

## Appendix S1:

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## **Appendix S2: Methods**

### **Economic evaluation**

This was a model-based cost-effectiveness analysis (CEA) that used published data, clinical data from the PENGUIN pilot study and a cost survey conducted to estimate the perioperative costs of oxygen

and SSI treatment among abdominal surgery patients. Separate models were built for each of the countries in the study because unit costs are different across countries. Clinical data were collected from PENGUIN pilot study in India and South Africa (Table S1). The evaluation assessed the costs and outcomes of high fraction of inspired oxygen (FiO<sub>2</sub>) compared to low FiO<sub>2</sub>. All the costs were reported in 2020 US dollars and outcomes were measured as SSI where SSI was defined as an infection of the only skin and subcutaneous tissue of the incision with either purulent drainage, organisms, fever, pain, swelling, heat, clinical or radiology diagnosis or the wound opened spontaneously within 30 days of surgery<sup>13</sup>.

Table S1: Hospitals from which PENGUIN pilot study clinical data were sourced

<b>Hospital name</b>	<b>Country</b>	<b>Hospital type</b>
Christian Medical Hospital, Ludhiana	India	Teaching hospital
Tata Memorial, Kolkata	India	Cancer hospital and research Centre
India Institute of Medical Sciences, Rishkesh	India	Teaching hospital
All India Institute of Medical Sciences, Bhubaneswar	India	Teaching hospital
Christian Medical College, Vellore	India	Teaching hospital
All India Institute of Medical Sciences, Jodhpur	India	Teaching hospital
Christian Hospital Chinchpada	India	General hospital
Government Medical College and Rajindra Hospital Patiala	India	Teaching hospital
Homi Bhaba Cancer Hospital Sangur	India	Cancer hospital
Government Medical College & Hospital Chandigarh	India	Teaching hospital
Amrita institute Kochi	India	Teaching hospital
Tata Memorial Hospital Mumbai	India	Teaching hospital
Groote Schuur Hospital	South Africa	Teaching hospital

Data on SSI incidence were collected from the PENGUIN pilot study questionnaire. The questionnaire was administered by a trained blinded assessor who asked standardised questions to establish whether the patient had an SSI.

Table S2: Unbundled data sourced from the PENGUIN Pilot study

<b>Variable</b>	<b>No. of patients with the event</b>	<b>Total sample</b>	<b>Missing outcome</b>
In-patient SSI	49	585	-
Unresolved in-patient SSI	20	38	11
Re-intervention following in-patient SSI	10	20	-
Post-discharge SSI*	8	444	92
Unresolved post-discharge SSI**	1	8	-
Post discharge re-intervention***	1	436	-

Sourced from unbundled/combined data of 585 high and low FiO<sub>2</sub> patients (558 from India and 27 from South Africa) participating in the PENGUIN pilot study. Post-discharge SSI\* stands for SSI occurring after the patient was discharged from the hospital. Unresolved post-discharge SSI\*\* stands for SSI that occurred after hospital discharge and did not resolve. Post discharge re-intervention\*\*\* stands for unresolved post discharge SSI that needed re-intervention.

### **Cost estimation**

#### *Sources of costs*

Direct healthcare resource use data were sourced from tertiary and teaching hospitals in Nigeria, India and South Africa that are part of Global Surgery Unit. Responses were received from nine of the 26 teaching and federal medical centres/tertiary hospitals that are part of the Global Surgery Unit in Nigeria. Responses were received from three teaching hospitals out of 21 hospitals that are part of the Global Surgery Unit in India and two tertiary hospitals in South Africa. Clinicians and hub managers from the hospitals completed an online questionnaire designed to capture perioperative and SSI treatment resource usage during abdominal surgery. The questionnaire in this Appendix was piloted in Nigeria before being iteratively improved and disseminated to the other participating centres and countries.

