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Estimating the Health and Economic Impact of Improved Management in Prevalent Chronic Obstructive Pulmonary Disease Populations in England, Germany, Canada, and Japan: A Modelling Study

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Introduction: COPD is a leading cause of morbidity and mortality globally. Management is complex and costly. Although international quality standards for diagnosis and management exist, opportunities remain to improve outcomes, especially in reducing avoidable hospitalisations.

Objective: To estimate the potential health and economic impact of improved adherence to guideline-recommended care for prevalent, on-treatment COPD populations in four high-income settings.

Methods: A disease simulation model was developed to evaluate the impact of theoretical improvements to COPD management, comparing outcomes for usual care and policy scenarios for interventions that reduce avoidable hospitalisations: 1) increased attendance (50% vs 31–38%) of early follow-up review after severe exacerbation hospitalisation; 2) increased access (30% vs 5–10%) to an integrated disease management (IDM) programme that provides guideline adherent care.

Results: For cohorts of 100,000 patients, Policy 1 yielded additional life years (England: 523; Germany: 759; Canada: 1316; Japan: 512) and lifetime cost savings (-£2.89 million; -€6.58 million; -$40.08 million; -¥735.58 million). For Policy 2, additional life years (2299; 3619; 3656) and higher lifetime total costs (£38.15 million; €35.58 million; ¥1091.53 million) were estimated in England, Germany and Japan, and additional life years (4299) and cost savings (-$20.52 million) in Canada. Scenarios found that the cost impact depended on the modelled intervention effect size.

Conclusion: Interventions that reduce avoidable hospitalisations are estimated to improve survival and may generate cost savings. This study provides evidence on the theoretical impact of policies to improve COPD care and highlights priority areas for further research to support evidence-based policy decisions.

Keywords: health intervention, exacerbations, re-admission, integrated care, economic evaluation

Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive respiratory disorder characterised by irreversible airflow limitation and symptoms including dyspnoea, persistent cough, and sputum production. Exacerbation of symptoms is common and occurs more frequently as the disease progresses.[1,2] Severe exacerbations are the primary cause of hospitalisation, and re-admission following discharge is common.[3,4]

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In 2019, COPD was the third leading cause of death worldwide, responsible for 3.23 million deaths.[5] The global cost of illness was estimated to be US$2.1 trillion in 2010 and is expected to more than double by 2030.[6] Hospitalisations and re-admissions are primary drivers of healthcare system costs, and their frequency is highly influenced by exacerbation frequency and severity.[7,8]

According to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) case definition (a fixed ratio value of forced expiratory volume in one second (FEV_1) to forced vital capacity (FVC): FEV1/FVC<0.7).,[9] the global prevalence of COPD was estimated at 10.3% (392 million cases, ages 30–79) in 2019.[10] Prevalence is higher in men, urban areas and high-income countries.[11]

Currently, no curative treatments exist for COPD. However, effective symptom management and slower disease progression can be achieved through pharmacological and non-pharmacological interventions.[12] GOLD describes international recommendations for the optimal diagnosis and management of COPD,[9] and many countries publish national guidelines to support best practices.[13–17] Despite this, challenges remain in delivering optimal care to patients. A recent study in high-income settings reported common barriers to include low consideration of COPD, underutilisation of effective pharmacological and non-pharmacological interventions, and sub-optimal management of exacerbations.[18]

Improvements in care for people with COPD are expected to reduce hospitalisations, improve patient outcomes, and increase life expectancy.[17,19,20] Interventions to identify undiagnosed patients, such as active case finding, improve patient outcomes and are cost-effective.[21–23] However, evidence on the health and economic benefit of interventions that provide optimal management in line with best practices is more limited.[24]

Early follow-up review post-discharge (within one month) is recommended in international guidelines[9] and quality standards[19] for patients hospitalised due to severe exacerbation and can reduce re-admission risk.[25] Despite this, uptake is low;[26,27] not attending early follow-up represents a missed opportunity to review and amend discharge therapy and may contribute to re-admissions and poor survival.[9]

Integrated disease management (IDM) programmes provide structured, multidisciplinary care and address the complex nature of managing COPD.[28] Administered by teams in both primary and secondary care settings, these programmes vary in composition. They often include pharmacological and non-pharmacological interventions (eg, treatment review, smoking cessation counselling, telemonitoring, etc.). Pulmonary rehabilitation is a well-known form of IDM; the organisation of two primary care programmes from Canada[29,30] and Germany[31] is detailed in Table S1. A recent meta-analysis of 52 studies found improvements in disease-specific quality of life, exercise capacity and respiratory-related hospital admissions for patients with IDM.[28] Despite this evidence of effectiveness, access and uptake remain limited.[31]

This study evaluates the potential health and economic impact of two policy scenarios to improve the management of prevalent, on-treatment COPD populations in England, Germany, Canada, and Japan, through interventions that align with recommendations in international quality standards on management.[19] The interventions were 1) early follow-up review after severe exacerbation hospitalisation and 2) provision of IDM to optimise COPD care.

Methods

Model Overview

A discrete-time cohort-level Markov state-transition model was developed to simulate the natural disease history for COPD. Consistent with prior models,[21,32,33] health states were based on GOLD airflow obstruction stages (GOLD I–IV).[9] While the GOLD ABE (ABCD pre-2023) clinical risk classifications are central to individualised therapeutic decision-making, spirometry remains a key prognostic measure for COPD, and the airflow obstruction stages are preferred for population-level modelling. Death was included as an absorbing state.

A lifetime horizon was assumed, and the cycle length was three months; a half-cycle correction was applied. In each cycle, simulated individuals either remain in their current GOLD stage, improve and move to the previous stage, or worsen and progress to the next stage while lung function typically declines over time, some improvements to earlier stages were observed in the source data and included in the disease progression model parameters.[21,34] Simulated individuals are also subject to risks of severe exacerbation hospitalisation, subsequent re-admission, and death. Deaths were determined by background COPD and in-hospital mortality. Severe exacerbation and background COPD mortality event risks were conditional upon GOLD stage.

The model predicts total life years, severe exacerbation hospitalisations (including re-admissions), in-hospital deaths, and lifetime costs for defined cohorts of patients. Modelled costs include inhaled medication, background disease management, hospitalisation, and intervention (ie, early follow-up review and IDM administration) costs.

