

## **Estimated neonatal survival of very preterm births across the care pathway: a UK cohort 2016-2020**

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## ABSTRACT

**Objective:** Currently used estimates of survival are nearly ten years old and relate to only those babies admitted for neonatal care. Due to ongoing improvements in neonatal care here we update estimates of survival for singleton and multiple births at 22<sup>+0</sup> to 31<sup>+6</sup> weeks gestational age across the perinatal care pathway by gestational age and birthweight.

**Design:** Retrospective analysis of routinely collected data

**Setting:** A national cohort from the United Kingdom and British Crown Dependencies

**Patients:** Babies born at 22<sup>+0</sup> to 31<sup>+6</sup> weeks gestational age from 1/1/2016 to 31/12/2020

**Interventions:** None

**Main outcome measures:** Survival to 28 days

**Results:** Estimates of neonatal survival are provided for babies: (1) alive at the onset of care during the birthing process (n=43,763); (2) babies where survival focused care was initiated (n=42,004); and (3) babies admitted for neonatal care (n=41,158). We have produced easy-to-use survival charts for singleton and multiple births. Generally, survival increased with increasing gestational age at birth and with increasing birthweight. For all births beyond 28 weeks and birthweights over 1000g, survival was over 95% at all three stages of care.

**Conclusions:** Survival estimates are a vital tool to support and supplement clinical judgement within perinatal care. These up-to-date, national estimates of survival to 28 days are provided based on three stages of the perinatal care pathway to support ongoing clinical care. These novel results are a key resource for policy and practice including counselling parents and informing care provision.

**What's Known on This Subject:**

Up-to-date neonatal survival estimates for preterm babies are vital for counselling parents and informing care.

Currently used estimates of survival were created using data which are nearly ten years old and relate to only those babies admitted for neonatal care.

**What This Study Adds:**

We provide easy to use neonatal survival charts by gestational age, multiplicity and birthweight which can be used for all babies born very preterm.

Estimates of survival to 28 days after birth are provided for babies alive at the onset of the birthing process; babies where active survival focused care was initiated; and babies admitted for neonatal care.

**How this study might affect research, practice or policy:**

These survival estimates based on different stages throughout the perinatal pathway allow, for the first time, ongoing counselling of parents through the early care pathway. The survival estimates are a key resource for policy and practice including counselling parents and informing care.

## INTRODUCTION

Reliable up-to-date estimates of survival for very preterm babies are a key resource for policy and practice including counselling parents and informing care. Babies born before 32 weeks gestational age account for 1% of all live births in the United Kingdom.<sup>1</sup> Whilst survival in this cohort has increased in recent years,<sup>2</sup> these babies still account for over half of all neonatal deaths.<sup>1</sup>

Statistical modelling of neonatal data has the potential to offer accurate evidence-based estimates of survival and, in combination with clinical assessment, can provide parents and clinicians with more information to improve care throughout the perinatal pathway.<sup>3</sup> With on-going improvements in survival following preterm birth it is vital that such results are kept up-to-date. Furthermore, models based on different points along the care pathway allow a flexible and dynamic approach to discussions around clinical decision-making and may assist parents' understanding during an extremely stressful time.

Many existing estimates of neonatal survival are derived using data from individual hospitals, often tertiary centres, rather than from a population based on residence or national data.<sup>4, 5</sup> The organisation of neonatal care into providers offering different levels of care means that survival estimates derived from a hospital-based cohort may not accurately reflect survival in the whole population. While estimates for neonatal survival exist, these are relatively out-of-date, based on regional data<sup>6</sup> or focused on neonatal care admissions.<sup>2</sup> These limitations support the need for a development of a new model using national data rather than re-calibration of historical models.

In this paper we use national data for the United Kingdom (UK) and British Crown Dependencies for births from 2016 to 2020 to develop a prediction model which aimed to describe neonatal survival for babies born at 22<sup>+0</sup> to 31<sup>+6</sup> weeks gestational age. We provide this by birthweight and gestational age for three different stages of care along the perinatal care pathway from the onset of the care during the birthing process through to admission for neonatal care.