Table S3: Resource use and unit cost questionnaire (Part A: to be completed by an anaesthetist)

Oxygen delivery costs and usage	
<b>Hospital Name</b>	_____
Resource Use	
Which of the following gases do you administer during surgery? <i>(Tick all that apply)</i>	<input type="checkbox"/> Oxygen <input type="checkbox"/> Medical air <input type="checkbox"/> Nitrous Oxide
Breathing system used? <i>(Tick all that apply)</i>	<input type="checkbox"/> Circle system <input type="checkbox"/> Other circuits
Oxygen supply for anaesthesia <i>(tick all that apply)</i>	<input type="checkbox"/> Oxygen concentrator in operating room <input type="checkbox"/> Oxygen cylinder <input type="checkbox"/> Pipeline from vacuum insulated evaporator (VIE) <input type="checkbox"/> Pipeline from oxygen cylinder manifold
Method of administering oxygen/ventilation	<input type="checkbox"/> Nasal prong <input type="checkbox"/> Non breathing face mask <input type="checkbox"/> Laryngeal mask airway (LMA) <input type="checkbox"/> Endotracheal tube (ETT)
On average, how long does laparotomy procedure take? <i>(minutes)</i>	Indicate time _____ min
For high FiO <sub>2</sub> , what is the average fresh gas flow rate used during surgery?	Fresh gas flow rate _____ (L/min)
Mixture to lower FiO <sub>2</sub> ? <i>(Tick all that apply)</i>	<input type="checkbox"/> Cylinder nitrous oxide <input type="checkbox"/> Pipeline nitrous oxide <input type="checkbox"/> Cylinder medical air
For low FiO <sub>2</sub> , what is the average fresh gas flow rate used during surgery?	Fresh gas flow rate _____ (L/min)

What are the average sizes of the cylinders for each of the gas delivery methods?

- Oxygen concentrator \_\_\_\_\_ (litres)
- Oxygen cylinder \_\_\_\_\_ (litres)
- (Pipeline)/ VIE \_\_\_\_\_ (litres)
- (Pipeline)/ manifold cylinders \_\_\_\_\_ (litres)

**Form completed by**

Full print name \_\_\_\_\_

Date form completed	D	D	M	M	Y	Y	Y	Y
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Table S4: Resource use and unit cost questionnaire (Part B: to be completed by Hub Manager)

Unit costs	
How much does it cost to refill oxygen concentrator? ( <i>Indicate zero if there is no cost</i> )	Indicate cost here _____
How much does it cost to refill the theatre oxygen cylinder?	Indicate cost here _____
How much does it cost to refill the VIE?	Indicate cost here _____
How much does it cost to refill the manifold cylinder?	Indicate cost here _____
What is the average cost of a surgical ward patient (per day)?	Indicate cost here _____
What is the average cost of disposables for in-patient wound dressing change?	Indicate cost here _____
What is the average cost of disposables for out-patient wound dressing change?	Indicate cost here _____
What is the average health worker cost for out-patient wound review (cost of nurse/doctor/community health worker)?	Indicate cost here _____
On average, how many out-patient wound reviews are made per patient?	Indicate number here _____
What is the most common empirical antibiotic used for treating surgical site infections?	Indicate antibiotic name here _____
On average, how much does the empirical antibiotic cost (overall treatment cost)?	Indicate cost here _____
What is the most frequent used post-operative painkiller?	Indicate painkiller name here _____
How much does the most frequent post-operative painkiller cost (overall treatment cost)?	Indicate cost here _____

What is the cost of wound swab cost including analysis (entire treatment cost per patient)?	Indicate cost here _____							
What is the average cost of re-intervention/reoperation for wound complication?	Indicate cost here _____							
<b>Form completed by</b>								
Full print name	_____							
Date form completed	D	D	M	M	Y	Y	Y	Y

To estimate the amount of FiO<sub>2</sub> gas utilised per patient, the fresh gas flow rate was multiplied by the duration of abdominal surgery and FiO<sub>2</sub> concentration rate. The cost of refilling manifold or cylinder was divided by the size of the manifold or cylinder to estimate the cost of the gas per litre. In the base-case, the median values of the concentration rates for both arms were used (90% and 28% FiO<sub>2</sub> concentration rates for high and low FiO<sub>2</sub> respectively). Then the amount of gas used the patient was multiplied with the cost of gas per litre.

