for details on the calculation of annual cost savings). The annual cost savings of biologics through exacerbation reduction per patient are as follows:

- **Tezepelumab** : RM 868
- **Benralizumab** : RM 1,055
- **Mepolizumab** : RM 995
- **Dupilumab** : RM 1,025

Figure 1.3
Comparison of OCS Dependence Costs

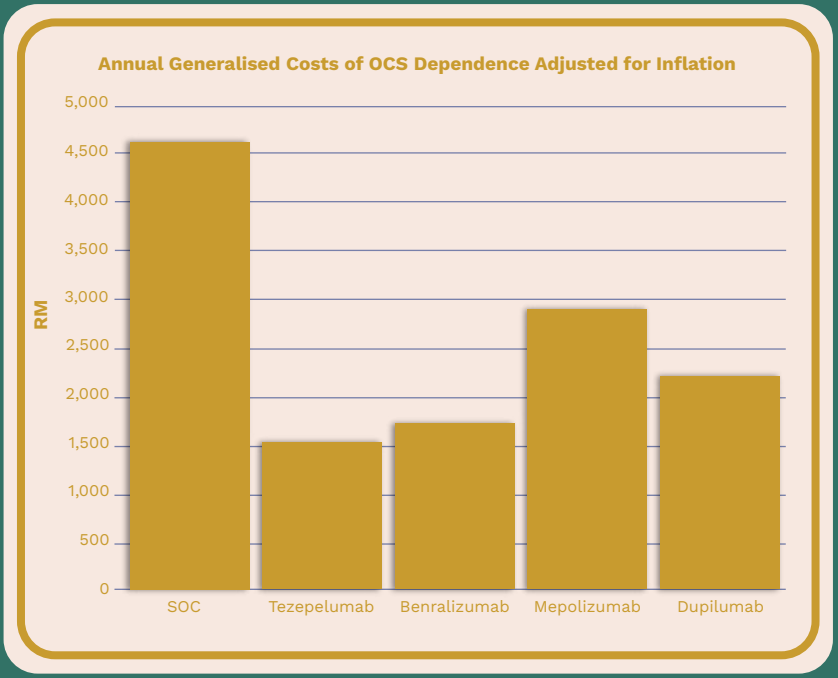


Figure 1.3 presents the comparison of the annual OCS dependence costs between SOC and various biologics, demonstrating that the biologics presented provide cost savings with lower OCS dependence costs (refer to Appendix A and D for details on the calculation of generalised costs).

The results in Figure 1.3 show that SOC incurs a higher annual OCS dependence cost than all biologics used in the cost comparison. The annual OCS dependence costs for SOC are RM 4,706, compared to RM1,546, RM1,741, RM2,941, and RM2,240 for Tezepelumab, Benralizumab, Mepolizumab, and Dupilumab, respectively. The OCS dependence costs for severe asthma patients on biologics, except for those on Mepolizumab, are less than half the OCS dependence costs for patients on SOC.

Figure 1.4
Annual Cost Savings of Biologics in OCS Dependence Costs

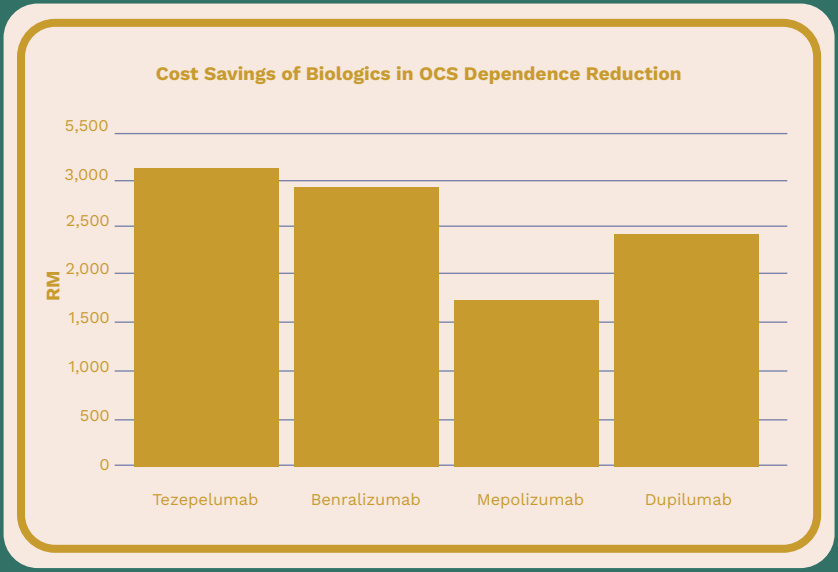


Figure 1.4 presents the base-case results of the expected annual cost savings through each biologic's OCS dependence reduction (refer to Appendix E for details on the calculation of annual cost savings). The annual cost savings of biologics through exacerbation reduction per patient are as follows:

- **Tezepelumab** : RM 3,159
- **Benralizumab** : RM 2,964
- **Mepolizumab** : RM 1,765
- **Dupilumab** : RM 2,466

Overall, the base case results show that biologics significantly reduce some of the costs associated with severe asthma exacerbations and OCS dependence. Hence, third-party payers, such as private insurance providers, can reduce the costs of hospitalisation and emergency treatments by providing coverage for biologics for severe asthma patients.

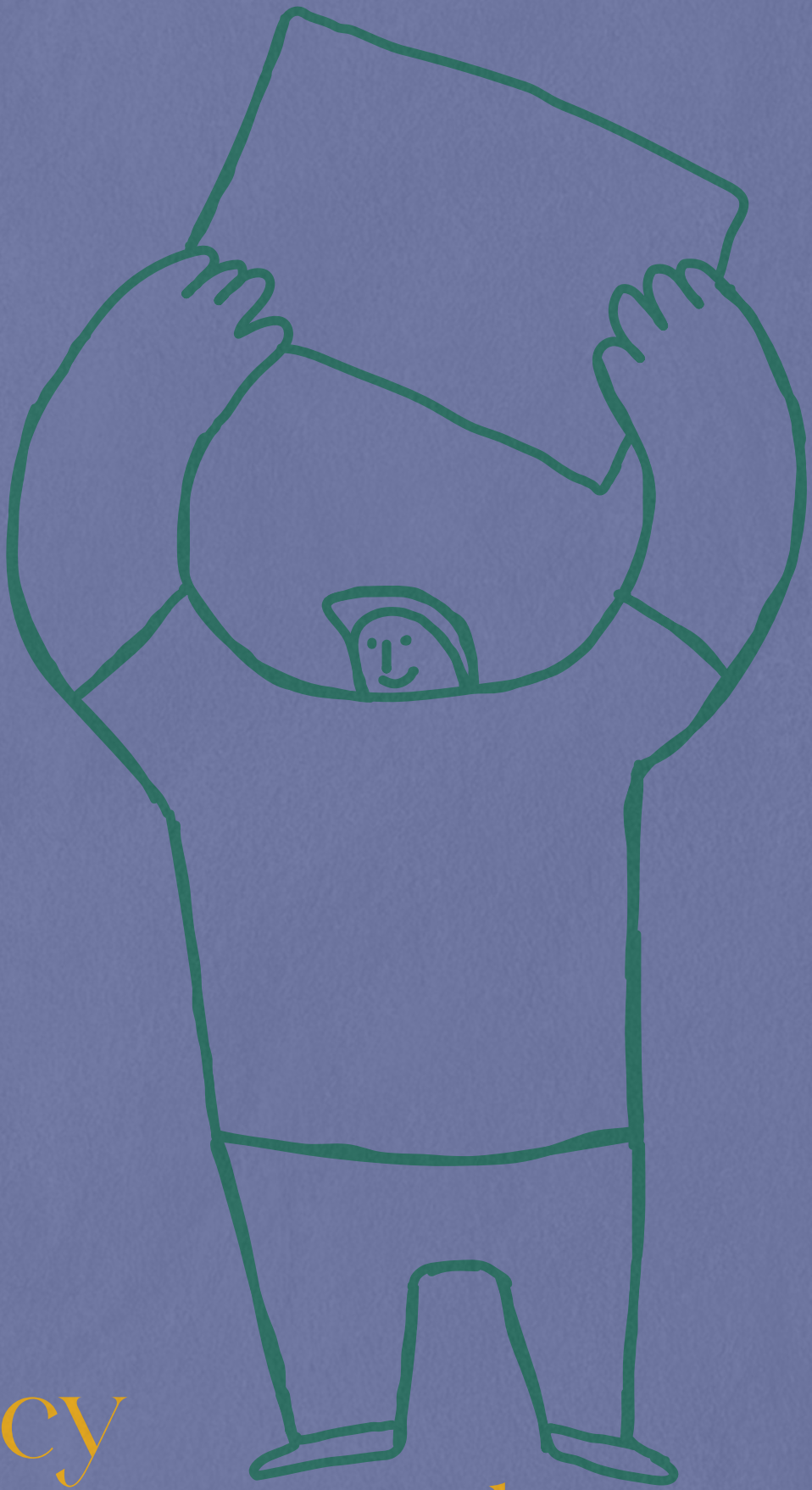
Sensitivity Analyses Results

One-Way Sensitivity Analysis

The OWSA results presented in the graphs in Appendix F to I show the impact of varying certain input parameters such as the cost of OCS dependence, exacerbation costs, OCS dependence and exacerbation rate reduction. The cost of OCS dependence and OCS dependence reduction have the largest impact on the marginal cost difference between each biologic and SOC. Negative cost difference indicates cost savings compared to SOC. The costs of exacerbation and exacerbation rate reduction contribute to a relatively smaller cost difference compared to the OCS-related factors. Overall, the OWSA exemplifies that biologics provide cost savings for all the ranges and values used in the analysis.