## **METHODS**

### **Data**

Data for births between 1 January 2016 and 31 December 2020 to mothers resident in the UK and British Crown Dependencies were obtained from the perinatal mortality surveillance programme (MBRRACE-UK). MBRRACE-UK has been commissioned by the Healthcare Quality Improvement Partnership (HQIP) to collect UK perinatal mortality surveillance data since 2013.<sup>1</sup> MBRRACE-UK links detailed information on all deaths reported by UK hospitals with birth notifications from the Patient Demographic Service (formerly the NN4B birth notification system) from NHS Digital for England, Wales and Isle of Man and birth and stillbirth and neonatal death registration data from the Office for National Statistics for England and Wales, National Records Scotland and Public Health Scotland for Scotland, Northern Ireland Maternity System for Northern Ireland, Health and Social Services Department (Bailiwick of Guernsey) and Health Intelligence Unit (Bailiwick of Jersey). Stillbirth and neonatal death registrations from statutory sources are used to optimise ascertainment of deaths and provide underlying information about all births.

### **Inclusion/exclusion**

We included data for all births from 22<sup>+0</sup> to 31<sup>+6</sup> weeks gestational age. We excluded babies where a congenital anomaly was recorded as the primary cause of death as these deaths have a particular underlying aetiology often unrelated to gestational age.

We imputed birthweight for births where birthweight was missing or considered implausible (birthweight outside the 0.4% and 99.6% centiles (based on sex and gestation specific birthweight centiles developed by MBRRACE-UK<sup>7</sup>) by assigning a birthweight from a normal distribution based on the mean and standard deviation for babies of the same gestational age, multiplicity of birth and survival status.

We investigated survival to 28 days relating to three different stages of care along the perinatal care pathway:

- (1) Babies alive at the onset of care for the birthing process, i.e. during labour, commencement of induction of labour or Caesarean section excluding those where death was confirmed before onset of care
- (2) Babies where survival-focused care was initiated, i.e. resuscitation or ventilation was provided following birth and/or the baby survived to be admitted for neonatal care.
- (3) Babies admitted to a neonatal care unit, i.e. the baby was known to be admitted for neonatal care and/or the baby survived beyond the first day after birth.

## Statistical analyses

Logistic regression models were developed to estimate the probability of survival to 28 days after birth for each of the three stages of care. Gestational age (measured in completed weeks), birthweight of the baby and multiplicity of birth (singleton versus multiple) were included in the model as these are known to be key predictors of survival.<sup>4</sup>

Non-linear functions were investigated for gestational age and birthweight using fractional polynomials,<sup>8</sup> with the final form selected using the change in deviance. Two-way interactions between the non-transformed variables were investigated between the main effects (gestational age, birthweight and multiplicity of birth) and retained in the model if their inclusion was statistically significant at the 5% level. Estimated survival percentages were calculated for babies according to week of gestational age at birth, multiplicity and birthweight in increments of 100 grams.

The overall model fit was assessed by investigating the Briers score for each of the optimised linear predictors where a score closer to 0 indicates a better fit of the model.<sup>9</sup> The internal validation of the model was checked by examining the calibration and discrimination (c-statistic and Hosmer-Lemeshow test) overall and in predefined subgroups based on birthweight (less than 50<sup>th</sup> centile v  $\geq 50^{\text{th}}$  centile), multiplicity (singleton versus multiple) and gestational age ( $22^{+0}-26^{+6}$  weeks;  $27^{+0}-29^{+6}$  weeks;  $30^{+0}-31^{+6}$  weeks).

## Funding

The MBRRACE-UK collaboration is commissioned by the Healthcare Quality Improvement Partnership (HQIP) to deliver the Maternal, Newborn and Infant Clinical Outcome Review Programme on behalf of NHS England, NHS Wales, Scottish Government, the Northern Ireland Department of Health and the States of Jersey Guernsey and the Isle of Man.

## RESULTS

There were 44,122 babies (33,173 singletons and 10,949 multiples) alive at the onset of care during the birthing process born at 22<sup>+0</sup> to 31<sup>+6</sup> weeks' gestational age in the UK and British Crown Dependencies between 01/01/2016 and 31/12/2020. A total of 359 babies were excluded because their primary cause of death was a congenital anomaly (0.8%).

There were 43,763 babies alive at the onset of care during the birthing process (around 8,800 babies per year). Birthweight was imputed due to being missing for 7086 (16%) births or implausible for 1,160 (2.7%) births. Survival-focused care was provided for 42,004 babies (96.0%) and 41,158 babies (94.0%) were admitted to a neonatal care unit. The observed survival is provided in Table 1 by week of gestational age and stage of care.

