

## Analysis of neonatal mortality data 2013-2014

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This document describes variations in neonatal mortality to discharge among infants born  $\leq 31^{+6}$  weeks gestation admitted to neonatal units contributing to the UK Neonatal Collaborative (UKNC). Neonatal units were informed of this planned analysis and have had opportunity to confirm the accuracy of mortality data for infants born in 2013 and 2014 that they entered into the Badger.Net platform, and improve on completeness of entries. It is these data, held in the National Neonatal Research Database, that form the basis of the analyses.

#### Methods

Data were extracted on infants born in 2013 and 2014 at  $\leq 31^{+6}$  weeks gestation, admitted to neonatal care, for whom the neonatal network of booking was known. Death was defined as death before discharge from neonatal care. Multiple imputation (applying the mi routine in Stata version 12) was used to impute missing outcome and covariate data; analysis of complete case data was also performed.

Neonatal networks in England were reconfigured from 23 networks to 13 Operational Delivery Networks (ODN) through mergers. We present 2013 and 2014 data for the original neonatal networks due to the variation in deployment of the new network infrastructure. Standardised Mortality Ratios (SMR) are presented for each neonatal network, assigning infants to the neonatal network of booking. Crude and adjusted SMR are presented for 2013 and 2014 combined.

The SMR was calculated as the observed number of deaths divided by the expected number of deaths. The observed number of deaths was averaged over the imputed datasets so infants with missing outcomes were included. For the unadjusted SMR, the expected number of deaths was calculated as the total number of infants in the multiplied by the overall mortality rate across all networks. For the adjusted SMR, the expected number of deaths was calculated by estimating the probability of death for each infant using logistic regression, and adding up the probabilities to obtain the expected number of deaths. 95% Confidence intervals for the SMR were calculated using Byar's approximation (Breslow 1994) with correction for multiple testing, controlling the false discovery rate at 5% (Benjamini and Hochberg 1995).

The logistic model used to estimate the probability of death was derived using data from babies born in  $\leq 31^{+6}$  weeks gestation in England in 2008-2014. Multivariable logistic regression was used with survival to discharge from neonatal care as the outcome. Predictor variables were gestational age (typically the best obstetric estimate from antenatal ultrasound), birth weight, sex, multiplicity of pregnancy (singleton/multiple), administration of any antenatal steroids (no/yes). Spline terms were used to model gestational age and birth weight and their interaction. The association between gestation and mortality is known to be different amongst singletons and multiples (Kiely 1998); a

similar interaction effect has been shown for birth weight (Buekens 1993). Interactions between multiple birth and gestational age/birth weight terms were therefore included.

As outcomes for infants from the same pregnancy are likely to be correlated, generalised estimating equations (GEE) were used to account for the lack of independence.

Funnel plots were used to illustrate the variation in SMR. Funnel plot limits were drawn corresponding to 2 and 3 standard deviations from the target SMR of 1 assuming the observed deaths follow a Poisson distribution. The limits were adjusted for multiple testing (Jones 2008) controlling the false discovery rate at 5%.

Note that if the SMR for a neonatal network lies outside the funnel, it will not necessarily have a confidence interval which excludes 1. This is because they have different interpretations: the confidence interval reflects uncertainty about the true SMR for that particular network, whereas the funnel plot limits reflect the variability we would expect to see in the SMR for similar neonatal networks. More specifically the confidence interval is the range in which we are 95% confident that the true SMR for the neonatal network lies, whereas the funnel plot limits represent the range in which we expect 95% of neonatal networks to lie.

## Results

A total of 15,255 infants were born in 2013-2014 at  $\leq 31^{+6}$  weeks gestation and admitted to neonatal care, for whom the neonatal network of booking was known; 8.9% of those for whom the outcome was known (1,327/14,837) died before discharge. The outcome was missing for 2.7% of infants. Infants with a missing outcome tended to be more vulnerable based on other neonatal characteristics. Antenatal steroid entries were missing for 0.5% of infants, and sex and multiple birth status SDS for  $<0.01\%$ . The prediction model fit the data well, giving an area under the ROC curve of 0.83 (95% confidence interval 0.82 to 0.84).