Table S5: Length of hospital stay (LoS)

Variable	Mean LoS in	Median LoS in	Distribution	Source
	days (SD)	days (IQR)		
SSI	16 (6)	16 (11)	Fixed	PENGUIN pilot trial <sup>9</sup>
No SSI	8 (4)	7 (5)	Fixed	PENGUIN pilot trial <sup>9</sup>
Re-intervention	18 (17)	15 (21)	Fixed	GlobalSurg Collaborative <sup>16</sup>

SD stands for standard deviation. The LoS were sourced from clinical trials data, and it was assumed that LoS are identical between the two arms in the current model.

Table S6: Resource use and unit costs: Nigeria

Resource use	Frequency	Time/cost (\$):	Cost	Distribution	Source
		mean (SD)	(Naira)		
Laparotomy duration: time, minute	1	120.00	N/A	Fixed	Survey
Reintervention	1	133.43 (76.92)	47,875.00	Gamma	Survey
Swab including analysis	1	16.65 (32.82)	5938.00	Gamma	Survey
Health worker outpatient wound review	1	18.12 (12.15)	6500.00	Gamma	Survey
Postoperative painkiller	1	11.43 (13.32)	4100.00	Gamma	Survey
Postoperative antibiotic	1	40.51 (53.40)	14,534.00	Gamma	Survey
Outpatient wound dressing change	1	3.38 (2.65)	1214.00	Gamma	Survey
In-patient wound dressing change	1	3.38 (2.59)	1213.00	Gamma	Survey
Surgical bed day	1	12.46 (18.30)	4471.00	Gamma	Survey
Discharge medications	1	8.93 (7.97)	11,600.00	Gamma	FALCON <sup>19</sup>
Healthcare revisit cost	1	26.08 (23.28)	N/A	Gamma	Imputed*
Purchased medications	1	23.05 (0.05)	N/A	Gamma	Imputed*
Oxygen cylinder refill per litre	N/A	0.01 (0.03)	5.19	Gamma	Survey
Manifold cylinder refill per litre	N/A	0.01 (0.02)	2.74	Gamma	Survey
Low FiO <sub>2</sub>	1	0.77 (2.54)	276.49	Gamma	Survey
High FiO <sub>2</sub>	1	9.37 (28.82)	3361.00	Gamma	Survey

Column 3 reports all resource use values in costs apart from duration of laparotomy which is reported in time (minutes). N/A means not applicable. SD means standard deviation. Survey refers to the survey in Appendix S2 above. \$ stands for 2020 US dollars while Naira stands for Nigerian Naira. \*Imputed refers to values imputed using the market-basket approach.

Table S7: Resource use and unit costs: India

Resource use	Frequency	Time/cost (\$): mean (SD)	Cost (Rupee)	Distribution	Source
Laparotomy duration: time, minute	1	86.67	N/A	Fixed	Survey
Reintervention	1	142.91 (192.09)	10,590.00	Gamma	Survey
Swab including analysis	1	9.67 (9.45)	716.67	Gamma	Survey
Health worker outpatient wound review	2	1.42 (1.81)	105.00	Gamma	Survey
Postoperative painkiller	1	5.4 (2.94)	400.00	Gamma	Survey
Postoperative antibiotic	1	37.34 (61.20)	2766.67	Gamma	Survey
Outpatient wound dressing change	1	1.8 (1.4)	133.33	Gamma	Survey
In-patient wound dressing change	1	3.26 (0.01)	241.67	Gamma	Survey
Surgical bed day	1	8.93 (9.73)	661.67	Gamma	Survey
Discharge medications	1	7.85 (9.26)	582.00	Gamma	PENGUIN pilot <sup>9</sup>
Healthcare revisit cost	1	35.01 (49.59)	2594.00	Gamma	PENGUIN pilot <sup>9</sup>
Purchased medications	1	28.62 (49.11)	2121.00	Gamma	PENGUIN pilot <sup>9</sup>
Oxygen cylinder refill per litre	N/A	N/A	N/A	Gamma	Survey
Manifold cylinder refill per litre	N/A	0.05 (0.05)	1.17	Gamma	Survey
Low FiO <sub>2</sub>	1	0.44 (2.54)	36.85	Gamma	Survey
High FiO <sub>2</sub>	1	4.77 (0.39)	353.36	Gamma	Survey

