APPENDIX 1 MODEL POPULATION

Table A1

Model population

Population	Stable	Post-hospital
Age (median)	67	73
Sex (% male)	53.9	46.9
Smoking status (% current smokers)	52.2	31.3
GOLD stage (% GOLD 3/ % GOLD 4)	50/50	50/50
Source	Studies included in systematic review [8]	2017 National UK COPD audit [9]

APPENDIX 2 MODEL ASSUMPTIONS

Model Assumptions

The starting cohort for the stable population was assumed to contain 50% with GOLD stage 3 and the remainder with GOLD stage 4 populations.

An estimate was applied for the utility loss from a cohort study of patients admitted to hospital followed up for 1 year.

The costs of usual care, NIV, and treating exacerbations were estimated with reference to best practice guidance and expert opinion.

No additional improvement in baseline utility was applied to either the stable or post-hospital population.

The effect of domiciliary NIV was assumed to last for up to 5 years and be driven primarily by a reduced risk of hospital admission and indirectly the associated reduction in mortality risk.

15% of patients were assumed to discontinue using domiciliary NIV after 3 months. These patients were assumed to incur costs but no benefits in the first 3 months and neither costs nor benefits beyond 3 months.

APPENDIX 3 MODEL TRANSITIONS

Both populations face risks of both moderate and severe exacerbation, and their routes through the model are slightly different, with entirely unique probabilities of moving between health states.

Stable health state transitions

As figure A1 shows in stable states patients can die from a disease-free mortality rate, live without an exacerbation, or experience an exacerbation.

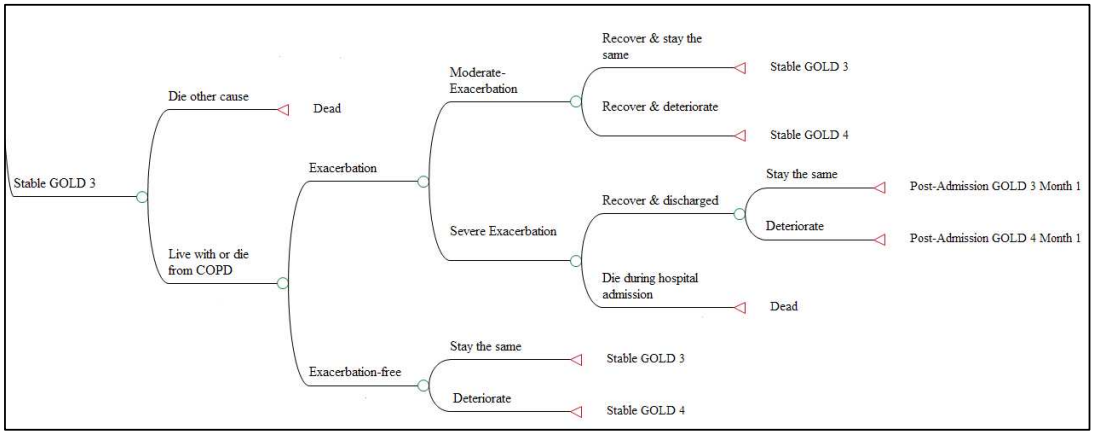

Figure A1 Stable health state transitions

The exacerbation may either be moderate and managed at home, or severe as to require hospital admission, the latter may also lead to death during admission. If they survive hospital admission the patient is effectively discharged and moves to the first month post-discharge state. Those who live without exacerbation, or experience only a moderate exacerbation (re)enter the stable health state. Figure A1 shows a pathway for a stable patient in GOLD stage 3; GOLD stage 4 pathway is identical except patients cannot move to GOLD stage 3.

Post-discharge health state transitions

An example of the post-discharge health state pathway in the first month post-discharge for GOLD stage 3 in the stable population is shown in Fig A2.

