

SUPPLEMENTARY MATERIALS

Study design and population

This was a retrospective, longitudinal, open-cohort study. Patients aged ≥ 12 years with a new asthma diagnosis or prevalent disease within 3 years of the index date and with evidence of short-acting β_2 -agonist (SABA) inhaler prescription and both baseline (12 months prior to the index date) and follow-up data were included in the Clinical Practice Research Datalink (CPRD), with hospital admission and outpatient consultation records for asthma from the Hospital Episode Statistics (HES) database. The CPRD is a primary care database of anonymised medical records from over 40 million patients visiting general practitioners in the UK,²² and HES database records are from visits to National Health Service (NHS) hospitals. Patients were identified using asthma Read codes. The index date was defined as the latest date of any of the following: 13th birthday, start of study period (1 January 2008), 1 year after the general practitioner practice began recording up-to-standard or research-quality data (CPRD quality control), 1 year after their continuous CPRD practice registration date or 1 year after first asthma Read code. The follow-up period ended at the earliest date of death, transfer out of CPRD, last date of CPRD data collection or end of study period (31 December 2019). Patients were excluded if they had less than 12 months of research-acceptable data, no current asthma, were at the highest 2016 Scottish Intercollegiate Guidelines Network/British Thoracic Society guidelines treatment step (continuous or frequent oral corticosteroid [OCS] use) and/or receiving non-asthma treatments including long-acting muscarinic antagonists/long-acting β_2 -agonists without inhaled corticosteroids (ICS) or regular OCS without ICS.

Supplementary Table 1: Unit costs by service based on NHS estimates

Healthcare Resource Utilisation	Unit Cost	Notes
Exacerbation – hospitalisation	£813	Weighted average of HRG codes DZ15M–R
Exacerbation – A&E	£263	Weighted average of Type 01 A&E attendances, excluding dental care
Exacerbation – primary care with OCS	£39.73	Primary care (£38.25)+prednisolone (£1.48)
Primary care consultation without OCS*	£38	Up 3.4% from last year
Outpatient consultation*	£157	Using national schedule of NHS costs, outpatient attendance respiratory medicine unit cost

*Non–exacerbation-related HCRU

A&E, accident and emergency; HCRU, healthcare resource utilisation; HRG, Healthcare Resource Group; NHS, National Health Service; OCS, oral corticosteroids.

Supplementary Table 2: Annual non-exacerbation-related HCRU rates and events in UK patients with asthma by SABA inhaler use and BTS treatment steps

Treatment	SABA group	Patients	Overall non-exacerbation-related HCRU		Primary care visits without OCS prescription*		Outpatient visits*	
			Rate	Events	Rate	Events	Rate	Events
No ICS	Overall	37,118	0.530	19,673	0.491	18,225	0.039	1,448
	SABA 1-2	26,736	0.479	12,807	0.448	11,978	0.031	829
	SABA ≥3	10,382	0.662	6,873	0.607	6,302	0.054	561
Low-dose ICS	Overall	69,684	0.656	45,713	0.626	43,622	0.029	2,021
	SABA 1-2	37,673	0.592	22,302	0.568	21,398	0.024	904
	SABA ≥3	32,011	0.727	23,272	0.692	22,152	0.035	1,120
Low-dose ICS+LABA	Overall	28,400	0.916	26,014	0.831	23,600	0.085	2,414
	SABA 1-2	10,861	0.828	8,993	0.753	8,178	0.075	815
	SABA ≥3	17,539	0.974	17,083	0.881	15,452	0.093	1,631
Medium-dose ICS±additional therapies	Overall	36,890	0.999	36,853	0.809	29,844	0.190	7,009
	SABA 1-2	13,049	0.856	11,170	0.731	9,539	0.125	1,631
	SABA ≥3	23,841	1.079	25,724	0.852	20,313	0.226	5,388
High-dose ICS±additional therapies	Overall	13,969	1.154	16,120	0.818	11,427	0.336	4,694
	SABA 1-2	3,198	0.983	3,144	0.757	2,421	0.226	723
	SABA ≥3	10,771	1.211	13,044	0.839	9,037	0.373	4,018

*Non-exacerbation-related HCRU

BTS, British Thoracic Society; HCRU, healthcare resource utilisation; ICS, inhaled corticosteroid; LABA, long-acting β_2 -agonist; OCS, oral corticosteroids; SABA, short-acting β_2 -agonist.