Figure 1 presents an overview of the model structure. The model was implemented in TreeAgePro 2021 (TreeAgePro Software, Williamstown, Massachusetts, USA).[35]

Inputs

The model was parameterised using published evidence on usual care (UC) for prevalent COPD populations in each country (Table 1). Data were obtained from population studies, prior modelling studies, national-level audits, and cost databases. Disease progression and severe exacerbation risk profiles were representative of single long-acting muscarinic antagonist (LAMA) therapy. All patients were assumed to be on-treatment. Intervention effects were based on the findings of retrospective population-based studies[25,36] for early follow-up review and randomised controlled trials (RCTs)[28,29] for IDM. A healthcare payer perspective was assumed. Costs reflect 2021/2022 prices. Future costs and benefits were discounted at country-specific rates: England, 3.5%; Germany, 3%; Canada, 1.5%; and Japan, 2%.

Further detail on the input sources and employed assumptions is provided in Supplemental S1.

Primary Analyses

Considerable gaps and uncertainty exist in the evidence on UC in each country and the intervention effect sizes. To assess the potential impact of improvements in care, primary analyses employed the most robust intervention effect evidence and assumed realistic uptake targets for the policy scenarios.

Early Follow-Up Review - Policy 1

- Intervention effect: the 90-day odds of re-admission were 66% (odds ratio [OR]: 0.34)[25] lower for patients attending early follow-up review within one month of severe exacerbation hospitalisation.
- Policy impact: assumed at 50%, the percentage of patients attending early follow-up review was increased for the policy. UC attendance levels ranged from 31.1–37.8% across settings.[26,53]

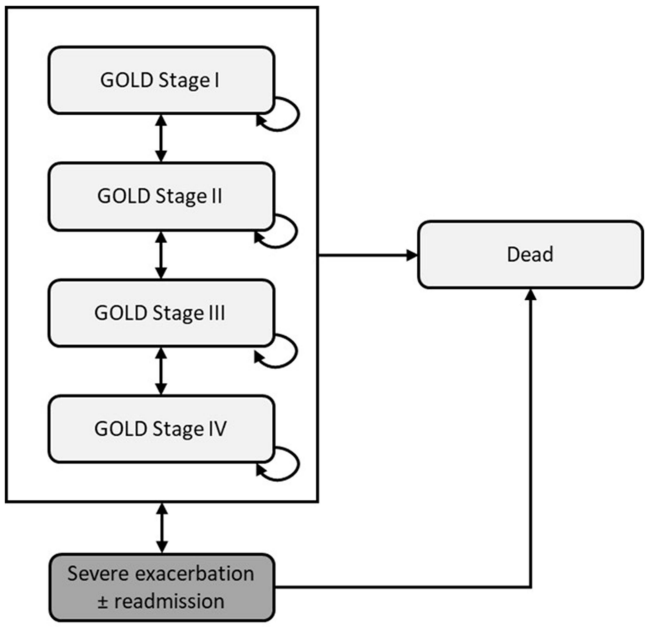

Figure 1 Schematic diagram of the model structure.
Abbreviation: GOLD, Global Initiative for Chronic Obstructive Lung Disease.

Table 1 Input Parameters Applied in the Model

Parameter Group	Parameter	England		Germany		Canada		Japan	
		Value	Source	Value	Source	Value	Source	Value	Source
Settings	Discount rate (costs and benefits)	3.5%	NICE[37]	3%	IQWiG, 2021[38]	1.5%	CADTH, 2017[39]	2%	Shiroiwa et al 2017[40]
Patient profile	Baseline age (years)	69.2	Adab et al 2017[41]	65.7	Worth et al 2016[42]	70.4	Maleki-Yazdi et al 2012[43]	74.8	Kobayashi et al 2018[44]
	Proportion female	0.38		0.40		0.41		0.10	
	Baseline GOLD stage distribution (Proportion)								
	GOLD I	0.244	Adab et al 2017[41]	0.176	Worth et al 2016[42]	0.12281	Maleki-Yazdi et al 2012[43]	0.2120	Kobayashi et al 2018[44]
	GOLD II	0.520		0.486		0.50877		0.5137	
	GOLD III	0.200		0.279		0.32982		0.1970	
	GOLD IV	0.036		0.059		0.03860		0.0773	
Clinical profiles	Disease progression and background COPD mortality								
	GOLD stage transitions and background COPD mortality	See original sources	THIN; Lambe et al 2019;[21] The Office for National Statistics 2018–20[45]	See original sources	Hettle et al 2012;[34] Leivseth et al 2013;[46] DESTATIS, 2018[47]	See original sources	Hettle et al 2012;[34] Leivseth, 2013;[46] Statistics Canada, 2016[48]	See original sources	Hettle et al 2012;[34] Leivseth et al 2013;[46] NIPSSR[49]
	Inhaled medication effect - disease progression odds ratio	0.85	Lambe et al 2019[21]	NA	Not applicable to the German model.	NA	Not applicable to the Canadian model.	NA	Not applicable to the Japanese model.
	Inhaled medication effect - all-cause mortality odds ratio	0.98	Karner et al 2012;[50] Lambe et al 2019[21]	NA	Not applicable to the German model.	NA	Not applicable to the Canadian model.	NA	Not applicable to the Japanese model.

	Severe exacerbation (3-monthly) probabilities								
	GOLD I	0.007	BLISS; Lambe et al 2019[21]	0.021	GOLD II assumed.	0.021	GOLD II assumed.	0.021	GOLD II assumed.
	GOLD II	0.019		0.021	Hettle et al 2012[34]	0.021	Hettle et al 2012[34]	0.021	Hettle et al 2012[34]
	GOLD III	0.066		0.050		0.050		0.050	
	GOLD IV	0.083		0.085		0.085		0.085	
	Inhaled medication effect - severe exacerbation odds ratio	0.85	Karner et al 2012;[50] Lambe et al 2019[21]	NA	Not applicable to the German model.	NA	Not applicable to the Canadian model.	NA	Not applicable to the Japanese model.
	Probability of re-admission within 90 days	0.307	European COPD Audit; Roberts et al 2012[51]	0.266	European COPD Audit; Roberts et al 2012[51]	0.350	Atwood et al 2022[26]	0.211	Matsui et al 2017[4]
	Probability of in-hospital death	0.050		0.038		0.038	European COPD Audit; Roberts et al 2012[51]	0.051	Shirakawa et al 2021[52]
Resource use and costs	Background disease management and inhaled medication costs (per annum)								
	GOLD I	£564.46	Table S2.	€784.25	Table S3.	$954.05	Table S4.	¥102,890.58	Table S5.
	GOLD II	£564.46		€855.63		$1061.59		¥108,313.14	
	GOLD III	£797.01		€965.81		$1578.67		¥170,695.30	
	GOLD IV	£1135.92		€1108.60		$2015.30		¥327,611.31	
	(Severe exacerbation) Hospitalisation [initial/re-admission]	£2768.42		€2946.66		$8999.94		¥708,551.66	
	Severe exacerbation hospitalisation early follow-up review	£98.84		€31.95		$109.70		¥27,051.41	
	Proportion attending early follow-up review - Usual care	0.378	NACAP COPD clinical audit 2019/20[27]	0.378	Value for England assumed.	0.311	Atwood et al 2022[26]	0.378	Value for England assumed.