Probabilistic Sensitivity Analysis

The PSA results in Appendix J to M quantify the probability of each biologic being cost-saving in terms of annual exacerbation costs and OCS dependence costs compared to SOC. The results showed that all biologics had a 100% probability of being cost-saving for both exacerbation and OCS dependence costs. The only exception was mepolizumab, where the probability of cost savings on OCS dependence costs compared to SOC was 99.66%. It should be noted that the iterations that were not cost-saving were outliers. Refer to Appendix M for more details.



Policy Recommendations

POLICY RECOMMENDATIONS

Establish standardised Eligibility Criteria to Optimise Resource Allocation.

Standardised eligibility criteria should be developed based on clinical guidelines to ensure private insurers effectively allocate resources. Coverage should prioritise patients who:

- Have a history of frequent exacerbations (e.g. two or more per year) requiring hospitalisation or systemic corticosteroid treatment.
- Demonstrate corticosteroid dependence, as reducing OCS use is linked with lower long-term healthcare costs and reduced risk of steroid-related comorbidities.

Improving Access for Adult-Onset Asthma Patients

A significant barrier to biologic coverage is the misconception that asthma is exclusively a childhood disease. Studies indicate that nearly half of middle-aged asthma patients develop the condition in adulthood and adult-onset asthma is often more severe and less likely to enter remission. Insurers should revise coverage policies to reflect this reality, ensuring that patients with adult-onset severe asthma receive equitable access to biologics.

Expand Coverage for Biologics Based on Long-Term Savings

Clinical and economic evidence demonstrates that biologics reduce severe asthma exacerbations and OCS dependence. The findings in this report indicate that:

- Annual exacerbation-related healthcare costs are significantly lower for patients receiving biologics than for those receiving SOC. For example, SOC annual exacerbation costs amount to RM1,223, whereas biologics reduce these costs to as low as RM168 for certain therapies.
- Biologics reduce OCS dependence, leading to lower long-term costs associated with steroid-induced comorbidities. For example, Tezepelumab reduces OCS dependence costs by RM3,159 per year per patient, generating substantial savings over time.

By covering biologics, private insurers can reduce claims related to hospital admissions, emergency visits, and complications arising from prolonged OCS use, ultimately improving their financial sustainability.

Shifting from Short-Term to Long-Term Cost Considerations

While biologics have higher initial costs, insurers should adopt a long-term perspective when evaluating their financial impact. By preventing costly emergency interventions and hospitalisations, biologics provide a return on investment that outweighs their upfront expense. Sensitivity analyses confirm that biologics remain cost-saving under varying economic conditions, further supporting their inclusion in insurance coverage.

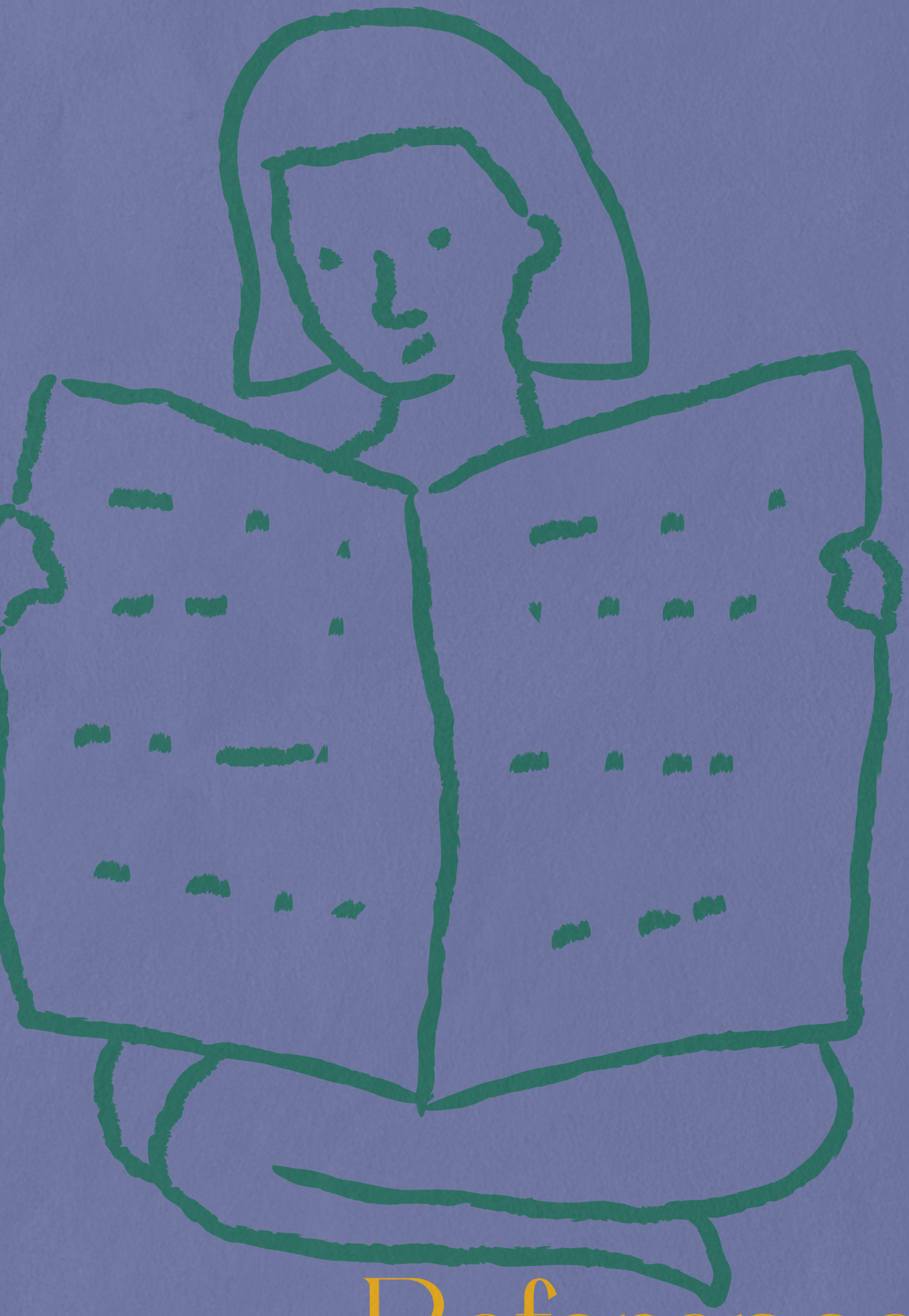
CONCLUSION: A CALL FOR BIOLOGICS COVERAGE BY PRIVATE INSURANCE PROVIDERS

This report's findings highlight the **significant clinical and economic benefits of biologics in treating severe asthma.** Despite their higher upfront costs, biologics have demonstrated their ability to substantially reduce exacerbation rates, leading to fewer hospitalisations and emergency department visits and reducing the long-term use of OCS. By minimising the reliance on OCS, biologics help prevent the development of serious corticosteroid-related complications. The sensitivity analyses also demonstrate that the results were robust.

To ensure that private insurance providers optimise coverage for severe asthma patients, it is essential to implement standardised eligibility criteria that incorporate corticosteroid dependence, exacerbation history, and treatment responsiveness.

Additionally, recognising the distinction between childhood and adult-onset asthma will help eliminate unnecessary barriers to biologics, ensuring that all eligible patients can receive the most effective treatment available.

In conclusion, private insurers can enhance the quality of care for their policyholders while achieving long-term cost savings by incorporating biologic therapies into their coverage plans. By taking a strategic and evidence-based approach to biologic reimbursement, insurers can play a pivotal role in reducing the economic burden of severe asthma, improving patient health outcomes, and ultimately delivering better value for both patients and the healthcare system as a whole.



References

REFERENCES

Alves, Sara, João Cavaleiro Rufo, and José Crispim. "Economic Evaluation of Biological Treatments in Patients with Severe Asthma: A Systematic Review." Expert Review of Pharmacoeconomics & Outcomes Research 23, no. 7 (June 9, 2023): 733–47. doi:10.1080/14737167.2023.2221435.