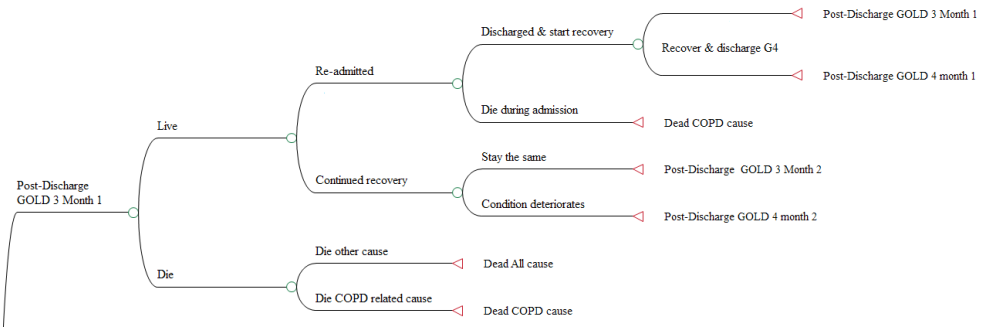

Figure A2 Pathway within a post-discharge health state for the stable population

From the post-discharge health state patients could either continue their recovery, die at home, or be readmitted where they could die during admission. If they survived hospital admission, they (re)entered one of the first month post-admission health states. If recovery continued without being readmitted, they moved to the second and then third post-admission health states where they faced similar pathways. The additional costs and utility losses associated with a non-severe exacerbation during the recovery period were considered negligible as patients were already assumed to have incurred higher costs and utility loss. The pathways within the post-discharge health states were almost identical for months 1- 3 but in month 3 patients could transition to a stable health state, although GOLD stage 3 patients were allowed to transition to a parallel GOLD stage 4 state. As noted above, the post-discharge health states were identical for both the stable and post-hospital populations.

APPENDIX 4

COPD-ADJUSTED ALL-CAUSE MORTALITY RATES, BY AGE AND SEX

Table A2 lists COPD adjusted all-cause mortality rates applied in the economic model. These were derived from ONS 2017-2019 all-cause and 2017 COPD-related mortality rates by sex and age for England.

Table A2

COPD-adjusted all-cause mortality rates, by age and sex

	All-cause mortality		Deaths caused by COPD		COPD-adjusted mortality	
Age (years)	Male (%)	Female (%)	Male (%)	Female (%)	Male (%)	Female (%)
60	0.760	0.504	3.049	3.823	0.736	0.486
61	0.831	0.549			0.806	0.528
61	0.922	0.626			0.894	0.603
63	1.018	0.671			0.987	0.646
64	1.095	0.726			1.061	0.699
65	1.203	0.799	6.502	7.478	1.124	0.739
66	1.333	0.857			1.246	0.793
67	1.444	0.938			1.350	0.868
68	1.574	1.033			1.472	0.956
69	1.729	1.130			1.617	1.045
70	1.829	1.244			1.710	1.151
71	2.028	1.334			1.896	1.234
72	2.233	1.524			2.087	1.410
73	2.550	1.735			2.384	1.605
74	2.812	1.917			2.629	1.773
75	3.140	2.144	6.642	6.410	2.932	2.006
76	3.512	2.422			3.278	2.266
77	3.884	2.731			3.626	2.556
78	4.352	3.096			4.063	2.898
79	4.810	3.448			4.490	3.227
80	5.398	3.846			5.040	3.600
81	6.001	4.363			5.608	4.084
82	6.651	4.896			6.209	4.582
83	7.540	5.627			7.039	5.266
84	8.476	6.394			7.913	5.983
85	9.466	7.246	5.031	3.056	8.990	7.025
86	10.683	8.309			10.148	8.056
87	11.859	9.346			11.262	9.061
88	13.336	10.643			12.665	10.318
89	14.985	11.894			14.231	11.531
90	15.953	13.439			15.150	13.028
91	17.906	15.076			17.005	14.615
92	19.695	16.708			18.704	16.197
93	21.504	18.434			20.423	17.871
94	23.809	20.447			22.611	19.822
95	26.101	22.821			24.788	22.124
96	28.671	25.077			17.229	24.310
97	30.411	26.706			28.881	25.890
98	32.589	29.126			30.950	28.236
99	36.954	30.953			35.095	30.007
100	38.439	34.336			36.505	33.287

APPENDIX 5

DISEASE PROGRESSION RATES APPLIED IN THE ECONOMIC MODEL

Table A4 lists the annual disease progression rates, obtained from a published COPD Markov model [16]

Table A5

Annual disease progression risks by age and smoking status

	GOLD stage 3 to GOLD stage 4	
Age (years)	Ex-smoker (%)	Smoker (%)
60	5.120	7.823
61	5.229	7.989
61	5.338	8.155
63	5.386	8.229
64	5.434	8.304
65	5.482	8.379
66	5.530	8.454
67	5.579	8.529
68	5.618	8.589
69	5.658	8.650
70	5.698	8.710
71	5.737	8.770
72	5.777	8.831
73	5.789	8.849
74	5.801	8.868
75	5.814	8.887
76	5.826	8.905
77	5.838	8.924
78	5.857	8.953
79	5.876	8.982
80	5.895	9.011
81	5.914	9.040
82	5.933	9.069
83	5.993	9.161
84	6.054	9.254
85	6.114	9.347
86	6.175	9.439
87	6.236	9.532
88	6.296	9.624
89	6.357	9.717
90	6.417	9.810
91	6.478	9.902
92	6.538	9.995
93	6.599	10.088
94	6.659	10.180
95	6.720	10.273
96	6.781	10.365
97	6.841	10.458
98	6.902	10.551
99	7.891	10.643
100	7.891	10.643

APPENDIX 6 DISTRIBUTIONS FOR PROBABILISTIC ANALYSES

As the standard error for the rate ratio on the natural scale isn't normally distributed for probabilistic sensitivity analysis to sample the parameter from a Normal distribution samples of the rate ratio were drawn form Ln(Rate Ratio), and then exponentiated for each draw.