Abbreviations: BLISS, Birmingham Lung Improvement StudieS; CADTH, Canadian Agency for Drugs and Technologies in Health; COPD, Chronic obstructive pulmonary disease; F, Female; GOLD, Global Initiative for Chronic Obstructive Lung Disease; IQWiG, Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen; M, Male; NA, Not applicable; NACAP, National Asthma and COPD Audit Programme; NICE, National Institute for Health and Care Excellence; NIPSSR, National Institute of Population and Social Security Research; ONS, Office of National Statistics; PHE, Public Health England; THIN, The Health Improvement Network; £, British Pound; €, Euro; $, Canadian dollar; ¥, Japanese Yen.

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IDM - Policy 2

- Intervention effect: patients receiving IDM were at reduced odds (36% lower; OR: 0.64[28]) of severe exacerbation hospitalisation across the modelled time horizon.
- Policy impact: the percentage of patients receiving lifelong management with IDM was assumed to be 30% in the policy, while UC levels were 5–10% across settings (Table 2).

Early follow-up review intervention costs reflected healthcare provider interactions for local practice (Tables S2–S5), while annual IDM administration costs were assumed to be £306, €346, $500, and ¥48,111. Intervention costs do not include additional costs due to treatment regimen changes, other non-pharmacological interventions, or other resource use.

Further information on the intervention effect data sources and assumptions made is provided in Supplemental S2. The impact of the policies was defined by differences in life years, severe exacerbation hospitalisations, in-hospital deaths, and total costs from UC.

Scenario and Uncertainty Analyses

Given considerable uncertainty in several key inputs and assumptions due to limited data, extensive scenario analyses were conducted to assess the impact for a range of intervention effect sizes and uptake levels and at alternative IDM administration costs (Table 2). One-way sensitivity analysis was conducted for all other key parameters.

Ethics approval was not required as no patient-specific information was used in this study.

Results

Primary Analyses

Table 3 presents discounted, primary analysis results for cohorts of 100,000 patients.

Policy 1

Increasing attendance of early follow-up review to 50% (from 37.8% in England, Germany and Japan, and 31.1% in Canada) resulted in fewer severe exacerbation hospitalisations (England: 1894; Germany: 3354; Canada: 5528; Japan: 1911) and fewer in-hospital deaths (England: 96; Germany: 127; Canada: 210; Japan: 97). Life year gains were predicted for all countries, ranging from 512 in Japan to 1316 in Canada.

While the costs of inhaled medication, background disease management, and early follow-up review were higher for the policy, hospitalisation costs were notably lower and the policy generated lifetime cost savings of £2.89 million, €6.58 million, $40.08 million, and ¥735.58 million.

Policy 2

Increasing IDM access to 30% (from 10% in England and Germany; from 5% in Canada and Japan) yielded fewer severe exacerbation hospitalisations (England: 8516; Germany: 16,153; Canada: 18,290; Japan: 14,412) and in-hospital deaths (England: 425; Germany: 613; Canada: 695; Japan: 735).

While this reduced hospitalisation-related costs, inhaled medication, background disease management, and IDM administration costs were higher for the policy, and the overall cost impact varied by country. In England, Germany, and Japan, the policy was estimated to generate additional life years (2299; 3619; 3656) at higher total lifetime costs (£38.15 million; €35.58 million; ¥1091.53 million), while in Canada, the policy generated 4299 additional life years at cost savings of $20.52 million.

Scenario and Uncertainty Analyses

Figures 2–5 show incremental differences between UC and the policies for different intervention effect sizes and uptake levels. As expected, for both policies, the number of hospitalisations avoided and life years gained increased with greater effect sizes and higher uptake levels. Estimated benefits were larger for Policy 2 than Policy 1, in all countries. The cost

Table 2 Overview of Usual Care and Policy Scenario Intervention Implementations

Early follow-up review								
Country	**Attendance (uptake) level**			**Per event review cost**	**Reference**	**90-day re-admission risk**		
	UC	**Reference**	**Policy [Primary analysis (scenario range)]**			**Base probability**	**Reference**	**Intervention effect [Primary analysis (scenario values)]**
England	37.8%	NACAP COPD clinical audit 2019/20[27]	50% (60% to 100%)	£98.84	Table S2.	30.7%	Roberts et al, 2012[51]	OR of re-admission: 0.34 (RR: 0.63, RR: 0.77, RR: 0.94) Based on: Gavish et al[25] – OR: 0.34* Sin et al[36] – RR: 0.77 (95% CI: 0.63 to 0.94).
Germany	37.8%	Value for England assumed.		€31.95	Table S3.	26.6%	Roberts et al, 2012[51]	
Canada	31.1%	Atwood et al 2022[26]		$109.70	Table S4.	35.0%	Atwood et al 2022[26]	
Japan	37.8%	Value for England assumed.		¥27,051.41	Table S5.	21.1%	Matsui et al 2016[4]	

(*Continued*)

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Table 2 (Continued).

IDM programme							
Country	**Participation (uptake) level**			**Per-patient annual IDM programme admin cost [Primary analysis (scenario range)]**	**Reference**	**Severe exacerbation (hospitalisation) risk**	
	UC	**Reference**	**Policy [Primary analysis (scenario range)]**			**Base probability**	**Intervention effect [Primary analysis (scenario range)]**
England	10%	Assumed[§].	30% (10% to 100%)	£306 (£50-£700)	$500 estimate for Canada based on early data from the Canadian BestCare programme[29] converted to local currency estimates[¥]; scenario range values assumed.	Table 1 (GOLD stage-specific severe exacerbation probabilities)	OR of severe exacerbation: 0.64 (OR: 0.50, OR: 0.81; RR: 0.40) Based on Poot et al[28] – OR: 0.64 (95% CI: 0.50, 0.81); Ferrone et al[29] – 0.40 (approximated).
Germany	10%	Achelrod et al 2016[31]		€346 (€50-€700)			
Canada	5%	Assumed[§]		$500 ($50-$700)			
Japan	5%	Assumed[§]		¥48,111 (¥7500–105,000)			

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Table 3 Cohort-Level (n=100,000) Discounted Primary Analysis Results by Country and Policy