AstraZeneca. "FASENRA approved for treatment of children aged 6 to 11 with severe asthma," April 11, 2024. https://www.astrazeneca-us.com/media/press-releases/2024/-fasenra-approved-for-treatment-of-children-aged-6-to-11-with-severe-asthma.html.

Barry, L. E., J. Sweeney, C. O'Neill, D. Price, and L. G. Heaney. "The Cost of Systemic Corticosteroid-Induced Morbidity in Severe Asthma: A Health Economic Analysis." Respiratory Research 18, no. 1 (June 26, 2017): 129. doi:10.1186/s12931-017-0614-x.

Bronnimann, S., and B. Burrows. "A Prospective Study of the Natural History of Asthma. Remission and Relapse Rates." Chest 90, no. 4 (October 1986): 480–84. doi:10.1378/chest.90.4.480.

Christian Jacob, Jennifer S. Haas, Benno Bechtel, Peter Kardos and Sebastian Braun. "Assessing Asthma Severity Based on Claims Data: A Systematic Review." The European Journal of Health Economics 18, no. 2 (March 1, 2016): 227–41. https://www.jstor.org/stable/pdf/44320090.pdf?refreqid=fastly-default%3A8d2da28d50fc23ce06639360237d48ea&ab_segments=0%2Fbasic_search_gsv2%2Fcontrol&initiator=&acceptTC=1.

Corren, J., T. Casale, Y. Deniz, and M. Ashby. "Omalizumab, a Recombinant Humanized Anti-IgE Antibody, Reduces Asthma-Related Emergency Room Visits and Hospitalizations in Patients with Allergic Asthma." The Journal of Allergy and Clinical Immunology 111, no. 1 (January 2003). doi:10.1067/mai.2003.49.

Corren, Jonathan, Jane R. Parnes, Liangwei Wang, May Mo, Stephanie L. Roseti, Janet M. Griffiths, and René van der Merwe. "Tezepelumab in Adults with Uncontrolled Asthma," September 7, 2017. doi:10.1056/NEJMoa1704064.

Department of Statistics Malaysia. "Monthly CPI Inflation by Division (2-Digit)." Accessed February 19, 2025. https://open.dosm.gov.my/data-catalogue/cpi_headline_inflation?division=overall&visual=table.

Fala, Loretta. "Nucala (Mepolizumab): First IL-5 Antagonist Monoclonal Antibody FDA Approved for Maintenance Treatment of Patients with Severe Asthma." American Health & Drug Benefits 9, no. Spec Feature (March 2016): 106. https://pmc.ncbi.nlm.nih.gov/articles/PMC5013851/.

Global Initiative for Asthma. "Global Strategy for Asthma Management and Prevention." Global Initiative for Asthma, 2022. https://ginasthma.org/wp-content/uploads/2022/07/GINA-Main-Report-2022-FINAL-22-07-01-WMS.pdf.

Habash, M., H. Guiang, I. Mayers, A. Quinton, V. Vuong, A. Dineen, S. Singh, D. Gibson, and A. P. Turner. "Cost-Effectiveness of Tezepelumab in Canada for Severe Asthma." Journal of Medical Economics 26, no. 1 (2023): 902–14. doi:10.1080/13696998.2023.2234235.

Hoy, S. M. "Tezepelumab: First Approval." Drugs 82, no. 4 (March 2022). doi:10.1007/s40265-022-01679-2.

Ibrahim, Muhammad Amin, Ahmad Izuanuddin Ismail, and Mohammed Fauzi Abdul Rani. "A Brief Review of Severe Asthma." Journal of Clinical and Health Sciences 6, no. 2 (September 1, 2021): 4–12. doi:10.24191/jchs.v6i2.14942.

Isamudin, Diyana, and Faiqah Kamaruddin. "DRG: Good Option but far from Adoption." New Straits Times, December 14, 2024. https://www.nst.com.my/business/economy/2024/12/1148150/drg-good-option-far-adoption.

Ivanova, J. I., R. Bergman, H. G. Birnbaum, G. L. Colice, R. A. Silverman, and K. McLaurin. "Effect of Asthma Exacerbations on Health Care Costs among Asthmatic Patients with Moderate and Severe Persistent Asthma." The Journal of Allergy and Clinical Immunology 129, no. 5 (May 2012): 1229–35. doi:10.1016/j.jaci.2012.01.039.

Jin, H. J. "Biological Treatments for Severe Asthma." Yeungnam University Journal of Medicine 37, no. 4 (October 2020): 262–68. doi:10.12701/yujm.2020.00647.

Kotoulas, Serafeim Chrysovalantis, Ioanna Tsiouprou, Eva Fouka, Athanasia Pataka, Despoina Papakosta, and Konstantinos Porpodis. "Omalizumab: An Optimal Choice for Patients with Severe Allergic Asthma." Journal of Personalized Medicine 12, no. 2 (January 26, 2022): 165. doi:10.3390/jpm12020165.

Lanier, B. Q., J. Corren, W. Lumry, J. Liu, A. Fowler-Taylor, and N. Gupta. "Omalizumab Is Effective in the Long-Term Control of Severe Allergic Asthma." Annals of Allergy, Asthma & Immunology : Official Publication of the American College of Allergy, Asthma, & Immunology 91, no. 2 (August 2003). doi:10.1016/S1081-1206(10)62170-9.

López-Tiro, Jesús, Angelica Contreras-Contreras, M. Eunice Rodríguez-Arellano, and Paula Costa-Urrutia. "Economic Burden of Severe Asthma Treatment: A Real-Life Study." The World Allergy Organization Journal 15, no. 7 (July 2022): 100662. doi:10.1016/j.waojou.2022.100662.

Maestrelli, Piero. "Natural History of Adult-Onset Asthma: Insights from Model of Occupational Asthma." American Journal of Respiratory and Critical Care Medicine 169, no. 3 (February 1, 2004): 331–32. doi:10.1164/rccm.2312012.

Maharita AR, Baihaqi M., Khairil Idham I., Anna Sani, Izzuna MMG. "Biologics in Severe Asthma: Health Technology Assessment." Malaysian Health Technology Assessment Section, January 2024. https://www.moh.gov.my/moh/resources/Penerbitan/MAHTAS/HTA/FR_BIOLOGICS_IN_SEVERE_ASTHMA.pdf.

Mansur, Adel H., S. Siravastava, V. Mitchell, J. Sullivan, and I. Kasujee. "Longterm Clinical Outcomes of Omalizumab Therapy in Severe Allergic Asthma: Study of Efficacy and Safety." Respiratory Medicine 124 (March 1, 2017): 36–43. doi:10.1016/j.rmed.2017.01.008.

McQueen, R. Brett, Danielle N. Sheehan, Melanie D. Whittington, Job F. M. van Boven, and Jonathan D. Campbell. "Cost-Effectiveness of Biological Asthma Treatments: A Systematic Review and Recommendations for Future Economic Evaluations." PharmacoEconomics 36, no. 8 (August 2018): 957–71. doi:10.1007/s40273-018-0658-x.

Ministry of Health Malaysia. "Pharmacoeconomic Guidelines for Malaysia," 2019. https://pharmacy.moh.gov.my/sites/default/files/document-upload/pharmacoeconomic-guidelines-malaysia-malaysia-second-edition-2019-final-page-adjustment.pdf.

National Institute for Health and Care Excellence (NICE),. "Benralizumab for Treating Severe Eosinophilic Asthma: Technology Appraisal Guidance," 2019. https://www.nice.org.uk/guidance/ta565/chapter/1-Recommendations.

————. "Dupilumab for Treating Severe Asthma with Type 2 Inflammation: Technology Appraisal Guidance," 2021. https://www.nice.org.uk/guidance/ta751/chapter/1-Recommendations.

————. "Mepolizumab for Treating Severe Eosinophilic Asthma: Technology App Guidance," 2021. https://www.nice.org.uk/guidance/ta671/chapter/1-Recommendations.

————. "Omalizumab for Treating Severe Persistent Allergic Asthma: Technology Appraisal Guidance," 2013. https://www.nice.org.uk/guidance/ta278/chapter/3-The-technology.

————. "Reslizumab for Treating Severe Eosinophilic Asthma: Technology Appraisal Guidance," 2017. https://www.nice.org.uk/guidance/ta479/chapter/1-Recommendations.

————. "Tezepelumab for Treating Severe Asthma: Technology Appraisal Guidance," 2023. https://www.nice.org.uk/guidance/ta880/chapter/1-Recommendations.

————. "What We Do." Accessed January 13, 2025. https://www.nice.org.uk/about/what-we-do.

Omar, Azza. Discussion on Treating Severe Asthma Patients with Biologics. Interview by Muhammad Daniel Kittu, Online Interview, January 23, 2025.

————. "National TB & Lung Diseases Conference: Latest Update on Severe Asthma Management." Presented at the National TB & Lung Diseases Conference, Royale Chulan Hotel, Kuala Lumpur, 21-23 June 2024.