Table A6

Distributions for hospital admissions rate ratios used in the probabilistic analysis

Definition All studies		
Post-hospital population	**Ln (Rate Ratio)**	**SE of Ln (Rate Ratio)**
Pooled mean	-0.706	0.131
Best case NIV	-1.099	0.296
Worst case NIV	0.502	0.126
Stable population		
Pooled mean	-0.501	0.116
Best case NIV	-1.061	0.115
Worst case NIV	0.154	0.338
Definition "UK-like" settings*		
Post-hospital population		
Pooled mean	-0.317	0.630
Best case NIV	-0.944	0.096
Worst case NIV	0.316	0.128
Stable population		
Pooled mean	-0.331	0.077
Best case NIV	-0.442	0.203
Worst case NIV	0.154	0.338

*UK like studies included studies from Italy, Poland, The Netherlands, Germany, and the UK

Abbreviations; SE (Standard Error)

APPENDIX 7 COSTING METHODS

Cost calculations were broken down into routine health-care visits, routine pharmacotherapy, moderate and severe exacerbations, and the cost of domiciliary NIV.

Routine health-care visits

Resource use for routine care were based upon assumptions made in the COPD diagnosis and management economic model report accompanying the National Institute for Health and Care Excellence (NICE) guidance (2018). It was assumed that GOLD stage 3 and 4 patients would attend, respectively, one and two assessments per year in secondary care. Unit costs reflect a mean of respiratory outpatient procedures. The NICE model (2018) also had an average of one and a half, and two, GP visits for stage 3 and 4 respectively, using unit costs for a standard 9.22-minute consultation. The NICE model (2018) also had four respiratory team visits for a Gold Stage 4 patient, and two for a Gold Stage 3 patient. Each visit was assumed to last 40 minutes and comprise 75% of a band 6 nurse and 25% of a band 7 nurse. Nurse time was costed using the per-hour patient facing time for each nurse, derived from the Unit Cost of Health and Social Care 2019[22]. Cost of spirometry were obtained from NHS reference costs 2010/2011 (DH, 2010) and inflated using the NHS cost inflation index [22]. Both the cost, and usage of home oxygen therapy were taken from Hertel et al. (2012), costs inflated using both the hospital and community health services index and the NHS cost inflation index [22]. As in the previous model [7] 75% of patients in each severity group were assumed to receive the flu vaccination, the cost of the which was assumed to be the average of the two flu jabs currently available for reimbursement for over 65-year olds (NHS England, 2019). Costs of routine care for GOLD stage 3 and 4 are shown in Table A7. The annual cost of routine healthcare was £478.95 in gold stage 3, and £927.99 in gold stage 4.

Smoking cessation and pulmonary rehabilitation are also recommended by NICE (2010) as usual care for COPD patients, however these costs are omitted from this model on the basis they are assumed to be the same in both strategies.

Table A7

Annual cost of routine healthcare by GOLD stage

Cost of routine healthcare			**Gold Stage 3**		**Gold Stage 4**	
Resource use type	Unit cost	Source	No. of visits	Weighted total cost*	No. of visits	Weighted total cost*
GP visit, 9.22 min standard consultation	£33.19	PSSRU [22]	1.5	£49.79	2	£66.38
Outpatient visit, mean of respiratory medicine outpatient procedures (NCL)	£157	NHS Reference costs, 2018/9 [35]	1	£157	2	£314
Respiratory team visit, 40 min visit from 75% band 6 nurse, 25% band 7 nurse	£70	PSSRU [22]	2	£140	4	£280
Spirometry test	£52	NHS Reference costs (2011)+	2	£104	3	£156
Home oxygen therapy	£17.17 per day	Hertel et al. (2012)+	1.22 days	£20.95	6.08 days	£104.40
Influenza vaccine, 73% of patients receive	£9.87	NHS England (2019)	0.73	£7.21	0.73	£7.21
Annual cost of routine healthcare			£478.95		£927.99	
Monthly cost of routine healthcare			£39.91		£77.33	

+Cost inflated to current value using HCHS inflation indices until 2015, and NHSCII from 2016 onwards, PSSRU [22]

Routine pharmacotherapy

Drug reference costs listed on the NHS Drug Tariff database in 2020 were used to estimate unit costs and are shown in Table A8. As there does not appear to be consistent drug inflation costs during the period (2018-2020) unit costs were not deflated. As the NICE economic model (2018) used to estimate routine healthcare compared the cost of different pharmacological strategies, no typical routine pharmacological treatment strategy is provided. Therefore, annual and monthly costs were calculated by applying the 2020 unit cost to ratios of pack cost to annual cost reported by NICE (2011). Where there was more than one drug in each treatment class, an overall average cost was applied.