Outcome	Policy 1 - Early Follow-Up Review			Policy 2 - IDM Programme		
	UC	Policy	Incr.	UC	Policy	Incr.
England						
Life years	900,160	900,683	523	899,922	902,221	2299
Hospitalisations[a] (inc. re-admission)	121,553	119,659	−1894	123,229	114,713	−8516
In-hospital deaths	6122	6026	−96	6161	5736	−425
Total costs	£820,814,581	£817,919,659	£2,894,922	£851,787,232	£889,937,616	£38,150,385
Inhaled medication	£359,151,999	£359,373,978	£221,979	£359,049,074	£360,022,610	£973,536
Background disease management	£195,560,145	£195,686,358	£126,213	£195,500,884	£196,053,080	£552,196
Hospitalisations[a] (inc. re-admission)	£263,355,648	£259,223,062	–£4,132,585	£267,005,286	£248,439,385	–£18,565,900
Early follow-up review	£2,746,789	£3,636,261	£889,473	£2,650,276	£2,465,993	–£184,284
IDM administration	–	–	–	£27,581,711	£82,956,548	£55,374,837
Cost-per-life year	–	–	–£5535	–	–	£16,594
Germany						
Life years	1,010,966	1,011,725	759	1,010,421	1,014,040	3619
Hospitalisations[a] (inc. re-admission)	234,949	231,595	−3354	237,277	221,124	−16,153
In-hospital deaths	8921	8794	−127	9007	8394	−613
Total costs	€1,476,508,442	€1,469,931,271	–€6,577,173	€1,516,318,643	€1,551,901,539	€35,582,897
Inhaled medication	€763,628,591	€764,204,858	€576,267	€763,214,411	€765,960,068	€2,745,657
Background disease management	€163,618,938	€163,753,880	€134,942	€163,520,512	€164,160,570	€640,058
Hospitalisations[a] (inc. re-admission)	€547,461,279	€539,590,096	–€7,871,184	€552,924,665	€515,019,259	–€37,905,405
Early follow-up review	€1,799,634	€2,382,437	€582,802	€1,735,887	€1,616,884	–€119,003
IDM administration	–	–	–	€34,923,168	€105,144,758	€70,221,590
Cost-per-life year	–	–	–€8666	–	–	€9832
Canada						
Life years	976,099	977,415	1316	974,796	979,095	4299
Hospitalisations[a] (inc. re-admission)	212,226	206,698	−5528	217,649	199,359	−18,290
In-hospital deaths	8062	7852	−210	8268	7573	−695
Total costs	$3,031,256,494	$2,991,173,028	–$40,083,468	$3,097,777,419	$3,077,260,900	–$20,516,518
Inhaled medication	$959,806,727	$961,137,566	$1,330,838	$958,487,488	$962,826,614	$4,339,126

(*Continued*)

Table 3 (Continued).

Outcome	Policy 1 - Early Follow-Up Review			Policy 2 - IDM Programme		
	UC	Policy	Incr.	UC	Policy	Incr.
Background disease management	$347,277,418	$347,795,816	$518,397	$346,762,048	$348,444,541	$1,682,494
Hospitalisations[a] (inc. re–admission)	$1,719,269,179	$1,674,345,109	–$44,924,070	$1,763,347,303	$1,614,720,233	–$148,627,070
Early follow-up review	$4,903,170	$7,894,537	$2,991,367	$4,810,679	$4,405,202	–$405,477
IDM administration	–	–	–	$24,369,901	$146,864,310	$122,494,409
Cost-per-life year	–	–	–$30,459	–	–	–$4772
Japan						
Life years	822,984	823,496	512	799,689	803,345	3656
Hospitalisations[a] (inc. re-admission)	159,457	157,546	−1911	172,665	158,253	−14,412
In-hospital deaths	8132	8035	−97	8806	8071	−735
Total costs	¥224,109,440,596	¥223,373,862,776	–¥735,577,820	¥238,398,978,647	¥239,490,512,644	¥1,091,533,997
Inhaled medication	¥60,259,150,280	¥60,297,217,978	¥38,067,698	¥59,096,395,015	¥59,371,416,079	¥275,021,064
Background disease management	¥62,593,811,158	¥62,639,624,248	¥45,813,090	¥67,307,362,854	¥67,675,545,015	¥368,182,161
Hospitalisations[a] (inc. re-admission)	¥100,069,590,911	¥98,865,970,763	– ¥1,203,620,148	¥108,434,797,319	¥99,348,989,604	– ¥9,085,807,715
Early follow-up review	¥1,186,888,247	¥1,571,049,786	¥384,161,539	¥1,636,720,201	¥1,499,578,570	–¥137,141,632
IDM administration	–	–	–	¥1,923,703,258	¥11,594,983,377	¥9,671,280,119
Cost-per-life year	–	–	–¥1,436,675	–	–	¥298,560

Notes: negative incremental values represent a reduction from UC. All reported costs are lifetime estimates. [a]Hospitalisations due to severe exacerbation.
Abbreviations: IDM, integrated disease management; UC, Usual care; Incr, incremental = (Policy - UC); £, British Pound; €, Euro; $, Canadian dollar; ¥, Japanese Yen; –, Not applicable.

impact varied with the effect size. Policy 1 was cost-saving for implementations where the intervention effect corresponded to a ≥23% reduction in the risk (odds/ probability) of re-admission in England and Japan; in Germany and Canada, the policy was cost-saving for all effect sizes. For Policy 2, cost savings were predicted for implementations where the intervention effect corresponded to a ≥36% reduction in severe exacerbation risk in Canada and a ≥50% reduction in Japan. The policy was associated with higher total costs for all effect sizes in England and Germany.

Table 4 shows the impact for alternative IDM administration cost levels. The policy was cost-neutral (ie, total policy costs equivalent to UC) at annual, per-patient administration costs of £95, €170, $584, and ¥42,681, under primary analysis intervention effect sizes and uptake levels.

Figures S1–S8 present tornado plots of incremental outcomes for one-way sensitivity analyses. As expected, parameters related to severe exacerbations, including severe exacerbation costs and event probabilities, and in-hospital mortality probabilities, were influential; results were also sensitive to variations in baseline age and cost and benefit discount rates. Notably, in some cases (Japan and Canada, Policy 2), the cost impact of the policy depended on the severe exacerbation cost level.