Supplementary Table 3: Annual exacerbation-related HCRU rates and events in UK patients with asthma by SABA inhaler use and BTS treatment steps

Treatment	SABA group	Patients	Overall exacerbation-related HCRU		Primary care visits with OCS prescription		A&E		Hospitalisations	
			Rate	Events	Rate	Events	Rate	Events	Rate	Events
No ICS	Overall	37,118	0.147	5,456	0.140	5,197	0.003	111	0.004	148
	SABA 1-2	26,736	0.116	3,101	0.111	2,968	0.002	53	0.003	80
	SABA ≥3	10,382	0.217	2,253	0.208	2,159	0.004	42	0.006	62
Low-dose ICS	Overall	69,684	0.158	11,010	0.151	10,522	0.003	209	0.004	279
	SABA 1-2	37,673	0.119	4,483	0.114	4,295	0.002	75	0.003	113
	SABA ≥3	32,011	0.199	6,370	0.189	6,050	0.004	128	0.006	192
Low-dose ICS+LABA	Overall	28,400	0.314	8,918	0.298	8,463	0.006	170	0.010	284
	SABA 1-2	10,861	0.221	2,400	0.213	2,313	0.003	33	0.006	65
	SABA ≥3	17,539	0.368	6,454	0.348	6,104	0.007	123	0.013	228
Medium-dose ICS±additional therapies	Overall	36,890	0.510	18,814	0.486	17,929	0.007	258	0.016	590
	SABA 1-2	13,049	0.305	3,980	0.294	3,836	0.005	65	0.007	91
	SABA ≥3	23,841	0.616	14,686	0.586	13,971	0.008	191	0.020	477
High-dose ICS±additional therapies	Overall	13,969	0.705	9,848	0.671	9,373	0.009	126	0.025	349
	SABA 1-2	3,198	0.433	1,385	0.414	1,324	0.005	16	0.013	42
	SABA ≥3	10,771	0.796	8,574	0.757	8,154	0.010	108	0.029	312

A&E, accident and emergency; BTS, British Thoracic Society; HCRU, healthcare resource utilisation; ICS, inhaled corticosteroid;

LABA, long-acting β_2 -agonist; OCS, oral corticosteroids; SABA, short-acting β_2 -agonist.

Supplementary Table 4: Extrapolation of HCRU costs to the broader UK asthma population by SABA inhaler use and BTS treatment steps

Treatment	SABA 1-2/year				SABA ≥3/year		
	% Patients (CPRD)	UK Patients	Cost per 1,000 Patients* (CPRD)	UK Population Cost	UK Patients	Cost per 1,000 Patients* (CPRD)	UK Population Cost
No ICS	20%	643,827	£26,746	£17,219,483	250,008	£45,448	£11,362,483
Low-dose ICS	37%	907,200	£27,324	£24,788,084	770,854	£44,795	£34,530,190
Low-dose ICS+LABA	15%	261,543	£44,642	£11,675,731	422,355	£69,691	£29,434,217
Medium-dose ICS±additional therapies	20%	314,232	£60,140	£18,897,834	574,113	£106,402	£61,087,045
High-dose ICS±additional therapies	8%	77,011	£121,429	£9,351,367	259,375	£208,457	£54,068,743
TOTAL		2,203,813		£81,932,499	2,276,705		£190,482,678
HCRU cost difference, high versus low		£108,550,179/year					

*Expressed as an average (i.e., sum of costs per 1,000 patients per year). QOF database estimate of 4,480,518 used for all calculations. This does not exclude patients <12 years of age.

BTS, British Thoracic Society; CPRD, Clinical Practice Research Datalink; HCRU, healthcare resource utilisation; ICS, inhaled corticosteroid; LABA, long-acting β_2 -agonist; SABA, short-acting β_2 -agonist; UK, United Kingdom.