In Tables 2-4 we display survival graphically using a grid approach for ease of use in practical situations and as seen in previous research.<sup>6</sup> The predicted survival for the midpoint birthweight of each hundred gram band is displayed. For example, at 24 weeks of gestational age, survival to 28 days for singletons babies between 300g and 800g ranged between 17-70% for babies alive at the onset of care during the birthing process, 31-73% for babies where active survival focused care was initiated, and 40-76% for babies admitted to a neonatal unit (Tables 2-4).

The results for multiple births were very similar (Tables 2-4). For singleton and multiple births of more than 28 weeks gestation at birth, over 90% of babies survived to 28 days across all birthweights over 1000g for all three stages of the perinatal care pathway.

Details of the final models are given in Appendix 1.

### Model fit

The model fit statistics are provided for the whole dataset and prior defined subgroups according to gestational age and birthweight (Table 5). The observed and predicted number of babies surviving is provided and can be used to investigate specific subgroups where the model over- or under-estimates survival. Overall, the model fit was good at all three stages of the care pathway (Briers scores: 0.07, 0.06 and 0.05). Generally, the Hosmer-Lemeshow test indicated good calibration, although there was a small number of subgroups where  $p < 0.01$ . Overall the discrimination of the models was good (c-statistics: 0.89, 0.86 and 0.85) although it was poorer (c-statistic around 0.62-0.65) in some of the subgroups based on gestational age at birth greater than 26 weeks.

## DISCUSSION

In this paper we have estimated the percentage of babies surviving to 28 days after birth for singleton and multiple births at 22<sup>+0</sup> to 31<sup>+6</sup> weeks gestational age using national data from the UK and British Crown Dependencies. We have provided graphical representations of the percentage of babies surviving for three different stages of the perinatal care pathway: (1) babies alive at the onset of care during the birthing process; (2) babies provided with survival-focused care; and (3) those who were admitted to neonatal care. Using national data for five years we were able to estimate survival for multiple births and babies born at the earliest weeks of gestational age where they may survive, particularly those born before 24 weeks of gestation. Previously, these groups have either not been included in estimates or included with very small sample sizes.

Use of national data provides a population-based overview of neonatal survival. Previous research in the UK<sup>6</sup> has predominantly investigated babies who were admitted to neonatal care, representing a biased cohort as these represent a highly selective subset of all babies. This is most marked at the earliest gestations where those babies who die following comfort care without admission to neonatal care have not been captured in previous estimates and these babies can represent a large cohort. For example of those babies born at 22 weeks less than 20% survived to be admitted for neonatal care. Our inclusion of this important group is unique and the results we provide can facilitate the counselling of parents about potential outcomes and how they change before, during and immediately following birth.

Comparison of our data with those from two previous neonatal mortality estimates in the UK<sup>6, 10</sup> demonstrates increases in survival over time with sustained improvements for all gestations up to 30 weeks with the largest improvements seen amongst the lower gestational age births. This confirms the need for these updated charts to inform future counselling of parents and clinical knowledge.

### Differences in adjustments

We made an a priori decision not to adjust for or make exclusions based on baby's ethnicity. Along with other work in similar fields we believe including ethnicity could exacerbate existing disparities between ethnic groups.<sup>11</sup> We do not think clinical decision-making over care initiation or continuation is or should be based on the ethnicity of a baby. Similarly, we did not provide separate survival estimates according to the sex of the baby as we believe any differences were likely to be so small that they would not be clinically meaningful for conversations with parents.



## **Clinical use of these charts**

These charts will help facilitate conversations between healthcare professionals and parents about the potential outcome for their baby (or babies). National estimates of survival are useful and vital to support clinical judgement and decision-making.<sup>3</sup> Both the British Association of Perinatal Medicine (BAPM)<sup>12</sup> and Yeoh et al<sup>13</sup> provide helpful guidance for such conversations with parents.