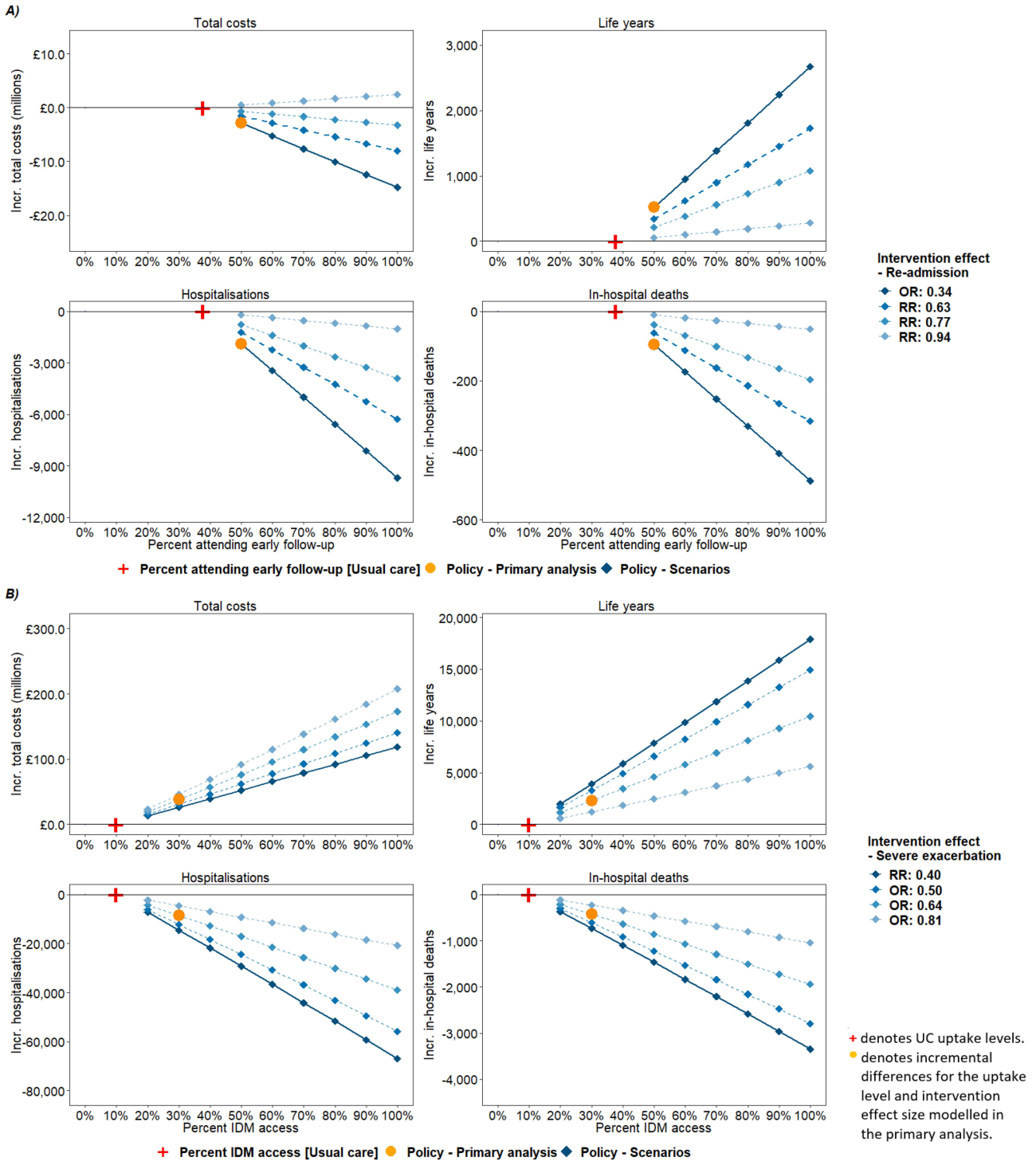

Figure 2 Cohort-level (n=100,000) incremental policy intervention scenario results by outcome - England. (**A**) Policy 1 - Early follow-up review: Values represent incremental differences between the policy intervention scenario and UC for the range of considered policy uptake levels and intervention effect sizes. (**B**) Policy 2 - IDM: Per A.
Abbreviations: IDM, integrated disease management; Incr, incremental (Policy - UC); OR, Odds ratio; RR, relative risk.

Discussion

Main Findings

This modelling study suggests a significant opportunity to realise health gains and potentially generate cost savings through better management of prevalent, on-treatment COPD populations, via increased uptake of two evidence-based interventions, in England, Germany, Canada and Japan. These findings are likely generalisable to other high-income settings.