Omar, Azza. Discussion on Treating Severe Asthma Patients with Biologics. Interview by Muhammad Daniel Kittu, Online Interview, January 23, 2025.

————. "National TB & Lung Diseases Conference: Latest Update on Severe Asthma Management." Presented at the National TB & Lung Diseases Conference, Royale Chulan Hotel, Kuala Lumpur, 21-23 June 2024.

Randall, J. R., R. Leigh, E. T. Crumley, S. Aponte-Hao, N. K. Vu, K. Martins, and S. Klarenbach. "The Efficacy and Safety of Biologic Drugs to Treat Severe Asthma: Rapid Review." CADTH Health Technology Review. Ottawa (ON), 2024.

Rojo-Tolosa, Susana, María Victoria González-Gutiérrez, José Antonio Sánchez-Martínez, Gonzalo Jiménez-Gálvez, Laura Elena Pineda-Lancheros, José María Gálvez-Navas, Alberto Jiménez-Morales, Cristina Pérez-Ramírez, and Concepción Morales-García. "Impact of Omalizumab in Patients with Severe Uncontrolled Asthma and Possible Predictive Biomarkers of Response: A Real-Life Study." Pharmaceutics 15, no. 2 (February 4, 2023): 523. doi:10.3390/pharmaceutics15020523.

Sardon-Prado, Olaia, Carolina Diaz-Garcia, Paula Corcuera-Elosegui, Javier Korta-Murua, Jose Valverde-Molina, and Manuel Sanchez-Solis. "Severe Asthma and Biological Therapies: Now and the Future." Journal of Clinical Medicine 12, no. 18 (September 8, 2023): 5846. doi:10.3390/jcm12185846.

Sculpher, M., F. Pang, A. Manca, M. Drummond, S. Golder, and H. Urdahl. "Generalisability in Economic Evaluation Studies in Healthcare: A Review and Case Studies." Health Technology Assessment 8, no. 49 (December 3, 2004). doi:10.3310/hta8490.

Sood, Akshay, Clifford Qualls, Mark Schuyler, Alexander Arynchyn, Jesse H. Alvarado, Lewis J. Smith, and David R. Jacobs Jr. "Adult-Onset Asthma Becomes the Dominant Phenotype among Women by Age 40 Years. the Longitudinal CARDIA Study." Annals of the American Thoracic Society 10, no. 3 (June 2013): 188–97. doi:10.1513/AnnalsATS.201212-115OC.

Tan, Daniel J., E. Haydn Walters, Jennifer L. Perret, John A. Burgess, David P. Johns, Adrian J. Lowe, Caroline J. Lodge, et al. "Clinical and Functional Differences between Early-Onset and Late-Onset Adult Asthma: A Population-Based Tasmanian Longitudinal Health Study." Thorax 71, no. 11 (November 2016): 981–87. doi:10.1136/thoraxjnl-2015-208183.

Trivedi, Michelle, and Eve Denton. "Asthma in Children and Adults-What Are the Differences and What Can They Tell Us About Asthma?" Frontiers in Pediatrics 7 (June 25, 2019): 256. doi:10.3389/fped.2019.00256.

Wang, Zhaoxin, Rui Liu, Ping Li, and Chenghua Jiang. "Exploring the Transition to DRGs in Developing Countries: A Case Study in Shanghai, China." Pakistan Journal of Medical Sciences 30, no. 2 (March 2014): 250–55. https://www.ncbi.nlm.nih.gov/pubmed/24772121.

World Bank Group. "World Development Indicators." Accessed February 21, 2025. https://databank.worldbank.org/reports.aspx?source=2&series=PA.NUS.PPP&country=MYS.

World Health Organisation. "Asthma," 2024. https://www.who.int/news-room/fact-sheets/detail/asthma.

Xu, Xiao, Caroline Schaefer, Agota Szende, Eduardo Genofre, Rohit Katial, and Yen Chung. "A Cost Comparison of Benralizumab, Mepolizumab, and Dupilumab in Patients with Severe Asthma- A US Third-Party Payer Perspective." Journal of Managed Care & Specialty Pharmacy 29, no. 11 (2023): 1193–1204.

Yong, Yee Vern, and Asrul Akmal Shafie. "How Much Does Management of an Asthma-Related Event Cost in a Malaysian Suburban Hospital?" Value in Health Regional Issues 15 (May 2018): 6–11. doi:10.1016/j.vhri.2017.05.001.

York Health Economics Consortium. "Probabilistic/Stochastic Sensitivity Analysis," 2016. https://yhec.co.uk/glossary/probabilistic-stochastic-sensitivity-analysis/.

———. "Sensitivity Analysis," 2016. https://yhec.co.uk/glossary/sensitivity-analysis/.

———. "Univariate/One Way Sensitivity Analysis," 2016. https://yhec.co.uk/glossary/univariate-one-way-sensitivity-analysis/.

APPENDICES

Appendix A: Summary of Generalised Cost per Year Adjusted for Inflation

Type of Cost	Original Cost from Study: Costs per exacerbation with SOC (2019) (USD)[50]	PPP Conversion Rate[51]	Generalised Cost per Exacerbation (RM)	Generalised Cost per Exacerbation Adjusted for Inflation	Generalised Cost of Exacerbation per Year Adjusted for Inflation
Costs of exacerbation with SOC	350	1.6	560	611	1,223

Annual Generalised Costs of OCS Dependence

Type of Cost	Average Cost from Study: Costs of OCS Dependence with SOC (2013) (GBP)[52]	PPP Conversion Rate[53]	Generalised Cost of OCS Dependence (International $)	PPP Conversion Rate[54]	Generalised Cost of OCS Dependence (RM)	Generalised Cost of OCS Dependence Adjusted for Inflation
Costs of OCS Dependence with SOC	3,568	0.7	2,498	1.5	3,746	4,706

Appendix B: Calculation of Exacerbation Costs with Biologics

- **Exacerbation Costs with Tezepelumab:**
  Average Exacerbation Reduction Per Year: 71%[55]
  [1,223 x (1-0.71)] = 355
- **Exacerbation Costs with Benralizumab:**
  Average Exacerbation Reduction Per Year: 86.25%[56]
  [1,223 x (1-0.8625)] = 168
- **Exacerbation Costs with Mepolizumab:**
  Average Exacerbation Reduction Per Year: 81.4%[57]
  [1,223 x (1-0.814)] = 227
- **Exacerbation Costs with Dupilumab:**
  Average Exacerbation Reduction Per Year: 83.83%[58]
  [1,223 x (1-0.8383)] = 198

[52] Barry et al., "The Cost of Systemic Corticosteroid-Induced Morbidity in Severe Asthma: A Health Economic Analysis."
[53] "World Development Indicators."
[54] Ibid.
[55] Corren et al., "Tezepelumab in Adults with Uncontrolled Asthma."
[56] Xu et al., "A Cost Comparison of Benralizumab, Mepolizumab, and Dupilumab in Patients with Severe Asthma- A US Third-Party Payer Perspective."
[57] Ibid.
[58] Ibid.

Appendix C: Calculation of Cost Savings with Biologics

- **Cost Savings with Tezepelumab:**
  Average Exacerbation Reduction Per Year: 71%[59]
  [1,223 x 0.71] = 868

- **Cost Savings with Benralizumab:**
  Average Exacerbation Reduction Per Year: 86.25%[60]
  [1,223 x 0.8625] = 1,055

- **Cost Savings with Mepolizumab:**
  Average Exacerbation Reduction Per Year: 81.4%[61]
  [1,223 x 0.814] = 995

- **Cost Savings with Dupilumab:**
  Average Exacerbation Reduction Per Year: 83.83%[62]
  [1,223 x 0.8383] = 1,025

Appendix D: Calculation of Annual OCS Dependence Costs with Biologics

- **Annual OCS Dependence Costs with Tezepelumab:**
  Average OCS Dependence Reduction Per Year:67.14%[63]
  [4,706 x (1-0.671425)] = 1,546

- **Annual OCS Dependence Costs with Benralizumab:**
  Average OCS Dependence Reduction Per Year: 63%[64]
  [4,706 x (1-0.63)] = 1,741

- **Annual OCS Dependence Costs with Mepolizumab:**
  Average OCS Dependence Reduction Per Year: 37.5%[65]
  [4,706 x (1-0.375)] = 2,941

- **Annual OCS Dependence Costs with Dupilumab:**
  Average OCS Dependence Reduction Per Year: 52.4%[66]
  [4,706 x (1-0.524)] = 2,240

[59] Corren et al., "Tezepelumab in Adults with Uncontrolled Asthma."
[60] Xu et al., "A Cost Comparison of Benralizumab, Mepolizumab, and Dupilumab in Patients with Severe Asthma- A US Third-Party Payer Perspective."
[61] Ibid.
[62] Ibid.
[63] Habash et al., "Cost-Effectiveness of Tezepelumab in Canada for Severe Asthma."
[64] Xu et al., "A Cost Comparison of Benralizumab, Mepolizumab, and Dupilumab in Patients with Severe Asthma- A US Third-Party Payer Perspective."
[65] Ibid.
[66] Ibid.