In order to obtain usage for each GOLD stage, the proportion of patients on each line of therapy by GOLD stage was obtained from data from a cohort of UK COPD patients in the Birmingham Lung Improvement (BLISS) study in the West Midlands [17]. As all patients were reported to be on an inhaled short-acting β_2-agonist (SABA), the assumptions of clinical experts on the previous model [7] regarding the number of delivery devices in each severity stage were used. Monthly costs for each GOLD stage are reported in Table A9.

Note, we acknowledge there is now a move to triple therapy inhalers (LAMA/LABA/ICS in one – Trelegy or Trimbow. However, at the time of conduct of most included RCTs these were not available. We accept it would reduce the costs of therapy; however model results were not sensitive to cost input parameters.

Table A8

Unit costs of pharmacotherapy

Class	Drug, Dose	Price per pack+	Annual cost adjusted*	Monthly cost (£)
SABA	Salbutamol 100 µg dose dry powder inhaler (Easyhaler Salbutamol)	£3.31	£24.17	£2.01
	Terbutaline 500 µg/ dose dry powder inhaler (Bricanyl)	£8.30	£121.17	£10.10
	SABA average cost			£6.06
ICS	Beclometasone 250 µg / dose inhaler CFC free Clenil Modulite	£16.29	£29.73	£2.48
SAMA	Ipratropium 20 µg/ dose inhaler CFC free	£5.56	£30.56	£2.55
LABA	Salmeterol 25 µg /dose inhaler CFC free	£29.26	£356	£29.67
LAMA	Tiotropium 18 µg inhalation powder capsules (Spiriva)	£33.50	£407.58	£33.97
LABA	Budesonide 200micrograms/dose / Formoterol 6micrograms/dose dry powder inhaler (Symbicort)	£28.00	£340.66	£28.39
And	Budesonide 400micrograms/dose / Formoterol 12micrograms/dose dry powder inhaler (Symbicort Turbohaler)	£28.00	£340.66	£28.39
ICS	Fluticasone propionate 500micrograms/dose / Salmeterol 50micrograms/dose dry powder inhaler (Seretide Accuhaler)	£32.74	£398.34	£33.19
	LABA and ICS average cost			£29.99

ICS, inhaled corticosteroids; LABA, long-acting β2-agonist; LAMA, long-acting muscarinic agonist; SAMA, short-acting muscarinic antagonist.

*Annual costs weighted using the ratio of pack price to annual cost reported in NICE (2011).

+NHS Drug Tariff database, 2020

Table A9

Pharmacotherapy by type, and monthly cost, by GOLD stage

		Proportion on type of pharmacotherapy					
Gold Stage and cost	**Assumed SABA's per month**	**SABA**	**ICS**	**LABA**	**LABA/ICS**	**LAMA**	**SAMA**
Gold Stage 3	2	1.00	0.01	0.05	0.68	0.62	0.04
Gold Stage 4	2.5	1.00	0.05	0.02	0.77	0.65	0.05
Monthly cost GOLD stage 3		£50.42					
Monthly cost GOLD stage 4		£54.71					

Cost of moderate exacerbation

Resource use for moderate exacerbations were based upon assumptions made in the COPD diagnosis and management economic model report accompanying the National Institute for Health and Care Excellent guidance (2018). As such, moderate exacerbations were expected to be usually managed in primary care through GP appointment, with a small proportion expected to visit A&E without admission or receive a number of visits from a respiratory team. A respiratory team was expected to comprise 75% of a band 6 nurse, and 25% a band 7 nurse. Note that cost of nurse time relative to the previous model is higher, as it is now adjusted to reflect patient facing cost [22]. Prescribed additional medication for a moderate exacerbation was assumed to be a course of prednisolone and antibiotics. Overall cost of a moderate exacerbation is shown in Table A10.