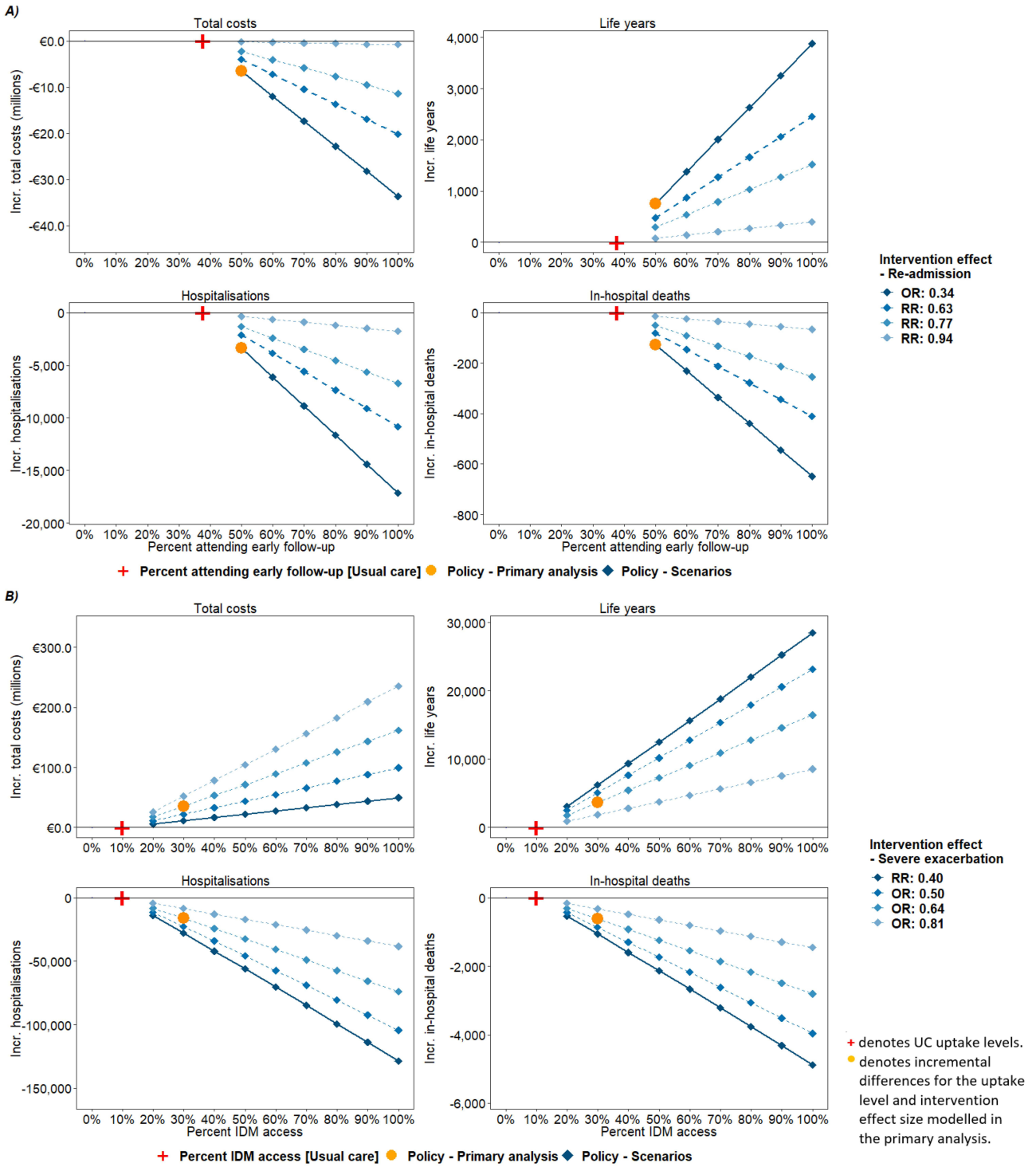

Figure 3 Cohort-level (n=100,000) incremental policy intervention scenario results by outcome - Germany. (**A**) Policy 1 - Early follow-up review: Values represent incremental differences between the policy intervention scenario and UC for the range of considered policy uptake levels and intervention effect sizes. (**B**) Policy 2 - IDM: Per A.
Abbreviations: IDM, integrated disease management; Incr, incremental (Policy - UC); OR, Odds ratio; RR, relative risk.

While increased attendance of early follow-up review after severe exacerbation hospitalisation (Policy 1) and increased access to IDM (Policy 2) are both predicted to reduce hospitalisations and improve survival, results suggest Policy 2 has a larger potential for impact. This highlights the importance of sustained, multidisciplinary care to prevent avoidable exacerbations and improve patient outcomes; all patients may achieve the benefits of IDM while the potential of early follow-up review is limited to patients experiencing severe exacerbation.

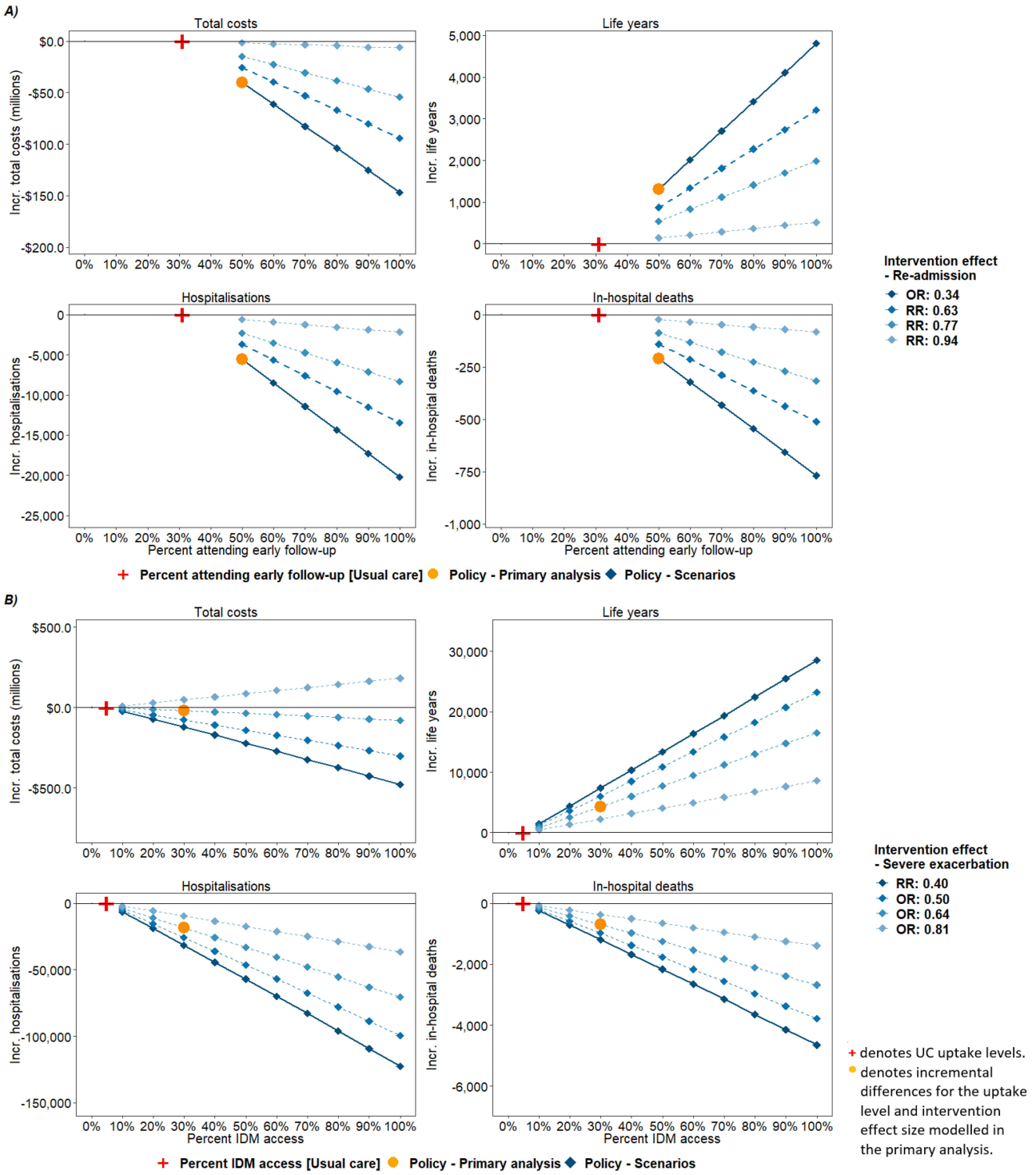

Figure 4 Cohort-level (n=100,000) incremental policy intervention scenario results by outcome - Canada. (**A**) Policy 1 - Early follow-up review: Values represent incremental differences between the policy intervention scenario and UC for the range of considered policy uptake levels and intervention effect sizes. (**B**) Policy 2 - IDM: Per A.

Abbreviations: IDM, integrated disease management; Incr, incremental (Policy - UC); OR, Odds ratio; RR, relative risk.

Policy 1, however, is likely of value to both patients and payers, with improved outcomes predicted at reduced total costs for a wide range of intervention effect sizes and across settings. This contrasts with Policy 2 where benefits come with higher total costs, except where cost savings were predicted in Canada and Japan under certain effect sizes.

