Supplementary Table 1: Essential treatments prescribed at admission that were included as predictors

Variable name	Description	Definition	
		Yes	No*
Intravenous antibiotics	Penicillin AND gentamicin are first line antibiotics prescribed together for possible severe bacterial infection.	Prescribed	Not prescribed
Intravenous fluids	Any prescription of an infusion of intravenous fluid e.g., 10% Dextrose	Prescribed	Not prescribed
Enteral feeds	Expressed breast milk or formula fed through nasogastric tube or cup	Prescribed	Not prescribed
Oxygen	Supplemental oxygen provided by any method e.g., nasal cannula	Prescribed	Not prescribed
Phenobarbital	Prescription of phenobarbital	Prescribed	Not prescribed

*****Reference category in the model

Supplementary Table 2: Symptoms and signs of severe illness considered as candidate predictors

Variable name	Description‡	Definition	
		Yes	No*
Difficulty feeding	Symptom: reported history of difficulty feeding	Present	Absent
Convulsions	Symptom: reported episode(s) of convulsions	Present	Absent
Central cyanosis	Sign: bluish or greyish discolouration of the tongue	Present	Absent
Severe Indrawing	Sign: severe (deep) lower chest indrawing	Present	Absent
Floppy/inability to suck	Sign: measure of altered consciousness in young infants (age 0-59 days)	Present	Absent

*****Reference category in the model. Documented that the patient did not have the symptom or sign present

‡Adapted from Opiyo N, English M. What clinical signs best identify severe illness in young infants aged 0-59 days in developing countries? A systematic review. Archives of Disease in Childhood. 2011;96(11):1052-9.

Supplementary Table 3: Distribution of predictors for patients included in the SENSS model derivation, updating and external validation

		Derivation (N = 5427)	Temporal Validation (N = 1627)	Model Updating* (N = 8848)	External Validation (N = 53909)
Predictor	**Levels**	**n (%)**	**n (%)**	**n (%)**	**n (%)**
Male	Yes	2937 (54.12)	961 (59.07)	4963 (56.09)	29384 (54.51)
	Missing	13 (0.24)	2 (0.12)	27 (0.31)	642 (1.19)
Birth weight	1000 grams & below (ELBW)	32 (0.59)	10 (0.61)	104 (1.18)	1243 (2.31)
	1001 - 1499 grams (VLBW)	136 (2.51)	45 (2.77)	379 (4.28)	3844 (7.13)
	1500 - 2499 grams (LBW)	1180 (21.74)	361 (22.19)	2123 (23.99)	13207 (24.5)
	2500 - 4000 grams (NBW)	3841 (70.78)	1125 (69.15)	5834 (65.94)	31285 (58.03)
	> 4000 grams (Macrosomia)	229 (4.22)	85 (5.22)	368 (4.16)	3352 (6.22)
	Missing	9 (0.17)	1 (0.06)	40 (0.45)	978 (1.81)
Difficulty feeding	Yes	225 (4.15)	134 (8.24)	971 (10.97)	7741 (14.36)
	Missing	575 (10.6)	199 (12.23)	1401 (15.83)	7248 (13.44)
Convulsions	Yes	29 (0.53)	25 (1.54)	218 (2.46)	1975 (3.66)
	Missing	571 (10.52)	199 (12.23)	1385 (15.65)	6845 (12.7)
Central cyanosis	Yes	222 (4.09)	64 (3.93)	450 (5.09)	1950 (3.62)
	Missing	570 (10.5)	216 (13.28)	1680 (18.99)	3013 (5.59)
Severe indrawing	Yes	429 (7.9)	62 (3.81)	314 (3.55)	3112 (5.77)
	Missing	620 (11.42)	234 (14.38)	2243 (25.35)	5299 (9.83)
Floppy/inability to suck	Yes	530 (9.77)	359 (22.07)	2561 (28.94)	17389 (32.26)
	Missing	852 (15.7)	217 (13.34)	1300 (14.69)	7886 (14.63)
Outcome	Alive	4900 (90.29)	1469 (90.29)	8134 (91.93)	46358 (85.99)
	Dead	508 (9.36)	152 (9.34)	696 (7.87)	7486 (13.89)
	Missing	19 (0.35)	6 (0.37)	18 (0.2)	65 (0.12)

*Data only from the same hospital used at derivation and temporal validation stage. Data collected between January 2016 – December 2020.