Column 3 reports all resource use values in costs apart from duration of laparotomy which is reported in time (minutes). N/A means not applicable. SD means standard deviation. Survey refers to the survey in Appendix S2. \$ stands for 2020 US dollars while Rupee stands for Indian Rupee

Table S8: Resource use and unit costs: South Africa

Resource use	Frequency	Time/cost (\$): mean (SD)	Cost (Rand)	Distribution	Source
Laparotomy duration: time, min	1	143.00	N/A	Fixed	Survey
Reintervention	1	932.14 (233.03)	15343.00	Gamma	Survey
Swab including analysis	1	81.00 (4.92)	81.00	Gamma	Survey
Health worker outpatient wound review	1	23.69 (5.92)	390.00	Gamma	Survey
Postoperative painkiller	1	6.68 (1.67)	110.00	Gamma	Survey
Postoperative antibiotic	1	31.03 (7.76)	510.72	Gamma	Survey
Outpatient wound dressing change	1	0.14 (1.00)	2.27	Gamma	Survey
In-patient wound dressing change	1	0.14 (0.03)	2.27	Gamma	Survey
Surgical bed day	1	61.54 (15.39)	1013.00	Gamma	Survey
Discharge medications	-	-	-	Gamma	Survey
Healthcare revisit cost	1	12.36 (21.82)	197.78	Gamma	PENGUIN pilot <sup>9</sup>
Purchased medications	1	13.56 (0.05)	0.10	Gamma	PENGUIN pilot <sup>9</sup>
Oxygen cylinder refill per litre	N/A	-	-	Gamma	PENGUIN pilot <sup>9</sup>
Manifold cylinder refill per litre	N/A	0.001 (0.001)	0.01	Gamma	Survey
Low FiO <sub>2</sub>	1	1.33 (0.33)	21.27	Gamma	Survey
High FiO <sub>2</sub>	1	4.27 (1.07)	68.38	Gamma	Survey

Column 3 reports all resource use values costs apart from duration of laparotomy which is reported in time (min). N/A means not applicable. SD means standard deviation. Survey refers to the survey in Appendix S2. Rands stand for South African Rands while \$ stands for 2020 US dollars.

Table S9: Median costs calculated from data used in Table S6-8

	<b>Nigeria</b>	<b>India</b>	<b>South Africa</b>
<b>Resource use</b>	<b>Median costs, \$ (IQR)</b>	<b>Median costs, \$ (IQR)</b>	<b>Median costs, \$ (IQR)</b>
Re-intervention	94.76 (101.03)	67.48 (180.63)	-
Swab including analysis	4.88 (4.53)	6.75 (9.11)	-
Health worker cost for outpatient wound review	20.90 (16.72)	1.42 (1.28)	-
Postoperative painkiller	8.36 (11.50)	4.05 (2.70)	-
Postoperative antibiotic	27.87 (22.30)	4.05 (53.98)	-
Outpatient wound dressing change	2.79 (2.79)	1.35 (1.35)	-
In-patient wound dressing change	2.79 (3.14)	2.70 (3.21)	-
Surgical bed day	8.36 (20.90)	6.75 (9.55)	-
Discharge medications	N/A*	5.00 (4.00)	-
Healthcare revisit cost	N/A*	11.00 (32.00)	15.00 (3.00)
Purchased medications	N/A*	13.00 (28.00)	11.00 (12.00)
Oxygen cylinder refill per litre	0.01 (0.73)	N/A	-
Manifold cylinder refill per litre	0.01 (4.81)	0.02 (0.01)	-
Low FiO <sub>2</sub>	0.49 (0.21)	0.53 (0.38)	-
High FiO <sub>2</sub>	4.13 (8.68)	5.85 (4.20)	-

IQR stands for interquartile range. Most South African data were from published average costs so we could not estimate the median. \*Could not estimate the median values as the costs were inputted.