Table A10

Cost of a typical moderate exacerbation

Resource use type	% requiring resource	Unit cost	Source	Weighted total cost*
GP visit, 9.22 min standard consultation	60%	£33.19	PSSRU [22]	£19.91
A&E visit without admission, weighted average of non-admitted	30%	£144.38	NHS reference costs (2019) [35]	£43.31
Respiratory team visit -cost per episode (6* 40 min visits *(75% band 6 nurse, 25% band 7).	10%	£420	PSSRU [22]	£42
Prednisolone 5mg tablets (six times a day for 5 days)	100% cohort, 1 per patient	£1.77	NHS Drug Tariff (2019)	£1.77
Amoxicillin 500mg capsules (3 times a day for 5 days)	100% of cohort, 2 per patient	£1.25	NHS Drug Tariff (2019)	£2.50
Prescription costs per consultation		£30.90	PSSRU [22]	£30.90
Estimated cost of moderate exacerbation				**£140.40**

*Weighted total cost, is the unit cost multiplied by % requiring the resource

Cost of severe exacerbation

As per the COPD diagnosis and management economic model report accompanying the National Institute for Health and Care Excellent guidance (2018) severe exacerbations were assumed to be managed in hospital with 70% requiring an ambulance journey to hospital. The cost of an ambulance journey was most recently available in 2015/6 reference costs and inflated using the NHS cost inflation index [22]. For the

hospital stay, the weighted mean was taken of all unit costs for non-elective long-stay for COPD. Previous version of NICE modelling (2010) also suggested that all patients should be followed up after discharge, this is included here, as in the previous model, and was assumed to be 30% by a band 5 community nurse, 30% by a GP, and 40% attending a respiratory outpatient appointment. The estimated cost of a severe exacerbation is shown in Table A11.

Table A11

Cost of a typical severe exacerbation

Resource use type	% requiring resource	Unit cost	Source	Weighted total cost*
Ambulance journey to A&E	70%	£251.92	NHS Reference costs (2015/6)+	£176.34
Hospital stay, mean NEL long-stay, COPD.	100%	£2,026	NHS Reference costs (2018/9) [35]	£2,026
Prednisolone 5mg tablets (six times a day for 5 days)	100% cohort, 1 per patient	£1.77	NHS Drug Tariff (2019)	£1.77
Amoxicillin 500mg capsules (3 times a day for 5 days)	100% of cohort, 2 per patient	£1.25	NHS Drug Tariff (2019)	£2.50
GP visit, 9.22 mins standard consultation	30%	£33.19	PSSRU (2018/9) [22]	£9.96
Outpatient appointment, follow up, mean of respiratory outpatient procedures	40%	£157.16	NHS Reference costs (2018/9) [35]	£62.86
Community nurse follow, 12 mins appointment, band 5	30%	£12.50	PSSRU (2018/9) [22]	£3.75
Estimated cost of severe exacerbation				**£2283.18**

*Weighted total cost, is the unit cost multiplied by % requiring the resource

+ Inflated using Health Service (HS) Index [22]

Cost of non-invasive ventilation

Table A11 shows the costs of providing the typical domiciliary NIV service. Both post-hospital and stable populations faced the same cost of providing NIV for an individual. In the base case, pricing information from suppliers of domestic NIV equipment was used to estimate the one-off equipment cost. Assumptions regarding machine type, and extent of the usage was identified by experts on the team. Four machines were identified as likely to be typical of the equipment to provide this service, Phillips Trilogy 100 and Dreamstation AVAPs, and ResMed Lumis 150 ST-A (iVAPS AE) and ResMed Stellar 100 (iVAPS AE). Each machine was assumed to be supplied 30% with humidification and 70% without, and all bundled with necessary modem and cloud-based remote monitoring facility. The Resmed Lumis 150 was assumed to represent 60% of the likely machine mix, 20% the Dreamstation AVAPs, and 10% each the Trilogy 100 and Stellar 100. It was assumed that each machine last five years and serves two patients on average during that time, the equipment cost is £2939.69 per patient. The cost of the machine was assigned monthly in the model and depreciated over 5 years at 3.5%. One-way sensitivity analysis was used to explore alternate costing assumptions supplied by the clinical expert, of machine cost £39.24 per month.

Table A11

Cost of providing the domiciliary NIV service

Equipment	Cost	Unit Cost source	Resource use Source
Equipment costs			
NIV equipment for domiciliary use	£2939.69	Supplier estimates	Clinician estimates of use of machines and cost estimate from firms
NIV equipment for domiciliary use monthly cost	£48.99		Depreciated over 5 years
Set-up costs			
NIV set-up and assessment month 1	£482.82	National Tariff Payment System 2019/20	Expert opinion
NIV Follow-up in m3: 1 x Consultant led outpatient app + 1 x Blood gas test	£157.16 + £194	NHS reference costs 2018/9	Expert opinion
Annual costs therefore			
2 x blood gas test conducted at routine follow up	2 * £194	NHS reference costs 2018/9	Expert opinion
1 x annual NIV assessment and consumable provision	£650	Estimate	Expert opinion
Monthly costs			
First 3 months	£294.32	Includes equipment and set-up costs	
>3 months	£90.58	Includes equipment and annual monitor and service costs	