Appendix E: Calculation of Annual Cost Savings from OCS Dependence Reduction with Biologics

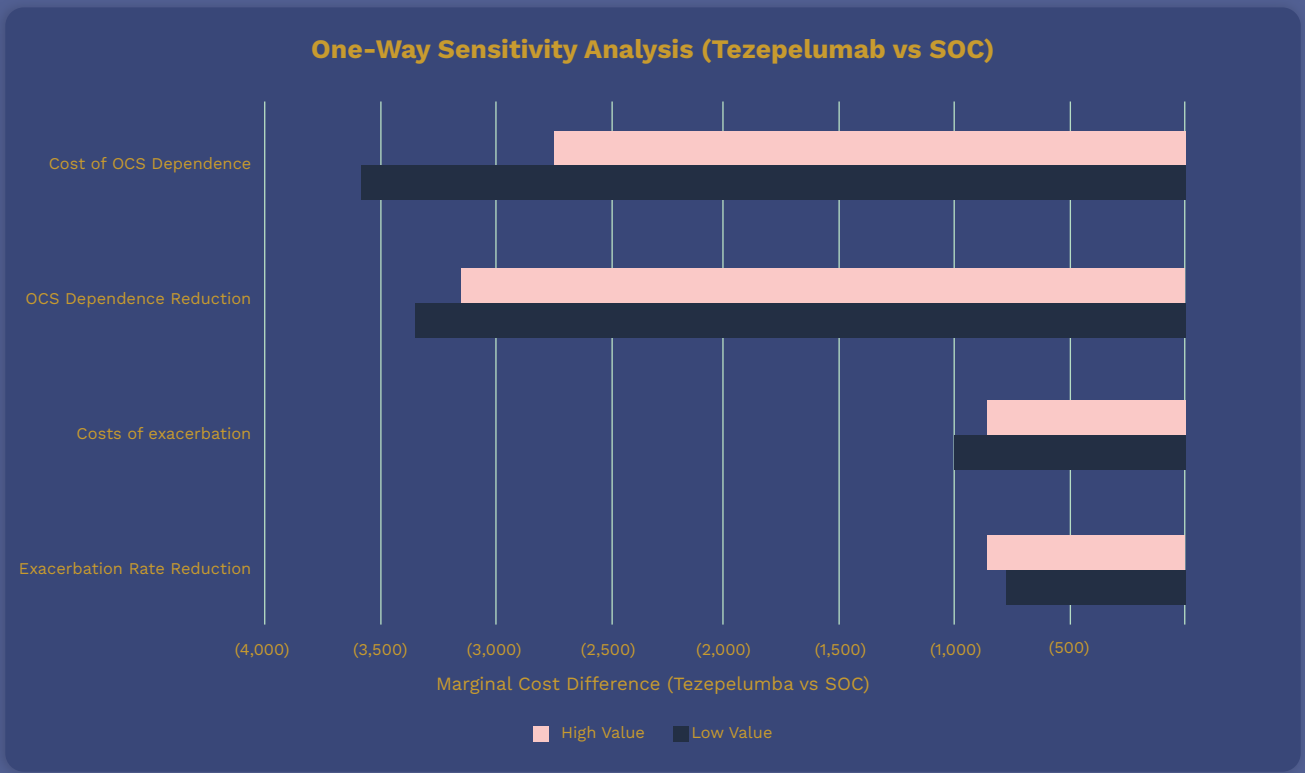
- **Annual Cost Savings from OCS Dependence Reduction with Tezepelumab:**
  Average OCS Dependence Reduction Per Year:67.14%[67]
  [4,706 x (1-0.671425)] = 3,159

- **Annual Cost Savings from OCS Dependence Reduction with Benralizumab:**
  Average OCS Dependence Reduction Per Year: 63%[68]
  [4,706 x (1-0.63)] = 2,964

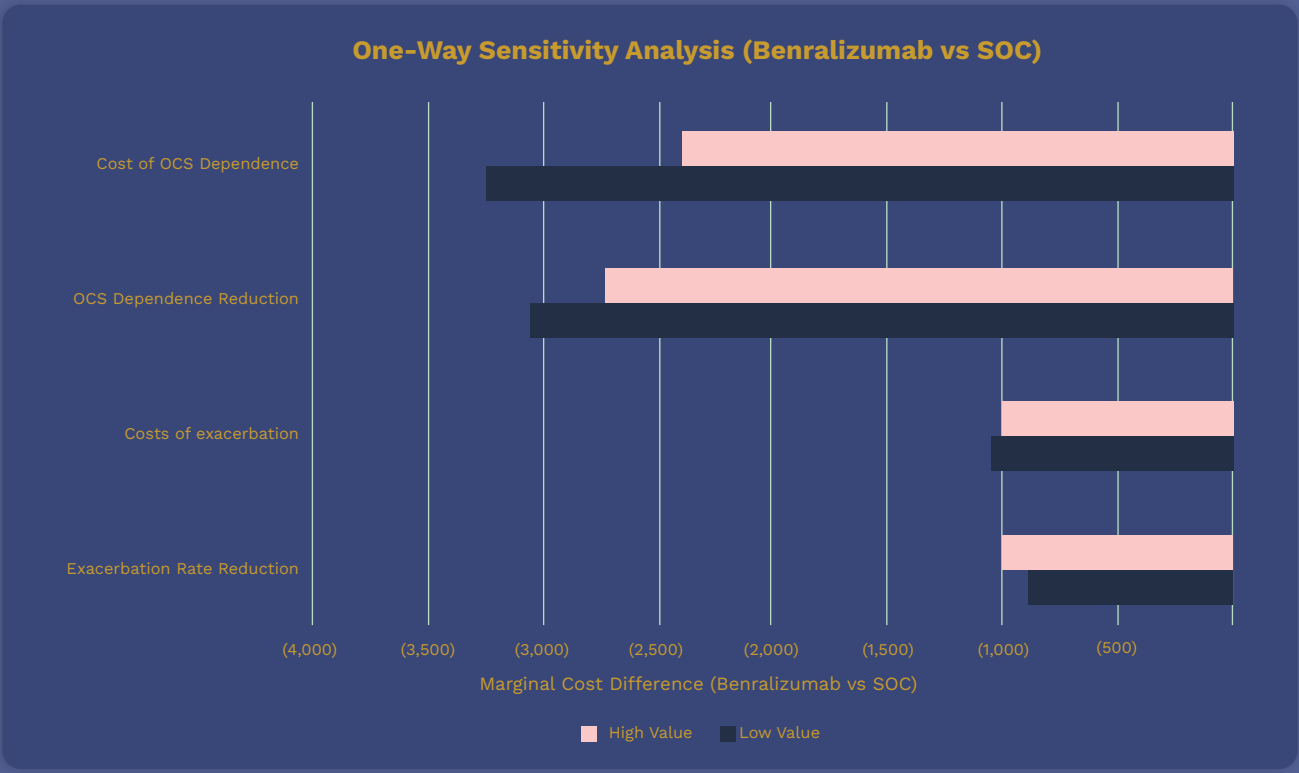
- **Annual Cost Savings from OCS Dependence Reduction with Mepolizumab:**
  Average OCS Dependence Reduction Per Year: 37.5%[69]
  [4,706 x (1-0.375)] = 1,765

- **Annual Cost Savings from OCS Dependence Reduction with Dupilumab:**
  Average OCS Dependence Reduction Per Year: 52.4%[70]
  [4,706 x (1-0.524)] = 2,466