### Market-basket cost imputation approach

The market-basket approach was used to estimate the cost of healthcare revisit in Nigeria.<sup>18</sup> Cost of nine items (resource use) available in Nigeria, India, and South Africa were collected from a survey as part of this study: Re-intervention, swab (including analysis), health worker for outpatient wound review, postoperative painkiller, empirical antibiotic, outpatient wound dressing change, in-patient wound dressing change, low FiO<sub>2</sub> and high FiO<sub>2</sub>. We collected the unit cost of the nine items in the three countries, multiplied each resource use by the associated frequency of use and summed the cost of the nine items to calculate the total cost of the basket in each country. Then, we divided the cost of the basket in Nigeria by the cost of the basket in India and South Africa to obtain the Nigeria-India Index and Nigeria-South Africa Index respectively.

The healthcare revisit cost in India and South Africa sourced from the PENGUIN pilot study were multiplied by the Nigeria-India index and Nigeria-South Africa index respectively. The results from

multiplying the Indian and South African healthcare revisit costs and the associated index were added and then divided by 2 to get a weighted average of healthcare revisit cost in Nigeria.

Table S10: Hospitals that provided healthcare resource use data

<b>Hospital name</b>	<b>Country</b>	<b>Type</b>
Christian Medical Hospital, Ludhiana	India	Teaching hospital
All India Institute of Medical Sciences, Jodhpur	India	Teaching hospital
Government Medical College and Rajindra Hospital Patiala	India	Teaching hospital
University Teaching Hospital Shika Zaria Nigeria	Nigeria	Teaching hospital
Federal medical centre Birnin, Kebbi Nigeria	Nigeria	Tertiary hospital
Aminu Kano Teaching Hospital, Kano	Nigeria	Teaching hospital
Federal Medical Centre Gusau, Zamfara	Nigeria	Tertiary hospital
Barau Dikko University Teaching Hospital, Kaduna	Nigeria	Teaching hospital
Federal Medical Centre Katsina	Nigeria	Teaching hospital
Obafemi Awolowo University Teaching Hospital, Ile-Ife, Osun state	Nigeria	Teaching hospital
Usmanu Danfodiyo University Teaching Hospital (UDUTH SOKOTO)	Nigeria	Teaching hospital
University College Hospital Ibadan	Nigeria	Teaching hospital
Groote Schuur Hospital	South Africa	Teaching hospital
University of Western Cape	South Africa	Teaching hospital

## **Sensitivity analysis**

Sensitivity analysis was conducted to test sensitivity of the model results to changes in model parameters inputs. Deterministic sensitivity analysis (DSA) was conducted to test sensitivity of the results to changes in individual model input parameters whilst probabilistic sensitivity analysis (PSA) was conducted to test the robustness of the results to simultaneous changes of multiple parameters in the model

### *Deterministic sensitivity analysis*

In the DSA, where necessary the ICER was calculated to show the incremental cost associated with reducing SSIs by one percentage point. Where the results showed dominance of either high or low FiO<sub>2</sub>, (being cheaper and more effective) the ICER was not calculated as dominance means cost-effective in favour of the arm that is cheaper and more effective.<sup>11</sup>

The following DSAs were conducted:

- I. Considered inclusion of travel costs to revisit the healthcare facilities (direct non-healthcare costs, defined as other costs beyond the healthcare costs that were incurred to access healthcare).<sup>11</sup> In this study the non-direct healthcare costs included costs for purchased medication and travel.
- II. High FiO<sub>2</sub> concentration rate was varied from 90% to 80% and 100% while low FiO<sub>2</sub> was varied from 28% to 21% and 35%.
- III. Considered the lower and upper bounds associated with SSI and reintervention rates, and SSI LoS (Table S11).
- IV. In the high FiO<sub>2</sub> arm, threshold analysis was conducted to identify values of SSI LoS and FiO<sub>2</sub> cost at which changes in the input parameters would change the base case results.