SMRs are shown on funnel plots both unadjusted (figure 1) and adjusted (figure 2) with neonatal networks numbered (see table 1 for key). Analysis of complete cases gave very similar results (largest absolute difference in SMR of 0.04).

## Comments

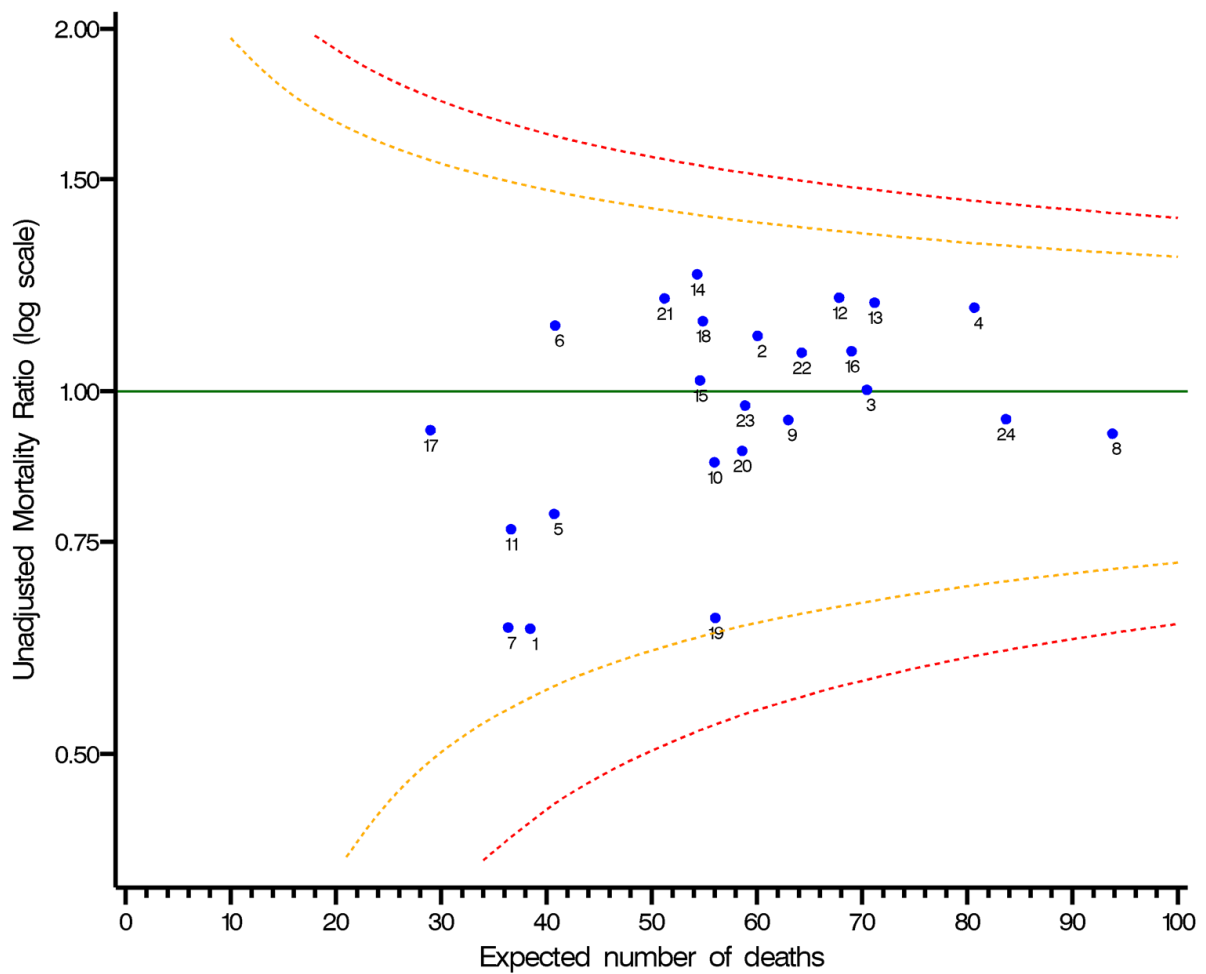
Two years of data have been combined in this report, giving improved power over the 2012 analysis. The average number of expected deaths in a network is 60. If a neonatal network with a patient case-mix leading to 60 expected deaths had a true underlying SMR of 1.3, the probability of the network's observed data falling above the 2 standard deviation upper control limit is around 60% (i.e. there would be 60% power to alert the network as having potentially unusual performance). This is before widening the limits to allow for multiple testing, so the power is further reduced.