Supplementary Table 4: Distribution of predictors for patients included in the NETS model derivation, updating and external validation

		Derivation (N = 4840)	Temporal Validation (N = 1443)	Model Updating* (N = 6610)	External Validation (N = 45090)
Indicator	**Levels**	**n (%)**	**n (%)**	**n (%)**	**n (%)**
Male	Yes	2605 (53.82)	850 (58.91)	3713 (56.17)	24719 (54.82)
	Missing	12 (0.25)	2 (0.14)	25 (0.38)	468 (1.04)
Birth weight	1000 grams & below (ELBW)	31 (0.64)	10 (0.69)	96 (1.45)	1083 (2.4)
	1001 - 1499 grams (VLBW)	115 (2.38)	40 (2.77)	366 (5.54)	3494 (7.75)
	1500 - 2499 grams (LBW)	1043 (21.55)	316 (21.9)	1717 (25.98)	11320 (25.11)
	2500 - 4000 grams (NBW)	3438 (71.03)	1002 (69.44)	4162 (62.97)	25932 (57.51)
	> 4000 grams (Macrosomia)	204 (4.21)	74 (5.13)	243 (3.68)	2478 (5.5)
	Missing	9 (0.19)	1 (0.07)	26 (0.39)	783 (1.74)
Enteral feeding	Yes	1380 (28.51)	598 (41.44)	1676 (25.36)	6053 (13.42)
	Missing	0 (0)	0 (0)	0 (0)	0 (0)
Intravenous antibiotics	Yes	1715 (35.43)	726 (50.31)	3914 (59.21)	21125 (46.85)
	Missing	0 (0)	0 (0)	0 (0)	0 (0)
Intravenous fluids	Yes	869 (17.95)	495 (34.3)	2812 (42.54)	19651 (43.58)
	Missing	0 (0)	0 (0)	888 (13.43)	8645 (19.17)
Oxygen prescribed	Yes	295 (6.1)	105 (7.28)	1462 (22.12)	7700 (17.08)
	Missing	0 (0)	0 (0)	0 (0)	0 (0)
Phenobarbital prescribed	Yes	141 (2.91)	77 (5.34)	664 (10.05)	4103 (9.1)
	Missing	0 (0)	0 (0)	0 (0)	0 (0)
Outcome	Alive	4374 (90.37)	1299 (90.02)	5950 (90.02)	38576 (85.55)
	Dead	447 (9.24)	138 (9.56)	649 (9.82)	6482 (14.38)
	Missing	19 (0.39)	6 (0.42)	11 (0.17)	32 (0.07)

* Data only from the same hospital used at derivation and temporal validation stage. Data collected between January 2016 – December 2020.

Supplementary Table 5: Distribution of predictors and missingness in SENSS external validation dataset by in-hospital mortality			
Predictors	**Present, n (%)**	**Missing, n (%)**	**Died, n (%)**
Difficulty feeding	7741 (14.36)	7248 (13.44)	2269 (29.31)
Convulsions	1975 (3.66)	6845 (12.7)	551 (27.9)
Central cyanosis	1950 (3.62)	3013 (5.59)	762 (39.08)
Severe Indrawing	3112 (5.77)	5299 (9.83)	1407 (45.21)
Floppy/inability to suck	17389 (32.26)	7886 (14.63)	4485 (25.79)
None	23559 (43.7)		965 (4.1)

Supplementary Table 6: Distribution of predictors in NETS external validation dataset by in-hospital mortality		
Predictors	**Prescribed, n (%)**	**Died, n (%)**
Intravenous antibiotics	21125 (46.85)	3541 (16.76)
Intravenous fluids	19651 (43.58)	3699 (18.82)
Enteral feeds	6053 (13.42)	279 (4.61)
Oxygen	7700 (17.08)	1830 (23.77)
Phenobarbital	4103 (9.1)	1116 (27.2)
None	8168 (18.11)	828 (10.14)