Supplementary Table 5: Extrapolation of HCRU costs to average asthma IC population (N=85,429) by SABA inhaler use and BTS treatment steps

Treatment	SABA 1-2/year				SABA ≥3/year		
	% Patients (CPRD)	IC Patients	Cost per 1,000 Patients* (CPRD)	IC Population Cost	IC Patients	Cost per 1,000 Patients* (CPRD)	IC Population Cost
No ICS	20%	12,276	£26,746	£328,320	4,767	£45,448	£216,646
Low-dose ICS	37%	17,297	£27,324	£472,629	14,698	£44,795	£658,379
Low-dose ICS+LABA	15%	4,987	£44,642	£222,618	8,053	£69,691	£561,215
Medium-dose ICS±additional therapies	20%	5,991	£60,140	£360,321	10,946	£106,402	£1,164,733
High-dose ICS±additional therapies	8%	1,468	£121,429	£178,300	4,945	£208,457	£1,030,916
TOTAL		42,020		£1,562,188	43,409		£3,631,889
HCRU cost difference, high versus low		£2,069,701/year					

*Expressed as an average (i.e., sum of costs per 1,000 patients per year). Percentages may not sum to 100% due to rounding.

BTS, British Thoracic Society; CPRD, Clinical Practice Research Datalink; HCRU, healthcare resource utilisation; IC, integrated care system; ICS, inhaled corticosteroid; LABA, long-acting β_2 -agonist; SABA, short-acting β_2 -agonist.

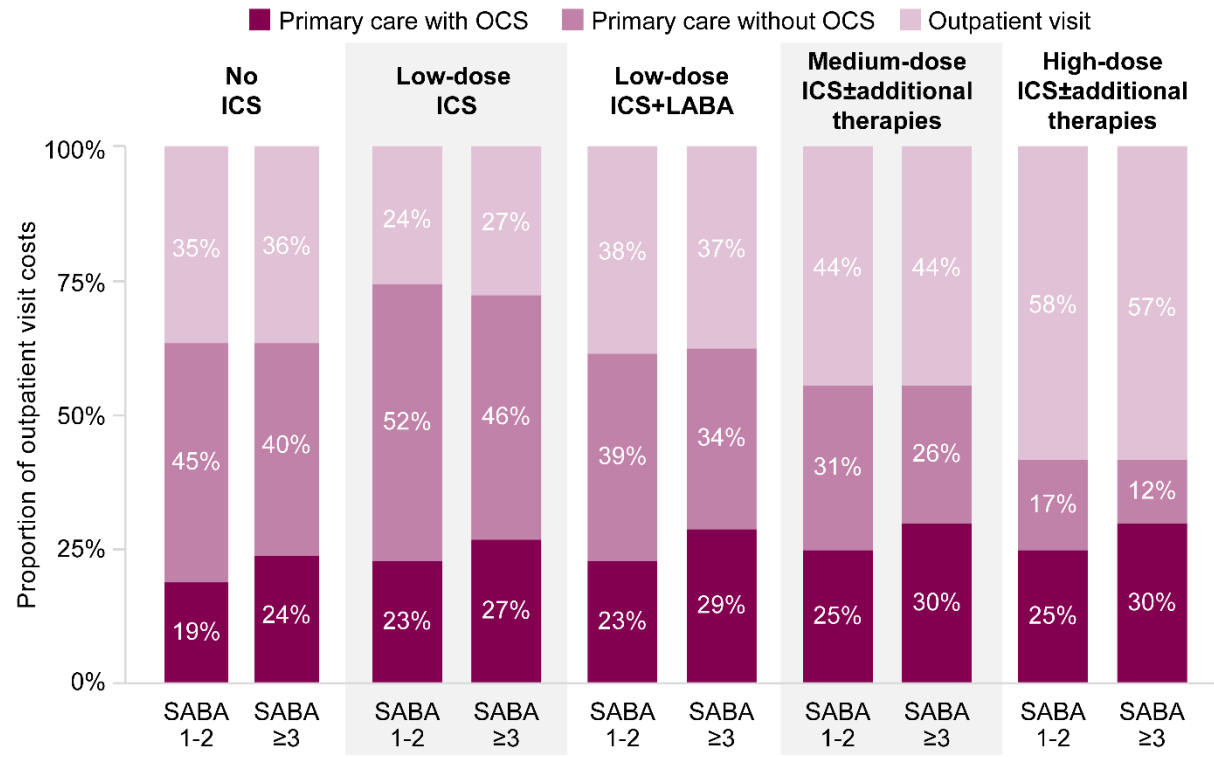
Supplementary Table 6: Extrapolation of HCRU costs to average PCN asthma population (N=50,000) by SABA inhaler use and BTS treatment steps