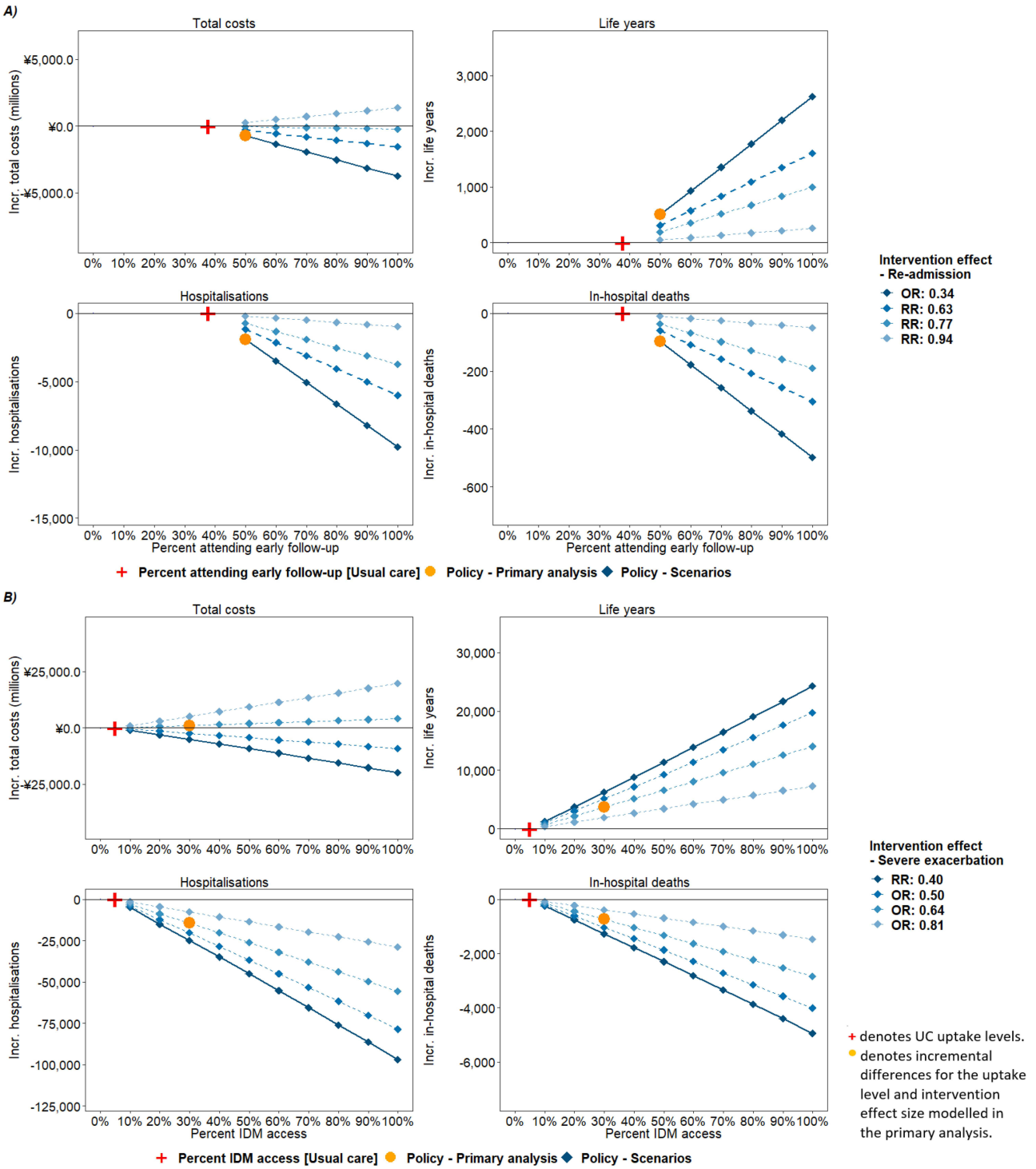

Figure 5 Cohort-level (n=100,000) incremental policy intervention scenario results by outcome - Japan. (**A**) Policy 1 - Early follow-up review: Values represent incremental differences between the policy intervention scenario and UC for the range of considered policy uptake levels and intervention effect sizes. (**B**) Policy 2 - IDM: Per A.
Abbreviations: IDM, integrated disease management; Incr, incremental (Policy - UC); OR, Odds ratio; RR, relative risk.

Sensitivity analyses found the cost impact for Policy 2 depended on the severe exacerbation cost level at primary analysis effect sizes in Canada and Japan. The cost impact at a given effect size depends on the underlying cost of COPD management, including during additional years of life, and the cost of the intervention, and the finding of directional

Table 4 Cohort-Level (n=100,000) Incremental Cost Estimates for IDM Programme Administration Cost Scenarios

Country	Primary Analysis			Scenario		
	Per-Patient Annual IDM Programme Admin Cost	Incr. Life Years	Incr. Total Costs	Per-Patient Annual IDM Programme Admin Cost	Incr. Total Costs	Incr. Cost-Per-Life Year
England	£306	2299	£38,150,385	£50	–£8,190,743	–£3562
				£100	£842,968	£367
				£150	£9,876,678	£4295
				£200	£18,910,388	£8224
				£300	£36,977,809	£16,082
				£400	£55,045,230	£23,940
				£500	£73,112,650	£31,797
				£600	£91,180,071	£39,655
				£700	£109,247,492	£47,513
Germany	€346	3619	€35,582,898	€50	–€24,480,201	–€6764
				€100	–€14,321,709	–€3957
				€150	–€4,163,217	–€1150
				€200	€5,995,274	€1657
				€300	€26,312,258	€7271
				€400	€46,629,242	€12,884
				€500	€66,946,225	€18,498
				€600	€87,263,209	€24,112
				€700	€107,580,192	€29,726
Canada	$500	4299	–$20,516,519	$50	–$130,761,487	–$30,414
				$100	–$118,512,046	–$27,565
				$150	–$106,262,605	–$24,716
				$200	–$94,013,165	–$21,867
				$300	–$69,514,283	–$16,169
				$400	–$45,015,401	–$10,470
				$500	–$20,516,519	–$4772
				$600	$3,982,362	$926
				$700	$28,481,244	$6625

(*Continued*)

Table 4 (Continued).

Country	Primary Analysis			Scenario		
	Per-Patient Annual IDM Programme Admin Cost	Incr. Life Years	Incr. Total Costs	Per-Patient Annual IDM Programme Admin Cost	Incr. Total Costs	Incr. Cost-Per-Life Year
Japan	¥48,111	3656	¥1,091,533,997	¥7500	–¥7,072,104,135	–¥1,934,553
				¥15,000	–¥5,564,462,147	–¥1,522,142
				¥22,500	–¥4,056,820,159	–¥1,109,731
				¥30,000	–¥2,549,178,171	–¥697,320
				¥45,000	¥466,105,805	¥127,502
				¥60,000	¥3,481,389,780	¥952,324
				¥75,000	¥6,496,673,756	¥1,777,146
				¥90,000	¥9,511,957,731	¥2,601,967
				¥105,000	¥12,527,241,707	¥3,426,789

Abbreviations: IDM, integrated disease management; Incr, incremental = (Policy - UC); £, British Pound; €, Euro; $, Canadian dollar; ¥, Japanese Y.

variations across and within countries, coupled with the absence of evidence for key parameters, highlights the need for further study to verify our findings.