## **Strengths/limitations**

In this work we present results from a large national cohort, rather than from a specific region or hospital. We have been able to investigate care throughout the perinatal pathway rather than a potentially biased subset, e.g. only those babies admitted to neonatal care. We have also focused on a cohort of babies alive at the onset of care during birthing process rather than only live births as this minimises the impact of the wide variation in the classification of deaths of babies born at less than 24 weeks as intrapartum losses or neonatal deaths.<sup>14</sup>

Our data relate to a time period encompassing the introduction of new guidance from BAPM in late 2019 which suggests potential provision of active care at 22 weeks of gestation.<sup>12</sup> Therefore there may be ongoing and future significant changes in survival and other outcomes in babies born at 22 weeks requiring regular updates to this analysis.

We followed the recommendations within the Transparent Reporting of Multivariable Prediction Model for Individuals Prognosis or Diagnosis (TRIPOD) statement when developing this work.<sup>15</sup> Overall the discrimination of the models was good although it was poorer in some of the subgroups based on gestational age at birth greater than 26 weeks. This finding is not unexpected because gestational age is a strong predictor of survival, and its effect will not be seen for subgroups defined over a narrow range of gestational ages.

A limitation of our work is that we only had information on survival for up to 28 days after birth and some babies may have died after this time whilst receiving neonatal care. However research has indicated that for babies born at <32 weeks' gestational age around half of deaths occur in the first 10 days after birth, and around 75% of deaths occurring within the first month<sup>16</sup>.

## **CONCLUSION**

In this work we have provided estimates of neonatal mortality for babies born at 22<sup>+0</sup> to 31<sup>+6</sup> weeks of gestational age to update and extend previous estimates. For the first time, estimates of survival have been provided using national data and at different points along the early care pathway, allowing for ongoing counselling of parents and care provision.

**Table 1:** Percentage and number of babies surviving to 28 days after birth by gestational age (weeks) for the three different stages throughout the perinatal pathway

Gestational age (weeks)	Percentage (number) of babies surviving to 28 days					
	Babies alive at the onset of care during the birthing process		Babies where active survival focused care was initiated		Babies admitted to a neonatal care unit	
22	4.5	(1548)	14.4	(485)	23.2	(302)
23	36.5	(1949)	44.0	(1,615)	50.6	(1,405)
24	64.7	(2454)	68.6	(2,312)	73.0	(2,173)
25	79.5	(2,566)	81.3	(2,507)	84.4	(2,415)
26	87.2	(3,228)	88.3	(3,186)	89.7	(3,137)
27	92.3	(3,867)	93.3	(3,827)	94.2	(3,790)
28	94.1	(5,178)	94.7	(5,146)	95.4	(5,109)
29	97.0	(5,693)	97.2	(5,680)	97.6	(5,654)
30	97.6	(7,588)	97.8	(7,572)	98.3	(7,533)
31	98.5	(9,692)	98.7	(9,674)	99.0	(9,640)
22 <sup>+0</sup> -31 <sup>+6</sup> weeks	87.1	(43,763)	90.8	(42,004)	92.7	(41,158)

**Table 2a Predicted percentage survival to 28 days after birth by birthweight and gestational age for singleton births alive at the onset of care during the birthing process**

	Gestation at birth (completed weeks)									
	22	23	24	25	26	27	28	29	30	31
Birthweight (grams)										
2200-2299										98%
2100-2199										98%
2000-2099									97%	98%
1900-1999									97%	98%
1800-1899									97%	98%
1700-1799								97%	97%	98%
1600-1699								97%	97%	98%
1500-1599							96%	97%	97%	98%
1400-1499							96%	97%	97%	98%
1300-1399						94%	96%	97%	97%	98%
1200-1299						94%	96%	97%	97%	97%
1100-1199					91%	94%	95%	96%	97%	97%
1000-1099					90%	93%	95%	96%	97%	97%
900-999				83%	90%	93%	95%	96%	97%	
800-899			70%	82%	89%	92%	94%	96%		
700-799	22%	46%	66%	80%	87%	91%	93%			
600-699	19%	40%	62%	76%	85%	89%				
500-599	14%	33%	53%	69%						
400-499	8%	21%	39%							
300-399	3%	8%	17%							

**Table 2b Predicted percentage survival to 28 days after birth by birthweight and gestational age for multiple births alive at the onset of care during the birthing process**