Treatment	% Patients (CPRD)	SABA 1-2/year			SABA ≥3/year		
		PCN Patients	Cost per 1,000 Patients* (CPRD)	PCN Population Cost	PCN Patients	Cost per 1,000 Patients* (CPRD)	PCN Population Cost
No ICS	20%	7,185	£26,746	£192,160	2,790	£45,448	£126,799
Low-dose ICS	37%	10,124	£27,324	£276,621	8,602	£44,795	£385,337
Low-dose ICS+LABA	15%	2,919	£44,642	£130,294	4,713	£69,691	£328,469
Medium-dose ICS±additional therapies	20%	3,507	£60,140	£210,889	6,407	£106,402	£681,696
High-dose ICS±additional therapies	8%	859	£121,429	£104,356	2,894	£208,457	£603,376
TOTAL		24,594		£914,320	25,406		£2,125,677
HCRU cost difference, high versus low				£1,211,357/year			

*Expressed as an average (i.e., sum of costs per 1,000 patients per year). Percentages may not sum to 100% due to rounding.

BTS, British Thoracic Society; CPRD, Clinical Practice Research Datalink; HCRU, healthcare resource utilisation; ICS, inhaled corticosteroid; LABA, long-acting β_2 -agonist; PCN, primary care network; SABA, short-acting β_2 -agonist.

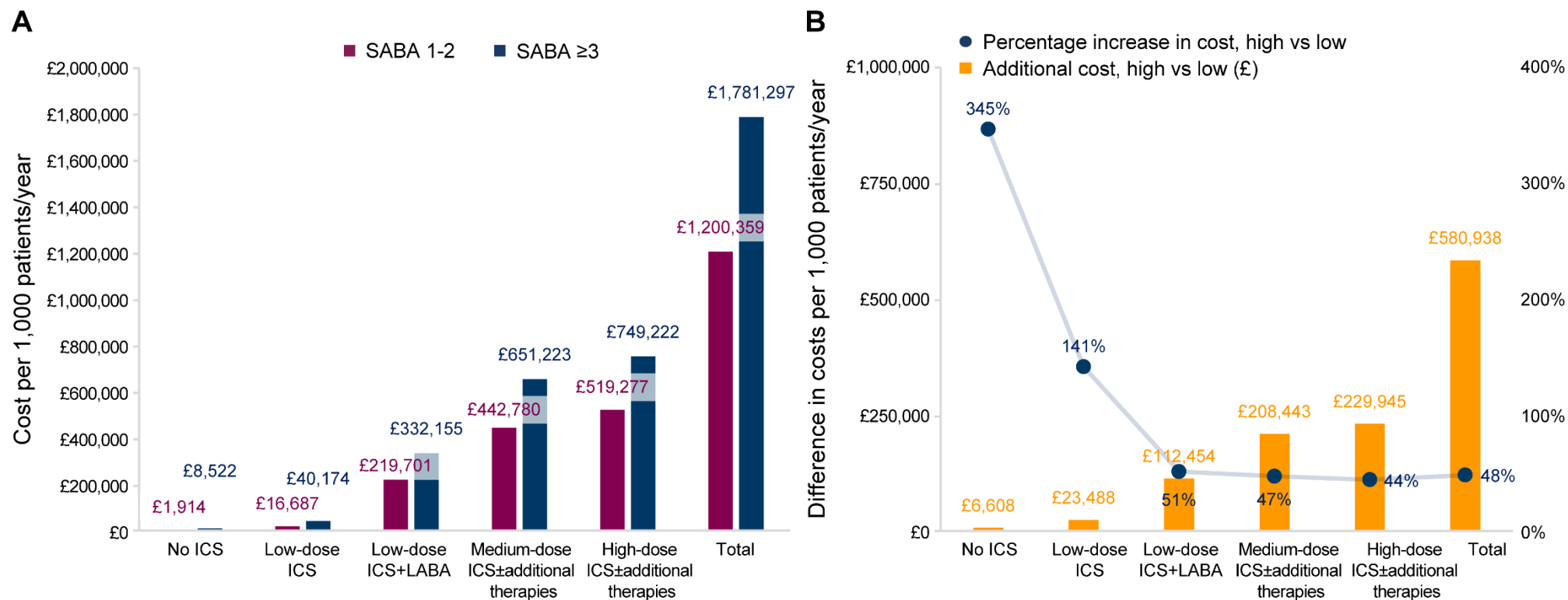
Supplementary Figure 1: HCRU cost drivers by SABA inhaler use and BTS treatment steps



Percentages may not sum to 100% due to rounding.