Initial set up of the machine, respiratory testing of the patient, and starting on domiciliary NIV was assumed to take place in an NIV clinic and last four hours, and be led by a respiratory team covered by the tariff DZ37A: NIV Supporter Assessment, 19yrs and over, in the National Tariff Payment System workbook 2019/2020 (NHS Improvement, 2019). Between 8 and 12 months, patients on domiciliary NIV

were assumed to have attended a follow-up clinic, where blood gases were checked and NIV pressure settings and/or masks adjusted as required. This service was assumed to be covered by the NHS reference cost for a consultant-led outpatient appointment [35] and National Tariff Payment System [34] tariff for conducting blood gas tests. The set-up and follow-up costs were applied as monthly costs spread evenly over the first 3 months of starting NIV.

From 3 months onwards follow up care included a 6-monthly check of a patient's NIV usage and blood gases, as well annual NIV equipment check and consumable replacement. As all patients are assumed to attend two annual respiratory appointments, the only additional cost was for conducting a blood gas check. Whilst, expert opinion and consultation with suppliers, concluded that costs associated with an annual NIV equipment check, which would be assumed to include device verification, consumable replacement and technical support, were estimated to be £650.

The estimated costs of providing a domiciliary NIV service were £1698.18 in the first year and £1086 in subsequent years. The estimate lies in between estimates of Tuggey et al. (2003) who estimate domiciliary NIV cost £1060 per year in 2003 prices and Clini et al. (2009) who estimated €1920 in 2008 prices.

Additional Refernces

Department of Health (2011). NHS 2010–11 Reference Costs. London: DH; 2011.

Department of Health and Social Care (2020). Electronic Drug Tariff. London: Department of Healt;. 2020 [online] available at http://www.drugtariff.nhsbsa.nhs.uk/#/00787224-DD/DD00787219/Home

Hertel N, Kotchie RW, Samyshkin Y, et al. Cost-effectiveness of available treatment options for patients suffering from severe COPD in the UK: a fully incremental analysis. Int J Chron Obstruct Pulmon Dis 2012;7:183–99. http://dx.doi.org/10.2147/COPD.S29820

NHS England (2019) Update on vaccines for 2019/20 seasonal flu vaccination programme , available online at https://www.england.nhs.uk/wp-content/uploads/2019/01/vaccines-for-19-20-seasonal-flu-vaccination-programme.pdf Accessed 29/06/20

NICE. Chronic Obstructive Pulmonary Disease: Costing report – Implementing NICE Guidance. NICE Clinical Guideline 101. NICE; 2011.

National Institute for Health and Care Excellence. (2018). *Chronic obstructive pulmonary disease in over 16s: diagnosis and management*. Nice guideline [NG115]. Retrieved from https://www.nice.org.uk/guidance/ng115

Tuggey JM, Plant PK, Elliott MW. Domiciliary non-invasive ventilation for recurrent acidotic exacerbations of COPD: an economic analysis. Thorax 2003;58:867–71. http://dx.doi.org/10.1136/thorax.58.10.867

APPENDIX 8 EXPECTED VALUE OF PERFECT INFORMATION

Value of information (VoI) analysis is essentially a quantitative method of assessing the marginal cost and value of further studies, and further translate it into information about the optimal design of additional research [25].

The EVPI uses the quantification of uncertainty from the PSA output, and calculates the net value of eliminating all uncertainty, such that the best treatment option could be selected in each model iteration. In this case, two expected value of perfect information (EVPI) analyses were conducted for both stable and post-hospital COPD populations in the UK. In this study, per person EVPI was estimated using the TreeAge software. Information about the chosen willingness to pay threshold, and units of cost and effect measures, and population expected to benefit were used to obtain the population level EVPI.

Population expected to benefit

In order to calculate the population expected to benefit, the original model used a population prevalence. Table A12 reports the sources used to update estimates of the stable and post-hospital populations. The UK COPD population was estimated using the 2.57% prevalence reported in Rayner et al. (2017). As reported in Haughney et al. (2013) the stable COPD population in either GOLD stage 3 or 4 was assumed to be 30.6% of the total COPD population. The authors did not report the proportion of patients in the 2007 GOLD stage admitted to hospital, but they did report on patients in each of the 2011 GOLD classifications (A-D) admitted to hospital at least once which was used to estimate the post-hospital population. However, because the decision relevance is thought to be ten-years, it is more appropriate to include new cases over that period also. NICE (2018) report that there are 80,443 incidence cases of COPD per year, unfortunately this incidence is not available by GOLD stage. Subsequently, estimates on the proportion of cases in GOLD stage from Haughney et al. were used to estimate the number of incidence cases in GOLD stage 3 and 4, as well as new post-hospitalisations. Accordingly, it was assumed that of the 80,443 incidence cases, 30.6% were stage 3 or 4, and 8.8% were post-hospitalisations.