Table S11: Parameter values used in deterministic sensitivity analysis

<b>Parameter</b>	<b>Base value</b>	<b>DSA value</b>
Costs included	Non-direct healthcare costs not included	Non-direct healthcare costs included
RRR	12.50%	5.20% 19.70%
<b>Low FiO<sub>2</sub></b>		
FiO <sub>2</sub> concentration	28%	21.00% 35.00%
SSI probability	0.08	0.06 0.11
Reintervention* probability	0.50	0.28 0.72
SSI LoS	15.61	9.56 21.66
<b>High FiO<sub>2</sub></b>		
FiO <sub>2</sub> concentration	90.00%	80.00% 100.00%
SSI probability	0.07	0.05 0.09
Reintervention* probability	0.50	0.28 0.72
SSI LoS	15.61	9.56 21.66

DSA value means the value that was used in the DSA in place of the base case input parameter value. RRR means relative risk reduction. Re-intervention\* stands for re-intervention following in-patient SSI. SSI LoS stands for length of hospital stay for patients who had an SSI.

### *Probabilistic sensitivity analysis (PSA)*

Joint uncertainty of multiple changes to the probabilities and costs were assessed using the PSA that was run for 10,000 Monte-Carlo simulations based on the distributions assigned to the parameters. Random values of the costs and probabilities were drawn based on the distributions assigned to the parameters for the 10,000 simulations. The Gamma distribution is restricted to a range from zero to positive infinity and can be used to characterize uncertainty of costs data.<sup>10</sup> Beta distribution can be used for proportions because it is restricted to a range from 0 to 1.<sup>10</sup> As such, costs were assigned a Gamma distribution while probabilities were assigned a Beta distribution.

### *Cost-effectiveness acceptability curves*

Uncertainty of the base case results across a range of CETs were assessed using the cost-effectiveness acceptability curves (CEACs).<sup>10</sup> The net monetary benefit (NMB) approach was used to calculate the probability of high and low FiO<sub>2</sub> being cost-effective.<sup>11</sup> Because of lack of specific thresholds for natural units as a measure of outcomes, GDP based CETs were used in all the three countries across a range of CETs. Using the thresholds, an intervention is considered cost-effective if it is less than three times a country's GDP per capita.<sup>29</sup>

The net monetary benefit was calculated as follows:

Net monetary benefit = CET \* difference in outcomes – difference in costs.

## **Appendix S3: Results**

### **Base case results**

The base case results based on the available evidence on the clinical effectiveness and the minimum important clinical difference (MID) of 12.5% shows that high FiO<sub>2</sub> is cost-effective as it is cheaper and more effective at reducing SSI compared to low FiO<sub>2</sub>.

### **Deterministic sensitivity analysis**

#### *Nigeria*

When the purchased medication and travel costs were included (DSA I), high FiO<sub>2</sub> reduced costs by \$6.45 (from \$6.18 in the base case) and SSIs by 1.05 percentage points. The results were sensitive to changes that were made in favour of low FiO<sub>2</sub>. For example, when the SSI probability in the low FiO<sub>2</sub> arm was reduced from 0.08 to 0.06, high FiO<sub>2</sub> was dominated as it increased costs by \$25.50 and increased SSIs by 1.20 percentage points (DSA III). The threshold analysis showed that the LoS of patients that had in-patient SSI in the intervention arm would have to increase from 15.61 to 22.38 days or the cost of high FiO<sub>2</sub> would have to increase from \$9.37 to \$10.02 for high FiO<sub>2</sub> not to be cost-effective (DSA IV). The rest of the results have been presented in Table S12.

Table S12: Deterministic sensitivity results (Nigeria)