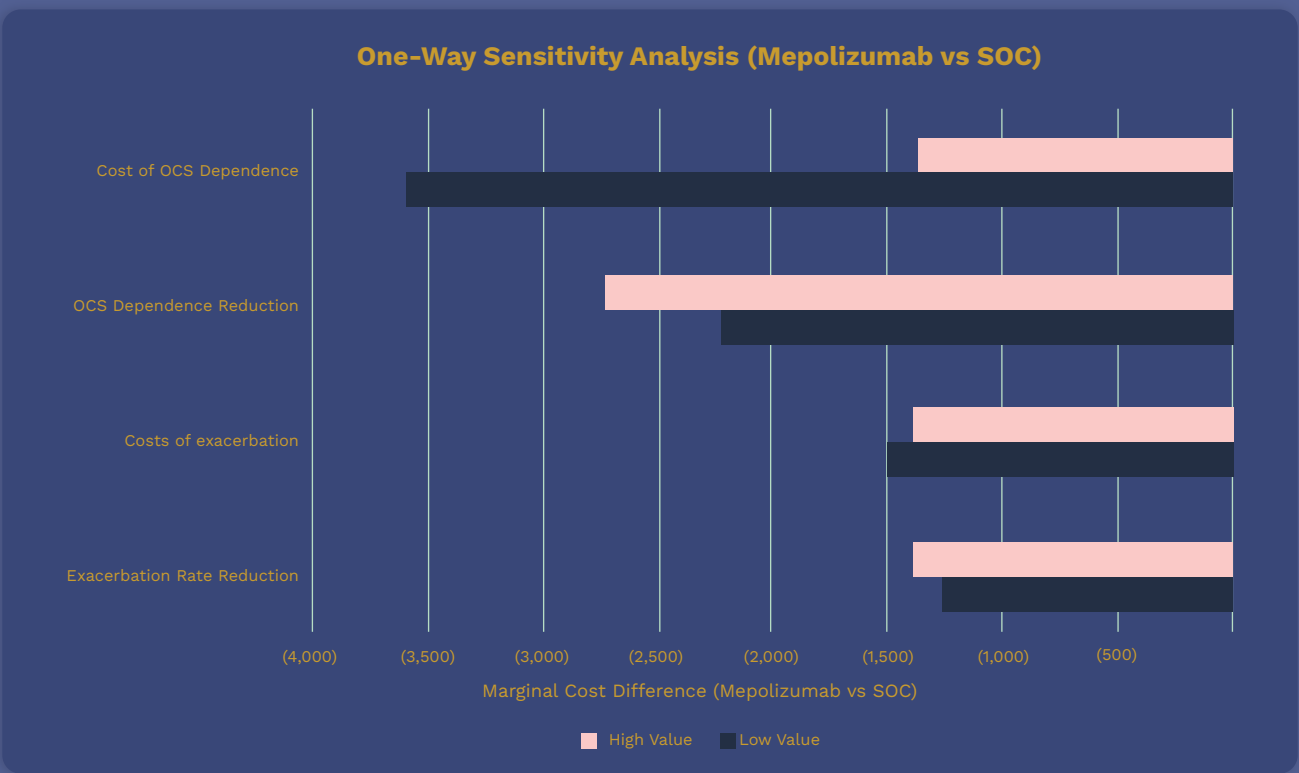
Appendix F: One-Way Sensitivity Analysis Results Comparing Tezepelumab vs SOC



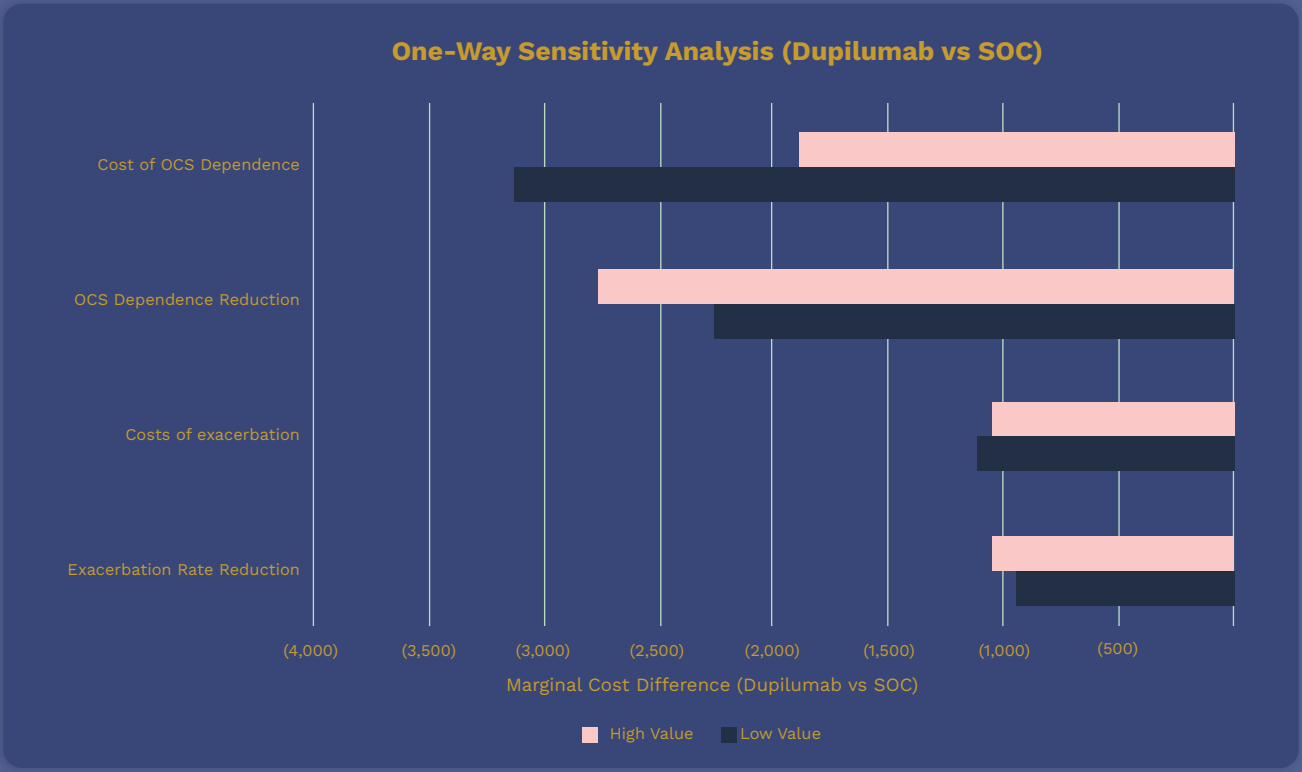
Appendix G: One-Way Sensitivity Analysis Results Comparing Benralizumab vs SOC



Appendix H: One-Way Sensitivity Analysis Results Comparing Mepolizumab vs SOC



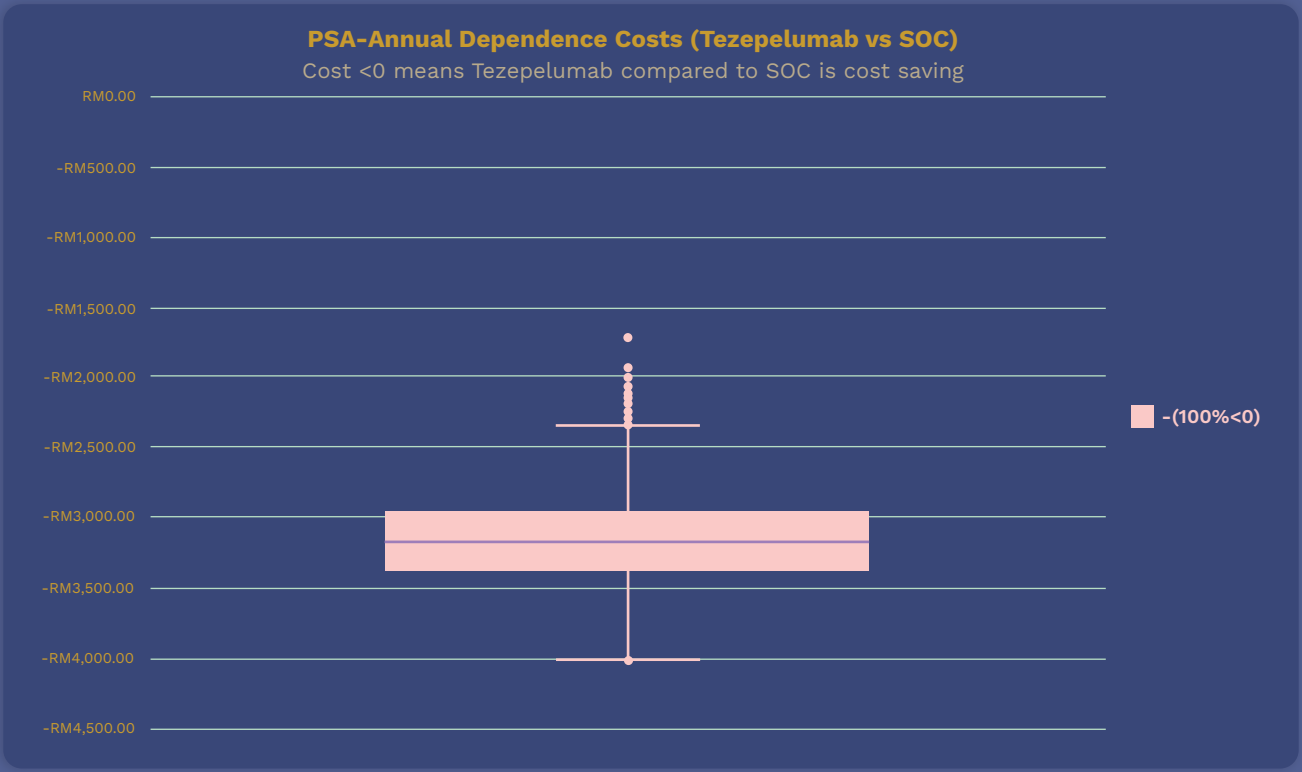
Appendix I: One-Way Sensitivity Analysis Results Comparing Dupilumab vs SOC