	Gestation at birth (completed weeks)									
	22	23	24	25	26	27	28	29	30	31
Birthweight (grams)										
2200-2299										100%
2100-2199										99%
2000-2099									99%	99%
1900-1999									99%	99%
1800-1899									99%	99%
1700-1799								99%	99%	99%
1600-1699								99%	99%	99%
1500-1599							98%	99%	99%	99%
1400-1499							98%	99%	99%	99%
1300-1399						97%	98%	98%	99%	99%
1200-1299						97%	98%	98%	99%	99%
1100-1199					95%	96%	97%	98%	98%	99%
1000-1099					94%	96%	97%	98%	98%	98%
900-999				88%	93%	95%	97%	97%	98%	
800-899			76%	87%	92%	95%	96%	97%		
700-799	26%	52%	72%	84%	90%	93%	95%			
600-699	21%	44%	66%	80%	87%	91%				
500-599	15%	35%	56%	72%						
400-499	8%	22%	40%							
300-399	3%	7%	16%							

**Table 3a Predicted percentage survival to 28 days after birth by birthweight and gestational age for singleton births where survival focused care was initiated**

	Gestation at birth (completed weeks)									
	22	23	24	25	26	27	28	29	30	31
Birthweight (grams)										
2200-2299										97%
2100-2199										97%
2000-2099									97%	98%
1900-1999									97%	98%
1800-1899									97%	98%
1700-1799								96%	97%	98%
1600-1699								97%	97%	98%
1500-1599							95%	97%	98%	98%
1400-1499							95%	97%	98%	98%
1300-1399						94%	96%	97%	98%	98%
1200-1299						94%	96%	97%	98%	98%
1100-1199					90%	94%	96%	97%	98%	98%
1000-1099					90%	94%	96%	97%	98%	98%
900-999				84%	90%	93%	95%	97%	98%	
800-899			73%	83%	89%	93%	95%	96%		
700-799	38%	56%	71%	81%	88%	92%	94%			
600-699	33%	51%	66%	78%	85%	90%				
500-599	27%	43%	60%	72%						
400-499	19%	33%	48%							
300-399	10%	19%	31%							

**Table 3b Predicted percentage survival to 28 days after birth by birthweight and gestational age for multiple births where survival focused care was initiated**

	Gestation at birth (completed weeks)									
	22	23	24	25	26	27	28	29	30	31
Birthweight (grams)										
2200-2299										99%
2100-2199										99%
2000-2099									99%	99%
1900-1999									99%	99%
1800-1899									99%	99%
1700-1799								99%	99%	99%
1600-1699								99%	99%	99%
1500-1599							98%	99%	99%	99%
1400-1499							98%	99%	99%	99%
1300-1399						97%	98%	99%	99%	99%
1200-1299						97%	98%	98%	99%	99%
1100-1199					94%	96%	97%	98%	99%	99%
1000-1099					94%	96%	97%	98%	99%	99%
900-999				88%	93%	95%	97%	98%	98%	
800-899			78%	87%	91%	94%	96%	97%		
700-799	42%	60%	74%	84%	89%	93%	95%			
600-699	35%	53%	68%	79%	86%	91%				
500-599	27%	43%	59%	72%						
400-499	17%	30%	45%							
300-399	9%	16%	27%							

**Table 4a Predicted percentage survival to 28 days after birth by birthweight and gestational age for singleton births admitted to a neonatal care unit**

	Gestation at birth (completed weeks)									
	22	23	24	25	26	27	28	29	30	31
Birthweight (grams)										98%
										98%
									97%	98%
									97%	98%
									98%	99%
								97%	98%	99%
								97%	98%	99%
							95%	97%	98%	99%
							96%	97%	98%	99%
						93%	96%	97%	98%	99%
						94%	96%	98%	98%	99%
					90%	94%	96%	98%	98%	99%
					91%	94%	96%	98%	98%	99%
				85%	91%	94%	96%	98%	98%	
			76%	85%	90%	94%	96%	97%		
	47%	62%	75%	84%	90%	93%	96%			
	43%	59%	72%	81%	88%	92%				
	38%	53%	66%	77%						
	29%	43%	56%							
	17%	27%	40%							

**Table 4b Predicted percentage survival to 28 days after birth by birthweight and gestational age for multiple births admitted to a neonatal care unit**