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**Figure 1**

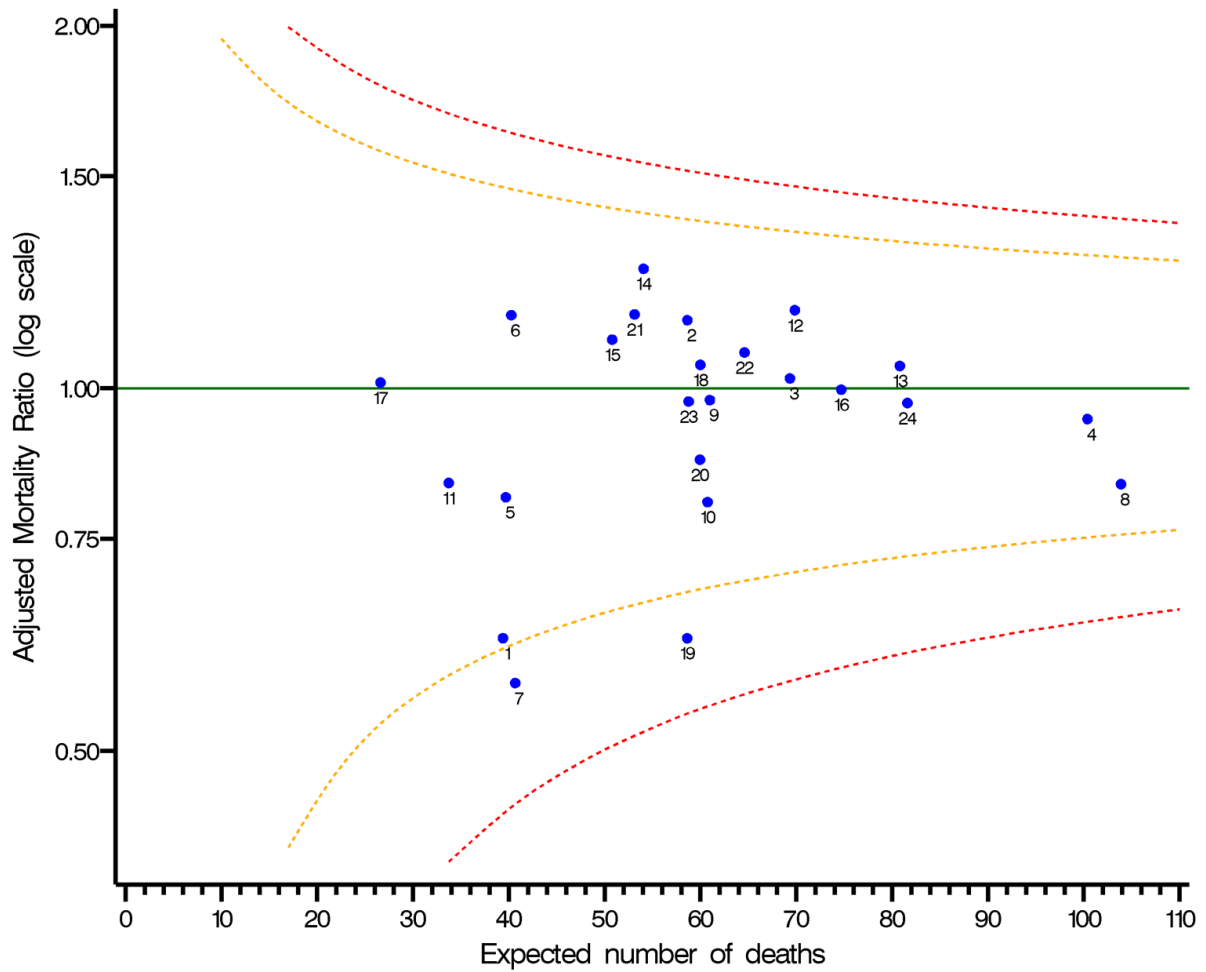
**Funnel plot for unadjusted SMR for babies live born  $\leq 31+6$  weeks gestation in 2013-2014 and admitted to neonatal care, by neonatal network of booking.**