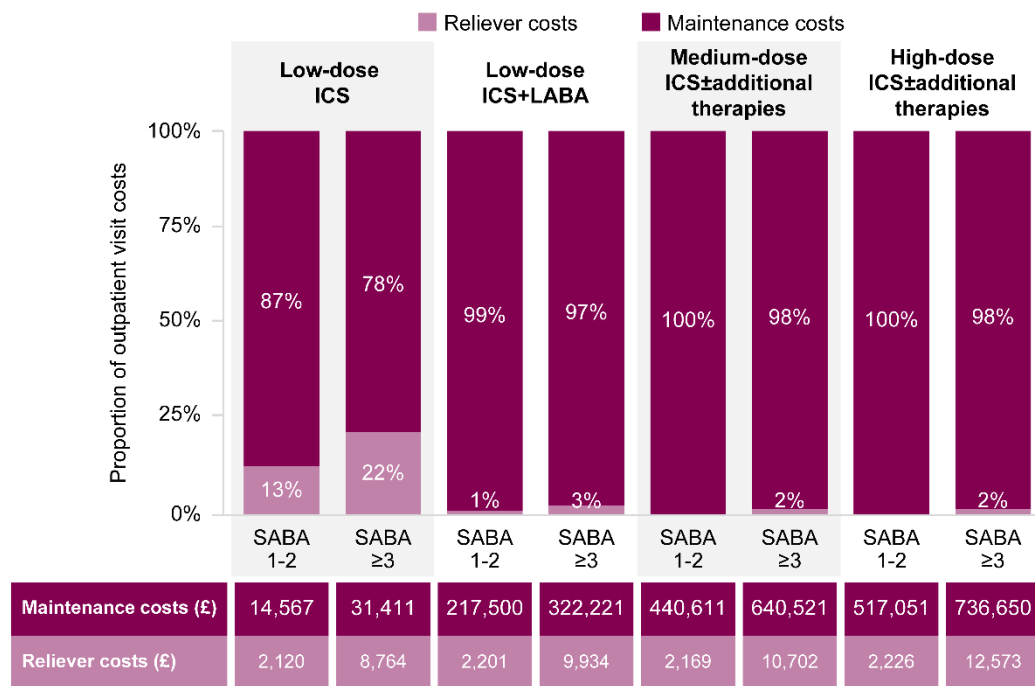
BTS, British Thoracic Society; HCRU, healthcare resource utilisation; ICS, inhaled corticosteroid; LABA, long-acting β_2 -agonist; OCS, oral corticosteroid; SABA, short-acting β_2 -agonist.

Supplementary Figure 2: Medication costs in UK patients with asthma by BTS treatment steps (A) Per 1,000 patients* (B) Cost differential: high-SABA versus low-SABA group (absolute and percentage differences)



*Expressed as an average (i.e., sum of costs per 1,000 patients per year). Estimates are subject to rounding
 BTS, British Thoracic Society; ICS, inhaled corticosteroid; LABA, long-acting β_2 -agonist; SABA, short-acting β_2 -agonist; UK, United Kingdom.