	Gestation at birth (completed weeks)									
	22	23	24	25	26	27	28	29	30	31
Birthweight (grams)										100%
										100%
									99%	100%
									99%	100%
									99%	100%
								99%	99%	100%
								99%	99%	100%
							98%	99%	99%	99%
							98%	99%	99%	99%
						97%	98%	99%	99%	99%
						96%	98%	99%	99%	99%
					94%	96%	98%	98%	99%	99%
					93%	96%	97%	98%	99%	99%
				88%	93%	95%	97%	98%	99%	
			79%	87%	91%	95%	96%	98%		
	48%	64%	76%	84%	90%	93%	96%			
	42%	57%	70%	80%	87%	91%				
	34%	48%	62%	73%						
	23%	36%	49%							
	12%	20%	30%							

**Table 5:** Model fit statistics for each of the three cohorts overall and by subgroups based on birthweight, multiplicity and gestational age at birth

Birth cohort	Variable	Overall	Birthweight		Gestational age (weeks)			Multiplicity	
			<50 <sup>th</sup> centile	≥50 <sup>th</sup> centile	22 <sup>+0</sup> -26 <sup>+6</sup>	27 <sup>+0</sup> -29 <sup>+6</sup>	30 <sup>+0</sup> -31 <sup>+6</sup>	Singleton	Multiple
<b>Alive at onset of birth process</b>	Number of babies	43763	21880	21883	11745	14738	17280	32853	10910
	Number surviving	38133	18834	19299	7221	13962	16950	28310	9823
	Predicted surviving	38133	18786	19345	7178	14050	16905	28310	9823
	C-statistic	0.89	0.89	0.88	0.83	0.63	0.62	0.88	0.92
	Hosmer-Lemeshow test	0.97	0.99	<0.001	0.76	<0.001	0.99	0.89	0.95
	Briers score	0.07	0.07	0.06	0.16	0.05	0.02	0.07	0.05
<b>Provided active survival focused care</b>	Number of babies	42004	20847	21157	10105	14653	17246	31412	10592
	Number surviving	38133	18834	19299	7221	13962	16950	28310	9823
	Predicted surviving	38133	18794	19339	7188	14011	16934	28310	9823
	C-statistic	0.86	0.86	0.85	0.76	0.62	0.64	0.84	0.89
	Hosmer-Lemeshow test	0.91	0.99	0.29	0.89	<0.001	0.99	0.89	0.73
	Briers score	0.06	0.06	0.06	0.16	0.04	0.02	0.07	0.05
<b>Neonatal admission</b>	Number of babies	41158	20341	20817	9432	14553	17173	30665	10493
	Number surviving	38133	18834	19299	7221	13962	16950	28310	9823
	Predicted surviving	38133	18784	19349	7189	13996	16948	28310	9823
	C-statistic	0.85	0.85	0.84	0.74	0.62	0.65	0.83	0.89
	Hosmer-Lemeshow test	0.15	0.80	0.01	0.98	<0.001	0.78	0.83	<0.001
	Briers score	0.05	0.05	0.05	0.15	0.04	0.01	0.06	0.04

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## **COMPETING INTERESTS**

None declared

## **ETHICS APPROVAL**

Approval gained for collection of patient identifiable data and access to statutory and routine data without consent:

England and Wales: National Information Governance Board ECC 5-05 (f)/2012 (from 10.10.2012) and the Confidentiality Advisory Group of the Health Research Authority 15/CAG/0119 (from 01.05.2015);

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Due to the different data privacy arrangements in Northern Ireland, only deidentified data are provided to MBRRACE-UK

#### **DATA AVAILABILITY**

Data may be obtained from a third party and are not publicly available. Data may be requested from the data controller, the Healthcare Quality Improvement Partnership (HQIP). A Data Access Request Form can be obtained from [https://www.hqip.org.uk/national-programmes/accessing-ncapop-data/%23.XQeml\\_IKhjU](https://www.hqip.org.uk/national-programmes/accessing-ncapop-data/%23.XQeml_IKhjU)

#### **AUTHOR CONTRIBUTIONS**

SES undertook the statistical analysis under the guidance and supervision of LKS. RA and BNM provided input to the statistical analysis and interpretation of results. AF provided critical clinical input. JJK and ESD provided oversight and knowledge of the data sources. LKS and SES wrote the first version of the manuscript. All authors contributed to the interpretation, revised the manuscript critically and approved the final version for submission.