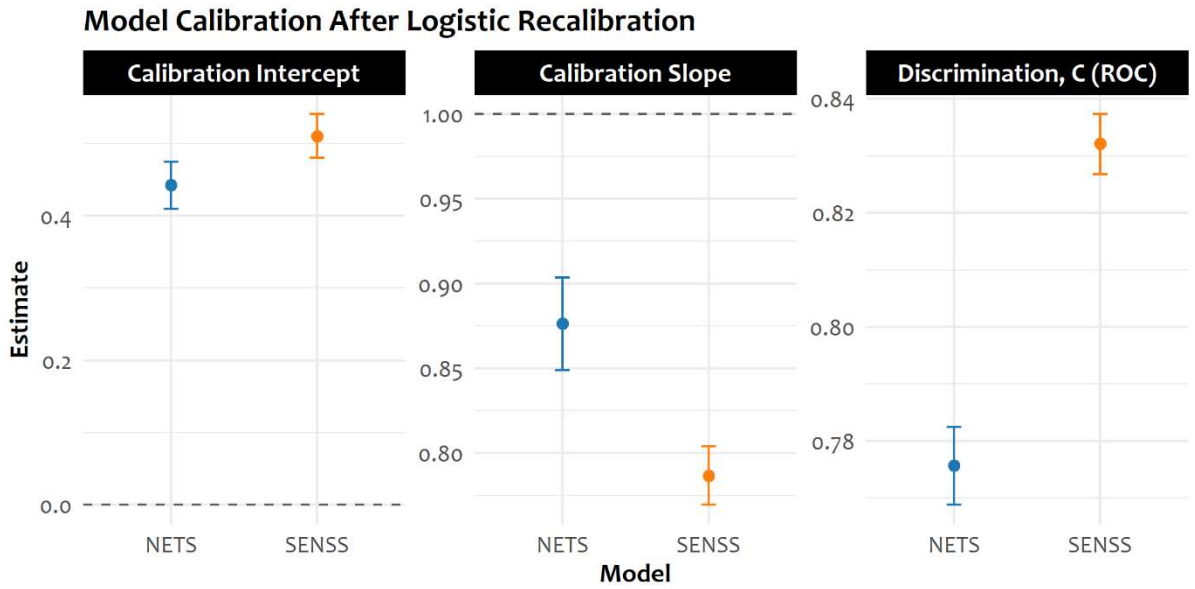
Supplementary Table 7: Hospital Specific Candidate Predictor Summaries‡																
Indicator	**H1***	**H2**	**H3**	**H4**	**H5**	**H6**	**H7**	**H8**	**H9**	**H10**	**H11**	**H12**	**H13**	**H14**	**H15**	**H16**
SENSS candidate predictors																
n	15902	1911	4188	1881	4285	3462	5493	1716	6587	6101	2338	3415	3370	2748	5356	1058
Mortality Rate	1356 (8.53)	397 (20.77)	455 (10.86)	364 (19.35)	893 (20.84)	384 (11.09)	594 (10.81)	421 (24.53)	390 (5.92)	837 (13.72)	349 (14.93)	543 (15.9)	306 (9.08)	671 (24.42)	725 (13.54)	157 (14.84)
Male	8861 (55.72)	1049 (54.89)	2289 (54.66)	1023 (54.39)	2176 (50.78)	1866 (53.9)	2880 (52.43)	1004 (58.51)	3648 (55.38)	3472 (56.91)	1266 (54.15)	1965 (57.54)	1810 (53.71)	1474 (53.64)	2873 (53.64)	589 (55.67)
Birth weight																
1000 grams & Below (ELBW)	146 (0.92)	45 (2.35)	67 (1.6)	84 (4.47)	154 (3.59)	75 (2.17)	51 (0.93)	41 (2.39)	103 (1.56)	176 (2.88)	90 (3.85)	106 (3.1)	68 (2.02)	75 (2.73)	93 (1.74)	15 (1.42)
1001 - 1499 grams (VLBW)	560 (3.52)	207 (10.83)	176 (4.2)	221 (11.75)	439 (10.25)	189 (5.46)	271 (4.93)	177 (10.31)	274 (4.16)	468 (7.67)	225 (9.62)	383 (11.22)	167 (4.96)	274 (9.97)	289 (5.4)	84 (7.94)
1500 - 2499 grams (LBW)	3664 (23.04)	446 (23.34)	747 (17.84)	587 (31.21)	1225 (28.59)	817 (23.6)	1261 (22.96)	460 (26.81)	1275 (19.36)	1618 (26.52)	741 (31.69)	936 (27.41)	741 (21.99)	784 (28.53)	1231 (22.98)	338 (31.95)
2500 - 4000 grams (NBW)	10800 (67.92)	955 (49.97)	3039 (72.56)	857 (45.56)	2019 (47.12)	2183 (63.06)	3548 (64.59)	850 (49.53)	4565 (69.3)	3165 (51.88)	1170 (50.04)	1741 (50.98)	2050 (60.83)	1424 (51.82)	3145 (58.72)	574 (54.25)
> 4000 grams (Macrosomia)	682 (4.29)	66 (3.45)	154 (3.68)	62 (3.3)	354 (8.26)	149 (4.3)	348 (6.34)	45 (2.62)	337 (5.12)	646 (10.59)	77 (3.29)	223 (6.53)	294 (8.72)	115 (4.18)	452 (8.44)	30 (2.84)
Difficulty feeding	1330 (8.36)	551 (28.83)	105 (2.51)	585 (31.1)	975 (22.75)	513 (14.82)	181 (3.3)	314 (18.3)	901 (13.68)	971 (15.92)	275 (11.76)	554 (16.22)	245 (7.27)	709 (25.8)	653 (12.19)	209 (19.75)
Convulsions	272 (1.71)	163 (8.53)	40 (0.96)	154 (8.19)	275 (6.42)	141 (4.07)	50 (0.91)	66 (3.85)	253 (3.84)	97 (1.59)	91 (3.89)	124 (3.63)	56 (1.66)	221 (8.04)	163 (3.04)	81 (7.66)
Central cyanosis	736 (4.63)	68 (3.56)	115 (2.75)	114 (6.06)	85 (1.98)	159 (4.59)	73 (1.33)	92 (5.36)	134 (2.03)	130 (2.13)	87 (3.72)	149 (4.36)	328 (9.73)	128 (4.66)	271 (5.06)	17 (1.61)