Parameter	Base case value	DSA value	Difference in costs	Difference in outcomes	ICER/Comment
Base case			-\$6.18	1.05%	High FiO <sub>2</sub> dominates
Non-direct healthcare costs included			-\$6.45	1.05%	High FiO <sub>2</sub> dominates
RRR	12.50%	5.20%	\$2.45	0.44%	\$562.46
		19.70%	-\$14.69	1.65%	High FiO <sub>2</sub> dominates
<b>Low FiO<sub>2</sub></b>					
FiO <sub>2</sub>	28.00%	21.00%	-\$5.99	1.05%	High FiO <sub>2</sub> dominates
		35.00%	-\$6.37	1.05%	High FiO <sub>2</sub> dominates
SSI	0.08	0.06	\$25.50	-1.20%	Low FiO <sub>2</sub> dominates
		0.11	-\$37.86	3.29%	High FiO <sub>2</sub> dominates
Reintervention*	0.50	0.28	\$37.90	1.05%	\$3,620.18
		0.72	-\$50.26	1.05%	High FiO <sub>2</sub> dominates
SSI LoS	15.61	9.56	\$0.14	1.05%	\$12.92
		21.66	-\$12.49	1.05%	High FiO <sub>2</sub> dominates
<b>High FiO<sub>2</sub></b>					
FiO <sub>2</sub> concentration	0.90	0.80	-\$7.22	1.05%	High FiO <sub>2</sub> dominates
		1.00	-\$5.14	1.05%	High FiO <sub>2</sub> dominates
SSI	0.07	0.05	-\$35.98	3.16%	High FiO <sub>2</sub> dominates
		0.09	\$23.62	-1.06%	Low FiO <sub>2</sub> dominates
Reintervention*	0.50	0.28	-\$44.75	1.05%	High FiO <sub>2</sub> dominates
		0.72	\$32.39	1.05%	\$3,093.88
SSI LoS	15.61	9.56	-\$11.70	1.05%	High FiO <sub>2</sub> dominates
		21.66	-\$0.65	1.05%	High FiO <sub>2</sub> dominates
<b>Threshold analysis</b>					
SSI LoS (days)	15.61	22.38	\$0.00	1.05%	\$0.00
High FiO <sub>2</sub> cost	\$9.37	\$10.02	\$0.00	1.05%	\$0.00

Re-intervention\* stands for re-intervention following in-patient SSI. ICER stands for incremental cost-effectiveness ratio. RRR stands for relative risk reduction. SSI LoS stands for length of hospital stay for patients who had an SSI.

### *India*

The results were similar to Nigeria as they were sensitive to changes that were made in favour of low  $\text{FiO}_2$  (Table S13). For example, when the probability of getting SSI was increased from 0.07 to 0.09 in the high  $\text{FiO}_2$  arm, high  $\text{FiO}_2$  was dominated as it increased costs by \$19.67 and increased SSIs by 1.06 percentage points (DSA IV).

Table S13: Deterministic sensitivity results (India)

Parameter	Base case value	DSA Value	Difference in costs	Difference in outcomes	ICER/Comment
Base case			-\$10.75	1.05%	High FiO <sub>2</sub> dominates
Non-healthcare costs included			-\$11.22	1.05%	High FiO <sub>2</sub> dominates
RRR	12.50%	5.20%	-\$1.94	0.44%	High FiO <sub>2</sub> dominates
		19.70%	-\$19.44	1.65%	High FiO <sub>2</sub> dominates
<b>Low FiO<sub>2</sub></b>					
FiO <sub>2</sub>	28.00%	21.00%	-\$10.64	1.05%	High FiO <sub>2</sub> dominates
		35.00%	-\$10.86	1.05%	High FiO <sub>2</sub> dominates
SSI	0.08	0.06	\$21.59	-1.20%	Low FiO <sub>2</sub> dominates
		0.11	-\$43.09	3.29%	High FiO <sub>2</sub> dominates
Reintervention*	0.50	0.28	\$36.47	1.05%	\$3,483.03
		0.72	-\$57.97	1.05%	High FiO <sub>2</sub> dominates
SSI LoS	15.61	9.56	-\$6.22	1.05%	High FiO <sub>2</sub> dominates
		21.66	-\$15.27	1.05%	High FiO <sub>2</sub> dominates
<b>High FiO<sub>2</sub></b>					
FiO <sub>2</sub> concentration	0.90	0.80	-\$11.28	1.05%	High FiO <sub>2</sub> dominates
		1.00	-\$10.22	1.05%	High FiO <sub>2</sub> dominates
SSI	0.07	0.05	-\$41.17	3.16%	High FiO <sub>2</sub> dominates
		0.09	\$19.67	-1.06%	Low FiO <sub>2</sub> dominates
Reintervention*	0.50	0.28	-\$52.06	1.05%	High FiO <sub>2</sub> dominates
		0.72	\$30.57	1.05%	\$2,919.31
SSI LoS	15.61	9.56	-\$14.71	1.05%	High FiO <sub>2</sub> dominates
		21.66	-\$6.79	1.05%	High FiO <sub>2</sub> dominates
<b>Threshold analysis</b>					
SSI LoS (days)	15.61	32.04	\$0.00	1.05%	\$0.00
FiO <sub>2</sub> cost	\$4.77	\$15.52	\$0.00	1.05%	\$0.00