Findings in the Context of Existing Literature

Early follow-up review after severe exacerbation hospitalisation has been shown to reduce re-admission rates[25,36] and mortality risks.[55] However, no prior studies have evaluated the value of improved attendance of early follow-up review in terms of health outcomes and costs.

Literature on the cost and effectiveness of IDM is mixed. Short-term studies in Italy[56] (2 years) and Poland[57] (six months) found that IDM reduced hospitalisations and was cost-effective. Assessing outcomes over three years, a large study of the German IDM programme found participants had reduced mortality risk (hazard ratio: 0.89, 95% confidence interval [CI]: 0.84–0.94) and higher total costs (€553 per year).[31] IDM can improve quality of life;[28–30] a recent cost-effectiveness analysis of IDM in Canadian primary care by Scarffe et al, found the programme dominated UC, with cost savings and higher quality-adjusted life years (QALYs) in the short- (1-year; within-trial) and long-term (30-years; model-based analysis).[58] Approximating the effect on severe exacerbation from the same RCT,[29] corresponding analyses from our study (Canada, Policy 2; RR: 0.40) corroborate this finding of improved health outcomes and cost savings and provide additional evidence on the impact at alternative uptake levels.

Notably, Scarffe et al, reported IDM to generate incremental lifetime QALYs (1.732) greater than incremental life years (0.244).[58] Our study did not evaluate QALYs. However, considering incremental cost-per-life year estimates from the primary analyses (England: £16,594; Germany: €9832; Japan: ¥298,560) and cost-per-QALY willingness-to-pay thresholds of £20,000,[37] €20,000, and ¥5,000,000, the policy is likely also cost-effective in these settings. There are no formal willingness-to-pay threshold exists in Germany or Japan, so the currency equivalent cost-per-QALY threshold for England has been assumed.[59]

Differences in findings across studies are likely due to variations in the composition of IDM and UC, evaluation follow-up time,[28] as well as measured outcomes and patient and provider factors.[60] IDM typically yields health benefits, mainly due to reduced exacerbation frequency, but the cost impact varies across settings. This is consistent with findings across the four countries in our study.

Strengths

The policies were selected to align with the international consensus statement on COPD management and designed to be feasible to implement in the study countries, ie based on improving existing management and reducing the variability of care.[19] Modelled intervention effects were based on the best available evidence, including data from a contemporary meta-analysis of 52 RCTs for IDM.[28] In practice, the interventions may be implemented differently according to local health services provisions and their costs and effect sizes vary accordingly. In addition, the achievable uptake will depend on the design of the associated policies, which may vary based on local-level infrastructure and existing care processes as well as budgetary considerations. Broad applicability of the findings was ensured through scenario analyses considering an extensive range of intervention effect sizes, uptake levels, and IDM administration costs.

Limitations

The management of COPD is highly complex and the care provision varies both on an individual basis and by setting. Capturing these intricacies and differences in outcomes between countries presents challenges. Where possible, country-specific data were used for UC profiles, and the impact of evaluated interventions was informed by published evidence. However, relevant data were lacking for many parameters, and differences exist in how studies measured outcomes or interventions. Combining this evidence robustly presented challenges requiring assumptions. The model framework makes these explicit, and sensitivity analyses highlight priority areas where further data on COPD care is needed.

The achievable impact of the policies may differ in practice in several ways. 1) Exacerbation history and symptom severity are core components of the GOLD ABE clinical assessment tool and key for therapeutic decision-making.[9] Based on these factors, both interventions may result in treatment changes (likely escalation), which were not modelled. Therefore, treatment costs may increase alongside slower disease progression rates and improved health outcomes. 2) Only the effect of IDM on severe exacerbations was modelled. IDM could beneficially impact disease progression, but limited data were available to inform this. Whilst our model captures the indirect effect of reductions in severe exacerbations on mortality, capturing the broader effects could yield more optimistic outcomes. 3) Studies of IDM report short-term (3–36 months) effects. Our model extrapolated these to a lifetime horizon, which may overestimate benefits in the case of waning. 4) The effects of IDM and early follow-up review were assumed to apply equally across patients, GOLD stages, and settings. In practice, not all patients may benefit equally from or be able to access these interventions; the effect may vary by disease stage and setting, and the benefits be greater for high-risk populations. Barriers such as distance from care may also limit the achievable impact.[9,25] However, this is a reasonable simplifying assumption for a population-level model, and a range of uptake and effect size scenarios were evaluated.

Policy Implications and Future Research

While the socio-economic burden of COPD is well established, the impact of policies that improve its management is less so. This study provides policymakers with evidence on the potential health and economic impact of improved COPD care in different healthcare settings by quantifying the potential value of policy scenarios to prevent and better manage severe exacerbations. Additionally, in making explicit the notable evidence gaps, priority areas for further research to support evidence-based policy decisions are highlighted.

Additional country-specific data on current and guideline-recommended care should be collected to support more robust assessment of the chosen interventions and to validate the impact shown in this study. Future studies could evaluate treatment-regimen changes due to early follow-up review and IDM, the impact on mild to moderate exacerbations which may also influence patients' disease trajectory,[61] and the impact in high-risk populations (eg, smokers). With prevalence estimates ranging from 5.1% to 13.5% for 40- to 64-year-olds high-income country prevalence is based on the GOLD case definition,[10] many COPD patients are of working age and the economic impact on patients and governments may be considerable.[9,62,63] Future studies could also assess the impact of improved outcomes on productivity losses ie, societal costs.

Conclusion

Preventing severe exacerbations is key to improving patient outcomes in COPD, and reductions in related hospitalisations will support healthcare system resilience and sustainability. This study provides evidence that suggests improved adherence to

early follow-up review post severe exacerbation hospitalisation (Policy 1) and increased access to IDM (Policy 2) can positively impact patient outcomes, reduce hospitalisations, and may generate cost savings across four high-income countries while highlighting priority areas for further research to support evidence-based policy decisions.

Abbreviations

CI, Confidence interval, COPD, Chronic Obstructive Pulmonary Disease; GOLD, Global Initiative for Chronic Obstructive Lung Disease; IDM, Integrated Disease Management; LAMA, Long-acting muscarinic antagonist; OR, Odds ratio; QALY, Quality-adjusted life year; RR, Relative risk; UC, Usual care.

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