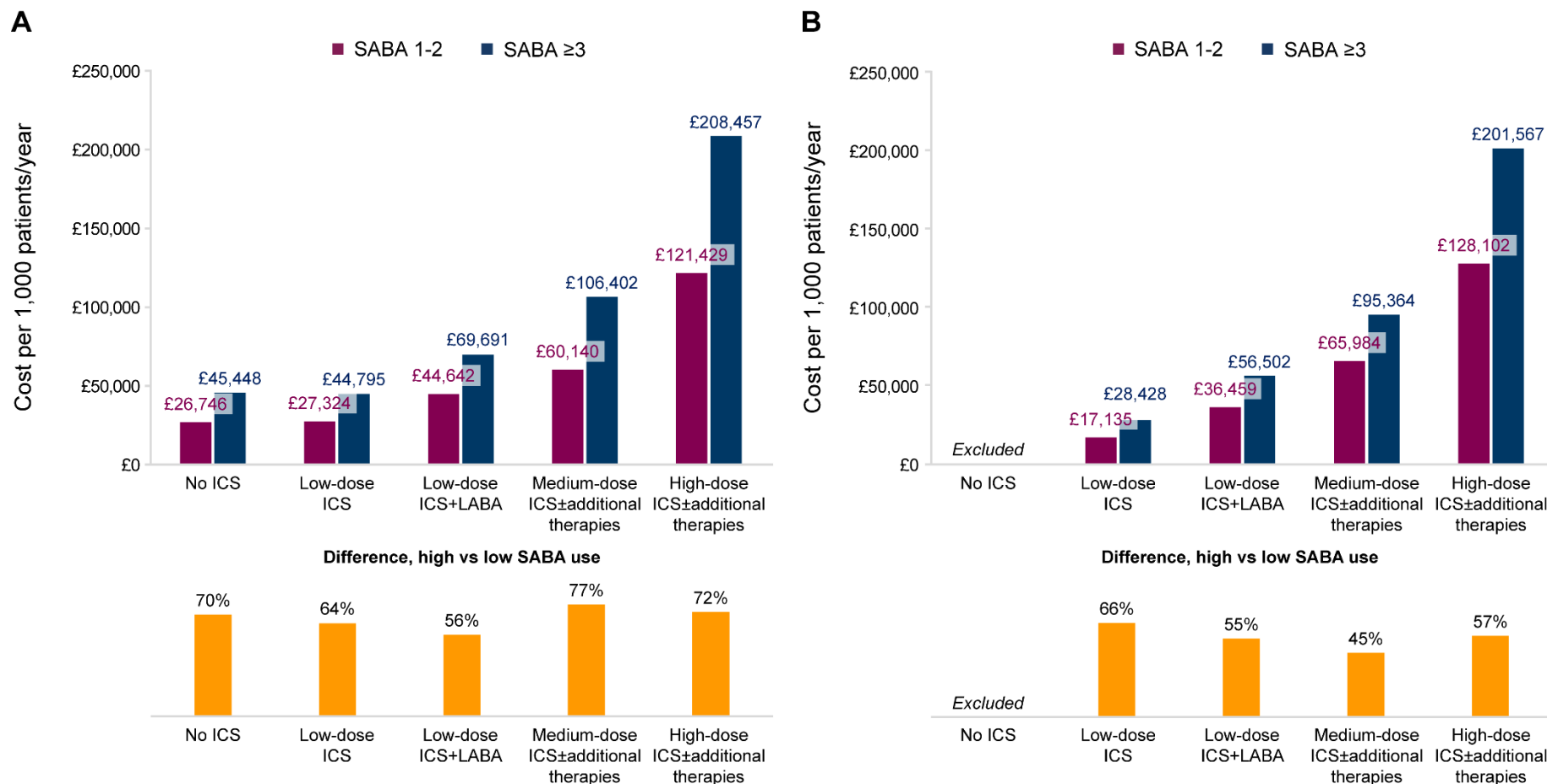
Supplementary Figure 3: Cost of maintenance and reliever medications in UK patients with asthma by SABA inhaler use and BTS treatment steps



Estimates are subject to rounding.

BTS, British Thoracic Society; ICS, inhaled corticosteroid; LABA, long-acting β_2 -agonist; SABA, short-acting β_2 -agonist; UK, United Kingdom.

Supplementary Figure 4: HCRU costs per 1,000 UK patients* with asthma by BTS treatment steps in (A) Full analysis cohort (B) Subgroup with $\geq 50\%$ PDC



*Expressed as an average (i.e., sum of costs per 1,000 patients per year).

BTS, British Thoracic Society; ICS, inhaled corticosteroid; LABA, long-acting β_2 -agonist; PDC, proportion of days covered; SABA, short-acting β_2 -agonist.