Re-intervention\* stands for re-intervention following in-patient SSI. ICER stands for incremental cost-effectiveness ratio. RRR stands for relative risk reduction. SSI LoS stands for length of hospital stay for patients who had an SSI.

### *South Africa*

The results were similar to Nigeria and India as there were sensitive to changes in probabilities that were in favour of low FiO<sub>2</sub>. For example, high FiO<sub>2</sub> was dominated when the probability of getting SSI in the intervention arm was increased from 0.07 to 0.09 as high FiO<sub>2</sub> increased cost by \$95.03 and SSIs by 1.06 percentage points (Table S14).

Table S14: Deterministic sensitivity results (South Africa)

<b>Parameter</b>	<b>Base case value</b>	<b>DSA value</b>	<b>Difference in costs</b>	<b>Difference in outcomes</b>	<b>ICER/Comment</b>
Base case			-\$93.31	1.05%	High FiO <sub>2</sub> dominates
Non-direct healthcare costs included			-\$93.37	1.05%	High FiO <sub>2</sub> dominates
RRR	12.50%	5.20%	-\$38.78	0.44%	High FiO <sub>2</sub> dominates
		19.70%	-\$147.09	1.65%	High FiO <sub>2</sub> dominates
<b>Low FiO<sub>2</sub></b>					
FiO <sub>2</sub>	28.00%	21.00%	-\$93.30	1.05%	High FiO <sub>2</sub> dominates
		35.00%	-\$93.31	1.05%	High FiO <sub>2</sub> dominates
SSI	0.08	0.06	\$106.89	-1.20%	Low FiO <sub>2</sub> dominates
		0.11	-\$293.51	3.29%	High FiO <sub>2</sub> dominates
Reintervention*	0.50	0.28	\$214.66	1.05%	\$20,502.30
		0.72	-\$401.27	1.05%	High FiO <sub>2</sub> dominates
SSI LoS	15.61	9.56	-\$62.12	1.05%	High FiO <sub>2</sub> dominates
		21.66	-\$124.49	1.05%	High FiO <sub>2</sub> dominates
<b>High FiO<sub>2</sub></b>					
FiO <sub>2</sub> concentration	0.90	0.80	-\$93.32	1.05%	High FiO <sub>2</sub> dominates
		1.00	-\$93.30	1.05%	High FiO <sub>2</sub> dominates
SSI	0.07	0.05	-\$281.64	3.16%	High FiO <sub>2</sub> dominates
		0.09	\$95.03	-1.06%	Low FiO <sub>2</sub> dominates
Reintervention*	0.50	0.28	-\$362.78	1.05%	High FiO <sub>2</sub> dominates
		0.72	\$176.16	1.05%	\$16,825.55
SSI LoS	15.61	9.56	-\$120.59	1.05%	High FiO <sub>2</sub> dominates
		21.66	-\$66.02	1.05%	High FiO <sub>2</sub> dominates
<b>Threshold analysis</b>					
SSI LoS (days)	15.61	36.30	\$0.00	1.05%	\$0.00
High FiO <sub>2</sub> cost	\$0.09	\$93.40	\$0.00	1.05%	\$0.00

Re-intervention\* stands for re-intervention following in-patient SSI. ICER stands for incremental cost-effectiveness ratio. RRR stands for relative risk reduction. SSI LoS stands for length of hospital stay for patients who had an SSI.