For the population EVPI and EVPPI estimates, the SAVI software does not incorporate a discount rate, and therefore the estimated number of patients over 10-years was discounted at 3.5%. In order to perform this calculation, the number of incidence cases per year (24,615 and 7079) were summed over nine years and multiplied by a discount factor using the formula, $\sum_{t=1}^{T} \frac{I_t}{(1+r)^t}$. Having estimated the discounted

incidence cases, these were then added to the discounted initial populations to produce a discounted 10-year population of 661,199 for stable end stage COPD, and 190,049 for post-hospital end-stage COPD.

Table A12

Population estimated applied in the Expected Value of Perfect Information (EVPI) analysis

Definition of Population	**Prevalence**	**Population Estimate**	**Source of estimate**
UK		66,436,000	ONS mid-2018 projection
Diagnosed with COPD	2.57% of population	1,707,000	Rayner et al. 2017
COPD Annual Incidence cases	0.19% of adult population	80,443	NICE (2018)
Stable end-stage COPD (GOLD 3&4)	30.6% of COPD population	522,000	Haughney et al. 2013
Stable End-stage COPD annual incidence cases		*24,615*	
Ten-year discounted COPD population		*661,199*	
Post-hospital end-stage COPD	8.8% of COPD population	150,000	Haughney et al. 2013
Post-hospital end-stage COPD incidence cases		*7,079*	
Ten-year post-hospital end-stage COPD population		*190,049*	

Additional References

Haughney J, Gruffydd-Jones K, Roberts J, Lee AJ, Hardwell A, McGarvey L. The distribution of COPD in UK general practice using the new GOLD classification. Eur Respir J 2014;43:993–1002. http://dx.doi.org/10.1183/09031936.00065013

L. Rayner, J. Sherlock, B. Creagh-Brown, J. et al. (2017) The prevalence of COPD in England: An ontological approach to case detection in primary care, Respiratory Medicine, 132 (217-225) https://doi.org/10.1016/j.rmed.2017.10.024

APPENDIX 9 SENSITIVTY ANALYSES: ALTERNATIVE MACHINE COST, LIFESPAN, AND ANNUAL MAINTENANCE COST OF NON-INVASIVE VENTILATION

Post Hospital Population

Varying NIV device cost

In the base case it was assumed the machine would cost £2939. Table A13 shows the impact of differing assumptions. The ICER rises to £14,764/QALY gained even when the device is assumed to cost £5000, but the cost-effectiveness likelihood is still 94%.

Table A13

One-way sensitivity analysis in the post-hospital population varying NIV device cost

NIV device cost	Cost-difference (£)	QALY difference	ICER (£/QALY)	Probability cost-effective+
2000	£4,124	0.424	£9726	100%
2939 (base case)	£4,799	0.424	£11,318	99.9%
4000	£5185	0.424	£12,229	98%
5000	£6,260	0.424	£14,764	94.4%

+ Cost-effective at £20,000/QALY

Abbreviations; ICER Incremental cost-effectiveness ratio; NIV Non-invasive ventilation; QALY (Quality-adjusted life-year)

Alternative machine lifespan

In the base case it was assumed the machine would be used continuously for 5 years, Table A14 shows the impact of differing assumptions. The ICER rises to £14,551/QALY gained even when the device is assumed to last only 3 years, but the cost-effectiveness likelihood is still 95%.

Table A14

One-way sensitivity analysis in the post-hospital population varying NIV device lifespan

NIV device lifespan	Cost-difference (£)	QALY difference	ICER (£/QALY)	Probability cost-effective+
3 years	£6,170	0.424	£14,551	94.7%
4 years	£5325	0.424	£12559	98.5%
5 years (base case)	£4,799	0.424	£11,318	99.9%

+ Cost-effective at £20,000/QALY

Abbreviations; ICER Incremental cost-effectiveness ratio; NIV Non-invasive ventilation; QALY (Quality-adjusted life-year)

Alternative costs of healthcare provision

Varying the cost of NIV set-up and hospital admission for severe exacerbation had little impact upon cost-effectiveness and results are not reported here. The ICER was however more sensitive to changes in the cost of annual NIV service, rising to £14,007/QALY gained where the annual service cost was £1000, however the likely cost-effectiveness was relatively unaffected falling to only 96%, shown in Table A15

Table A15

One-way sensitivity analysis in the post-hospital population varying cost of annual NIV maintenance