Appendix J: Probabilistic Sensitivity Results Comparing Tezepelumab vs SOC

X: mean
Lines in the box: Median =-RM 1,207
Lower of Box: First quartile (Q1) = -RM 1,381
Upper of Box: Third quartile (Q3) = -RM 1,053
Lower whisker: Min or Q1-Interquartile range(IQR)*1.5 (larger of the two) = -RM1,872
Upper whisker: Max or Q3+IQR*1.5 (lower of the two) = -RM562

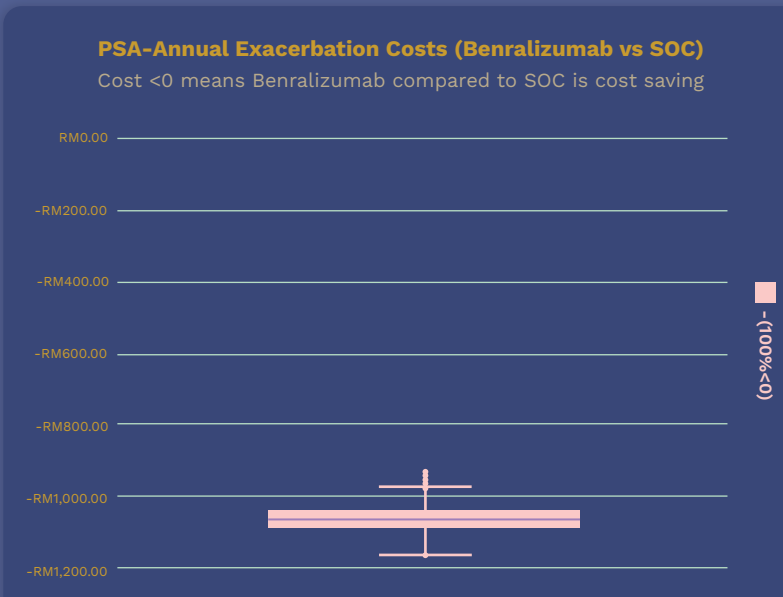
Values outside the whiskers' range are considered outliers and represented by dots.



X: mean
Lines in the box: Median =-RM3,178
Lower of Box: Q1 = -RM3,377
Upper of Box: Q3 = -RM 2,960
Lower whisker: Min or Q1-IQR*1.5 (larger of the two) = -RM 4,002
Upper whisker: Max or Q3+IQR*1.5 (lower of the two) = -RM2,335

Values outside the whiskers' range are considered outliers and represented by dots.

Appendix K: Probabilistic Sensitivity Results Comparing Benralizumab vs SOC

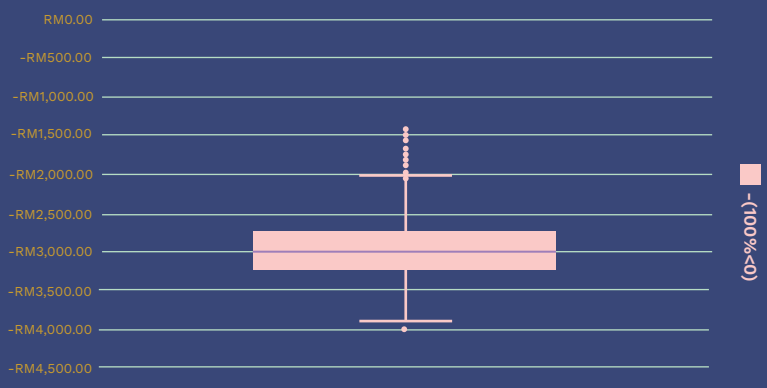


X: mean
Lines in the box: Median =-RM3,178
Lower of Box: Q1 = -RM3,377
Upper of Box: Q3 = -RM 2,960
Lower whisker: Min or Q1-IQR*1.5 (larger of the two) = -RM 4,002
Upper whisker: Max or Q3+IQR*1.5 (lower of the two) = -RM2,335

Values outside the whiskers' range are considered outliers and represented by dots.

PSA-Annual OCS Dependence Costs (Benralizumab vs SOC)

Cost <0 means Benralizumab compared to SOC is cost saving



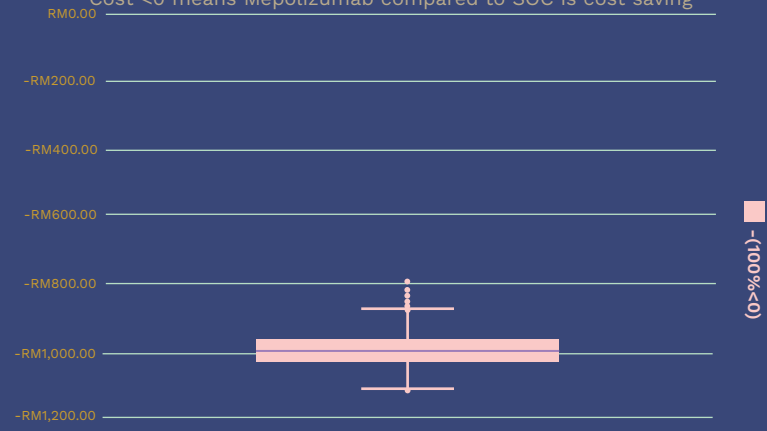
X: mean
Lines in the box: Median =-RM2,981
Lower of Box: Q1 = -RM3,206
Upper of Box: Q3 = -RM2,735
Lower whisker: Min or Q1-IQR*1.5 (larger of the two) = -RM3,912
Upper whisker: Max or Q3+IQR*1.5 (lower of the two) = -RM2,029

Values outside the whiskers' range are considered outliers and represented by dots.

Appendix L: Probabilistic Sensitivity Results Comparing Mepolizumab vs SOC

PSA-Annual OCS Dependence Costs (Mepolizumab vs SOC)

Cost <0 means Mepolizumab compared to SOC is cost saving

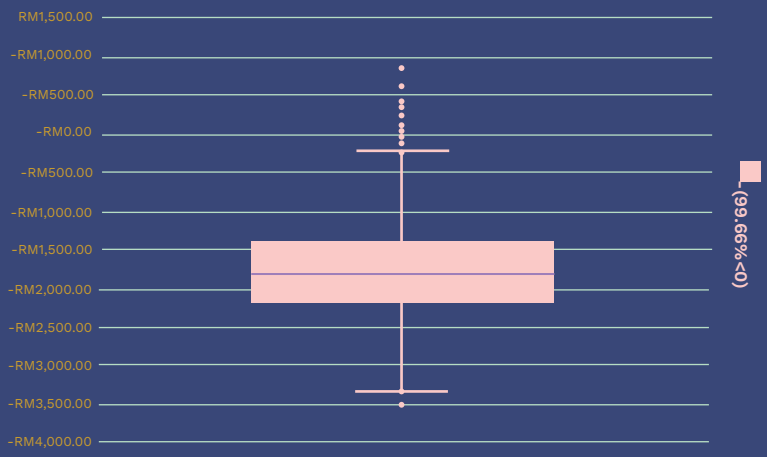


X: mean
Lines in the box: Median =-RM999
Lower of Box: Q1 = -RM1,028
Upper of Box: Q3 = -RM968
Lower whisker: Min or Q1-IQR*1.5 (larger of the two) = -RM1,118
Upper whisker: Max or Q3+IQR*1.5 (lower of the two) = -RM877

Values outside the whiskers' range are considered outliers and represented by dots.

PSA-Annual OCS Dependence Costs (Mepolizumab vs SOC)

Cost <0 means Mepolizumab compared to SOC is cost saving



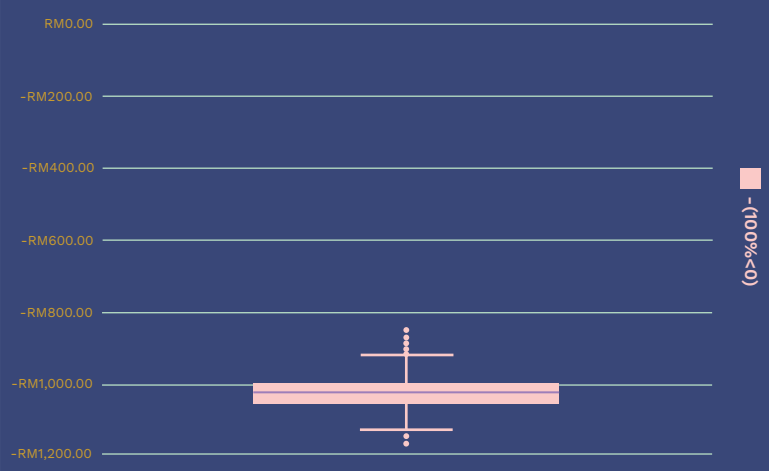
X: mean
Lines in the box: Median =-RM1,803
Lower of Box: Q1 = -RM2,171
Upper of Box: Q3 = -RM1,392
Lower whisker: Min or Q1-IQR*1.5 (larger of the two) = -RM3,340
Upper whisker: Max or Q3+IQR*1.5 (lower of the two) = -RM223

Values outside the whiskers' range are considered outliers and represented by dots.