Severe indrawing	805 (5.06)	140 (7.33)	112 (2.67)	217 (11.54)	180 (4.2)	289 (8.35)	133 (2.42)	87 (5.07)	257 (3.9)	475 (7.79)	98 (4.19)	256 (7.5)	140 (4.15)	355 (12.92)	316 (5.9)	57 (5.39)
Floppy/inability to suck	3450 (21.7)	801 (41.92)	378 (9.03)	949 (50.45)	1816 (42.38)	1451 (41.91)	745 (13.56)	586 (34.15)	1888 (28.66)	3377 (55.35)	685 (29.3)	1147 (33.59)	811 (24.07)	1072 (39.01)	1325 (24.74)	358 (33.84)
NETS candidate predictors																
n	11938	923	3535	1202	1994	2259	3098	897	5588	5916	1607	2605	1217	1432	2612	785
Mortality Rate	1176 (9.85)	217 (23.51)	385 (10.89)	233 (19.38)	416 (20.86)	298 (13.19)	499 (16.11)	233 (25.98)	326 (5.83)	810 (13.69)	267 (16.61)	445 (17.08)	181 (14.87)	367 (25.63)	443 (16.96)	125 (15.92)
Male	6646 (55.67)	522 (56.55)	1918 (54.26)	651 (54.16)	1063 (53.31)	1255 (55.56)	1657 (53.49)	531 (59.2)	3092 (55.33)	3366 (56.9)	871 (54.2)	1508 (57.89)	654 (53.74)	790 (55.17)	1378 (52.76)	455 (57.96)
Birth weight																
1000 grams & Below (ELBW)	131 (1.1)	34 (3.68)	59 (1.67)	56 (4.66)	85 (4.26)	68 (3.01)	47 (1.52)	25 (2.79)	93 (1.66)	173 (2.92)	67 (4.17)	92 (3.53)	42 (3.45)	53 (3.7)	81 (3.1)	12 (1.53)
1001 - 1499 grams (VLBW)	504 (4.22)	152 (16.47)	147 (4.16)	169 (14.06)	216 (10.83)	162 (7.17)	246 (7.94)	140 (15.61)	241 (4.31)	452 (7.64)	180 (11.2)	350 (13.44)	131 (10.76)	183 (12.78)	224 (8.58)	76 (9.68)
1500 - 2499 grams (LBW)	2910 (24.38)	275 (29.79)	643 (18.19)	447 (37.19)	598 (29.99)	610 (27)	913 (29.47)	306 (34.11)	1121 (20.06)	1590 (26.88)	556 (34.6)	773 (29.67)	332 (27.28)	511 (35.68)	765 (29.29)	277 (35.29)
2500 - 4000 grams (NBW)	7889 (66.08)	434 (47.02)	2559 (72.39)	496 (41.26)	848 (42.53)	1317 (58.3)	1764 (56.94)	405 (45.15)	3823 (68.41)	3072 (51.93)	753 (46.86)	1210 (46.45)	647 (53.16)	633 (44.2)	1371 (52.49)	405 (51.59)
> 4000 grams (Macrosomia)	504 (4.22)	28 (3.03)	127 (3.59)	34 (2.83)	247 (12.39)	102 (4.52)	128 (4.13)	21 (2.34)	310 (5.55)	629 (10.63)	51 (3.17)	180 (6.91)	65 (5.34)	52 (3.63)	171 (6.55)	15 (1.91)
Intravenous antibiotics	5743 (48.11)	315 (34.13)	2148 (60.76)	741 (61.65)	256 (12.84)	987 (43.69)	1892 (61.07)	280 (31.22)	1330 (23.8)	3015 (50.96)	1176 (73.18)	1966 (75.47)	251 (20.62)	382 (26.68)	1051 (40.24)	638 (81.27)
Intravenous fluids	4158 (34.83)	315 (34.13)	2651 (74.99)	743 (61.81)	739 (37.06)	844 (37.36)	1278 (41.25)	692 (77.15)	1740 (31.14)	3930 (66.43)	1131 (70.38)	1929 (74.05)	533 (43.8)	628 (43.85)	1543 (59.07)	609 (77.58)
Enteral feeds	3485 (29.19)	6 (0.65)	31 (0.88)	91 (7.57)	240 (12.04)	230 (10.18)	147 (4.74)	53 (5.91)	2658 (47.57)	993 (16.78)	55 (3.42)	19 (0.73)	185 (15.2)	21 (1.47)	228 (8.73)	11 (1.4)