NIV annual service cost	Cost-difference (£)	QALY difference	ICER (£/QALY)	Probability cost-effective+
550	£4,453	0.424	£10,502	100%
650 (base case)	£4,799	0.424	£11,318	99.9%
750	£5127	0.424	£12,091	98.9%
850	£5466	0.424	£12,891	98.2%
1000	£5939	0.424	£14,007	96.3%

+ Cost-effective at £20,000/QALY

Abbreviations; ICER Incremental cost-effectiveness ratio; NIV Non-invasive ventilation; QALY (Quality-adjusted life-year)

Stable Population

Varying NIV device cost

In the base case it was assumed the machine would costs £2939. Table A16 shows the impact of differing assumptions. The ICER falls to £23,738/QALY gained when the device is assumed to cost £2000, but the cost-effectiveness likelihood is still only 17%.

Table A16

One-way sensitivity analysis in the stable population varying NIV device cost

NIV device cost	Cost-difference (£)	QALY difference	ICER (£/QALY)	Probability cost-effective+
2000	£7,359	0.310	£23,738	17.3%
2939 (base case)	£8,488	0.310	£27,380	4%
4000	£9,730	0.310	£31,387	0%

+ Cost-effective at £20,000/QALY

Abbreviations; ICER Incremental cost-effectiveness ratio; NIV Non-invasive ventilation; QALY (Quality-adjusted life-year)

Alternative machine lifespan

In the base case it was assumed the machine would be used continuously for 5 years, Table A17 shows the impact of differing assumptions. The ICER rises to £30,161/QALY gained even when the device is assumed to last only 4 years, 0% likely to be cost-effective.

Table A17

One-way sensitivity analysis in the stable population varying NIV device lifespan

NIV device lifespan	Cost-difference (£)	QALY difference	ICER (£/QALY)	Probability cost-effective+
4 years	£9,350	0.310	£30,161	0%
5 years (base case)	£8,488	0.310	£27,380	4%

+ Cost-effective at £20,000/QALY

Abbreviations; ICER Incremental cost-effectiveness ratio; NIV Non-invasive ventilation; QALY (Quality-adjusted life-year)

Alternative costs of healthcare provision

Varying the cost of NIV set-up and hospital admission for severe exacerbation had little impact upon cost-effectiveness and results are not reported here. The ICER was however more sensitive to changes in the cost of annual NIV service, falling to £25,577/QALY gained where the annual service cost was £550, however the likely cost-effectiveness was relatively unaffected rising to only 8%, shown in Table A18

Table A18

One-way sensitivity analysis in the stable population varying cost of annual NIV maintenance

NIV annual service cost	Cost-difference (£)	QALY difference	ICER (£/QALY)	Probability cost-effective+
550	£7,929	0.310	£25,577	8%
650 (base case)	£8,488	0.310	£27,380	4%
750	£9,065	0.310	£29,241	1%

+ Cost-effective at £20,000/QALY

Abbreviations; ICER Incremental cost-effectiveness ratio; NIV Non-invasive ventilation; QALY (Quality-adjusted life-year)

APPENDIX 10 SUBGROUP ANALYSES

Table A19 Disease severity, sex and age sub-groups post-hospital population

Subgroup	Cost-difference (£)	QALY difference	ICER (£/QALY)	Probability cost-effective+
Base case	+£4,799	0.424	£11,318	99.9%
All GOLD stage 3	+£4,719	0.433	£10,898	100%
All GOLD stage 4	+£4,857	0.416	£11,678	99%
All male	+£4,749	0.430	£11,044	99.5%
All female	+£4,827	0.417	£11,575	99.3%
55 start age	+£4,788	0.426	£11,239	99.5%
65 start age	+£4,784	0.426	£11,230	99.5%

+ Cost-effective at £20,000/QALY

Abbreviations; ICER Incremental cost-effectiveness ratio; NIV Non-invasive ventilation; QALY (Quality-adjusted life-year)

Table A20 Disease severity, sex and age sub-groups stable population

Subgroup	Cost-difference (£)	QALY difference	ICER (£/QALY)	Probability cost-effective+
Base case	+£8,488	+0.310	£27,380	4%
All GOLD stage 3	+£9,311	+0.257	£36,230	0%
All GOLD stage 4	+£7,671	+0.363	£21,132	43%
All male	+£8,337	+0.305	£27,334	4%
All female	+£8,661	+0.312	£27,750	3%
55 start age	+£9,359	+0.328	£28,533	4%
75 start age	+£7,658	+0.269	£28,468	3%

+ Cost-effective at £20,000/QALY

Abbreviations; ICER Incremental cost-effectiveness ratio; NIV Non-invasive ventilation; QALY (Quality-adjusted life-year)