Appendix M: Probabilistic Sensitivity Results Comparing Dupilumab vs SOC

PSA-Annual OCS Exacerbation Costs (Dupilumab vs SOC)

Cost <0 means Dupilumab compared to SOC is cost saving

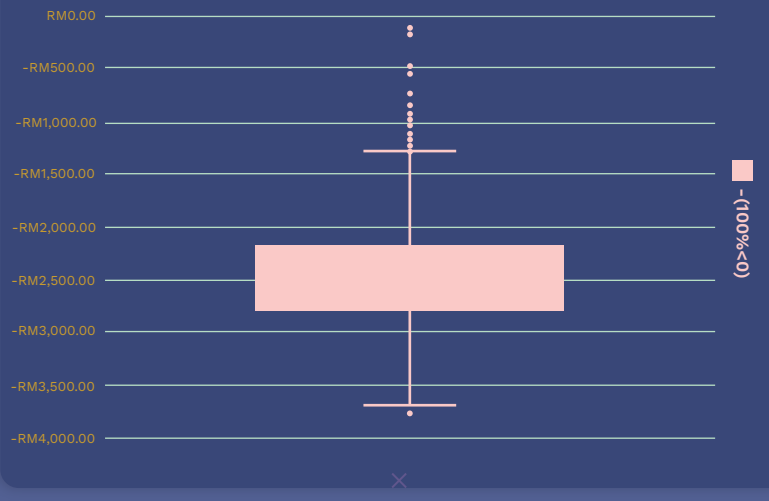


X: mean
Lines in the box: Median =-RM1,028
Lower of Box: Q1 = -RM1,052
Upper of Box: Q3 = -RM999
Lower whisker: Min or Q1-IQR*1.5 (larger of the two) = -RM1,132
Upper whisker: Max or Q3+IQR*1.5 (lower of the two) = -RM920

Values outside the whiskers' range are considered outliers and represented by dots.

PSA-Annual OCS Dependence Costs (Dupilumab vs SOC)

Cost <0 means Dupilumab compared to SOC is cost saving



X: mean
Lines in the box: Median =-RM2,495
Lower of Box: Q1 = -RM2,781
Upper of Box: Q3 = -RM2,182
Lower whisker: Min or Q1-IQR*1.5 (larger of the two) = -RM3,679
Upper whisker: Max or Q3+IQR*1.5 (lower of the two) = -RM1,284

Values outside the whiskers' range are considered outliers and represented by dots.

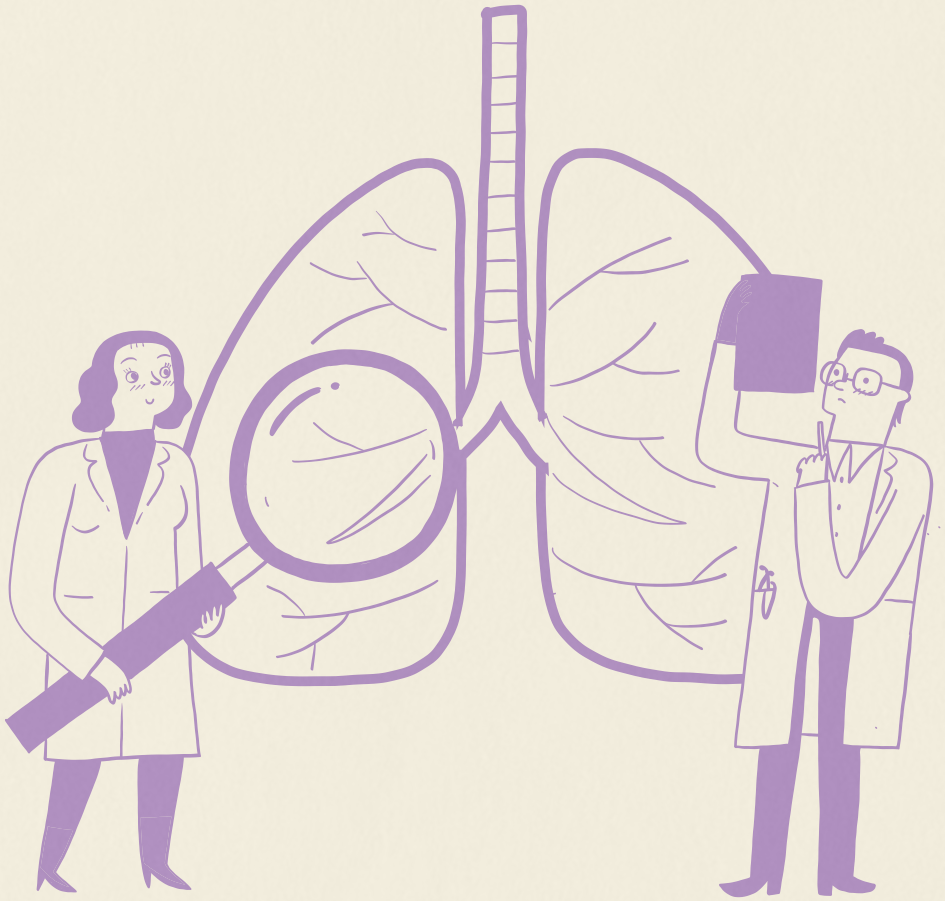
Appendix N: Limitations

There are several limitations to this report. The severe asthma exacerbation cost data utilised was based in Mexico, where hospitals use Diagnostic Related Groups as a classification system to manage costs[71] compared to Malaysian hospitals that use a fee-for-service payment model[72]. While studies such as the management of asthma-related event costs in a Malaysian Suburban Hospital were available, it does not include exacerbation costs caused by severe asthma, and the cost amounted to RM 1,777.86[73] which is higher than the exacerbation cost used in calculating the cost savings of biologics. Despite using a more conservative figure for exacerbation cost, biologics are still shown to be cost-saving.

Omalizumab was excluded from the cost-minimisation model due to issues with comparability of exacerbation reduction. The available clinical trial studies separate the treatment course into two distinct phases: the "stable-steroid phase" and the "steroid-reduction phase"[74,75,76]. This segmentation of treatment phases complicates direct comparisons with other biologics, as the other studies included do not explicitly distinguish the exacerbation reduction data in a phased approach, making it difficult to isolate the impact of the biologic on exacerbation reduction without considering the potential confounding effects of ongoing steroid treatment during the initial stable-steroid phase. As a result, the data derived from studies involving omalizumab might not be directly comparable, which could affect the generalisability of the findings. Real-world studies were an alternative option available[77,78], but using data from such studies would have undermined the comparability of the results as the exacerbation reduction data from the other biologics were sourced from clinical trials. Hence, it was decided that Omalizumab would be excluded from the model. This exclusion is a methodological consideration and does not impede the broader cost-saving potential of biologics.

The newest biologic for severe asthma, Tezepelumab—approved in 2021[79]—may have less extensive data on exacerbation reduction compared to older biologics such as Dupilumab, Benralizumab and Mepolizumab, which were approved in 2018, 2017 and 2015,[80,81,82] respectively. Future studies would be needed to address this to provide a clearer picture of Tezepelumab's impact on exacerbation reduction.

[71] Wang et al., "Exploring the Transition to DRGs in Developing Countries: A Case Study in Shanghai, China."
[72] Isamudin and Kamaruddin, "DRG: Good Option but far from Adoption."
[73] Yong and Shafie, "How Much Does Management of an Asthma-Related Event Cost in a Malaysian Suburban Hospital?"
[74] Kotoulas et al., "Omalizumab: An Optimal Choice for Patients with Severe Allergic Asthma."
[75] Corren et al., "Omalizumab, a Recombinant Humanized Anti-IgE Antibody, Reduces Asthma-Related Emergency Room Visits and Hospitalizations in Patients with Allergic Asthma."
[76] Lanier et al., "Omalizumab Is Effective in the Long-Term Control of Severe Allergic Asthma."
[77] "Longterm Clinical Outcomes of Omalizumab Therapy in Severe Allergic Asthma: Study of Efficacy and Safety."
[78] Rojo-Tolosa et al., "Impact of Omalizumab in Patients with Severe Uncontrolled Asthma and Possible Predictive Biomarkers of Response: A Real-Life Study."
[79] Hoy, "Tezepelumab: First Approval."
[80] Sardon-Prado et al., "Severe Asthma and Biological Therapies: Now and the Future."
[81] "FASENRA approved for treatment of children aged 6 to 11 with severe asthma."
[82] Fala, "Nucala (Mepolizumab) First IL-5 Antagonist Monoclonal Antibody FDA Approved for Maintenance Treatment of Patients with Severe Asthma."



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