Oxygen	1776 (14.88)	98 (10.62)	1213 (34.31)	572 (47.59)	272 (13.64)	913 (40.42)	251 (8.1)	257 (28.65)	1277 (22.85)	552 (9.33)	190 (11.82)	278 (10.67)	94 (7.72)	335 (23.39)	175 (6.7)	172 (21.91)
Phenobarbital	814 (6.82)	142 (15.38)	213 (6.03)	174 (14.48)	202 (10.13)	206 (9.12)	273 (8.81)	100 (11.15)	398 (7.12)	317 (5.36)	193 (12.01)	217 (8.33)	95 (7.81)	188 (13.13)	214 (8.19)	157 (20)

*Hospital used in the SENSS and NETS model derivation and temporal validation stage.
‡Observations missing data on the outcome variable or all the candidate predictor variables omitted from analysis for objective two

Model recalibration approaches evaluated

Supplementary Figure 1 illustrates our attempt at logistic recalibration approach using the model updating dataset before model revision was considered. Model recalibration approaches like logistic recalibration are explained in detail elsewhere [1, 2]. We explored logistic recalibration because intercept recalibration would not suffice given the poor performance of both calibration slope and intercept from the original SENSS and NETS models (Figure 2). In logistic recalibration, intercepts and coefficients for corresponding linear predictors are estimated in order to update the regression coefficients [1, 2]. This method is meant to correct miscalibration of the predicted probabilities from the original SENSS and NETS and SENSS model (Figure 2), such that there is no general over- or underestimation of risks and such that predicted risks are on average not overly extreme or overly modest [1, 2].



Supplementary Figure 1: Model logistic recalibration results. SENSS: Score for Essential Neonatal Symptoms and Signs; NETS: Neonatal Essential Treatment Score.

While the logistic recalibration is one of the simpler approaches to model updating, it works best when the new dataset has a case-mix that is similar in both the updating and the external validation datasets [1]; This does not appear to be the case in our study given the differing levels of the predictor and outcome variables across the derivation, temporal validation, updating and external datasets (Table1, Supplementary Table 3, Supplementary Table 4) and as illustrated by Supplementary Figure 1. The

level of the NETS model discrimination is also concerning (Figure 2), and the strength of the association between some predictors and the outcome could arguably be substantially different in the external validation population given the differences in the presence of some predictors and the outcome rate between the derivation, updating, and external validation datasets (Table1, Supplementary Table 3, Supplementary Table 4).

Logistic recalibration of SENSS and NETS models illustrated by Supplementary Figure 1 used the parameters in equation 1 and 2 for SENSS and NETS models respectively. The recalibrating dataset (SENSS: n=8848, NETS: n=6610), was from the original derivation hospital but was not included in the model development or internal validation and is represented by the *Model updating* column in Supplementary Table 3 and 4.

$$LP_{SENSS\,(recalibrated)} = \alpha_1 + \beta_1 \times LP_{SENSS\,(original)} \quad (1)$$

Where: $\alpha_1 = -1.3884,\ \beta_1 = 0.7179$

$$LP_{NETS\,(recalibrated)} = \alpha_2 + \beta_2 \times LP_{NETS\,(original)} \quad (2)$$

Where: $\alpha_2 = -1.6255,\ \beta_2 = 0.5316$

Supplementary References

1. Su, T.-L., et al., *A review of statistical updating methods for clinical prediction models.* Statistical methods in medical research, 2018. **27**(1): p. 185-197.
2. Van Calster, B., et al., *Validation and updating of risk models based on multinomial logistic regression.* Diagnostic and prognostic research, 2017. **1**(1): p. 1-14.