Control limits show 2 and 3 standard deviations from the mean after correction for multiple testing, assuming observed deaths follow a Poisson distribution. Numbers correspond to neonatal networks in table 1.

**Figure 2**

**Funnel plot for adjusted SMR for babies live born  $\leq 31+6$  weeks gestation in 2013-2014 and admitted to neonatal care, by neonatal network of booking.**



Control limits show 2 and 3 standard deviations from the mean after correction for multiple testing, assuming observed deaths follow a Poisson distribution. Adjusted for gestation, birth weight SDS, sex, antenatal steroids accounting for correlation within multiple birth sets and missing data. Numbers correspond to neonatal networks in table 1.

**Table 1**

Unadjusted and adjusted SMR for babies live born  $\leq 31+6$  weeks gestation in 2013-2014 and admitted to neonatal care, by neonatal network of booking

Code	Booked neonatal network code	Total infants	Raw SMR	Adj SMR
1	100106	422	0.64(0.33,1.1)	0.62(0.32,1.07)
2	100109	659	1.11(0.76,1.56)	1.14(0.78,1.6)
3	100142	773	1(0.69,1.4)	1.02(0.71,1.42)
4	100108	885	1.17(0.86,1.56)	0.94(0.69,1.26)
5	100012	447	0.79(0.45,1.28)	0.81(0.46,1.31)
6	100162	448	1.13(0.71,1.7)	1.15(0.72,1.72)
7	100011	399	0.64(0.32,1.12)	0.57(0.29,1)
8	100059	1,029	0.92(0.66,1.24)	0.83(0.6,1.12)
9	100088	691	0.95(0.63,1.36)	0.98(0.65,1.4)
10	100071	614	0.87(0.56,1.3)	0.8(0.51,1.19)
11	100078	402	0.77(0.42,1.28)	0.83(0.45,1.4)
12	100113	744	1.2(0.85,1.63)	1.16(0.83,1.58)
13	100115	781	1.18(0.85,1.6)	1.04(0.75,1.41)
14	100209	596	1.25(0.86,1.75)	1.26(0.86,1.76)
15	100111	599	1.02(0.67,1.48)	1.1(0.72,1.59)
16	100208	757	1.08(0.76,1.49)	1(0.7,1.38)
17	100118	318	0.93(0.5,1.57)	1.01(0.54,1.71)
18	100524	602	1.14(0.77,1.62)	1.05(0.71,1.48)
19	100196	615	0.65(0.38,1.02)	0.62(0.37,0.98)
20	100070	643	0.89(0.58,1.31)	0.87(0.57,1.28)
21	100150	562	1.19(0.8,1.7)	1.15(0.77,1.64)
22	100222	705	1.08(0.74,1.5)	1.07(0.74,1.5)
23	100210	646	0.97(0.65,1.4)	0.98(0.65,1.41)
24	100110	918	0.95(0.67,1.3)	0.97(0.69,1.33)

## References

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- Buekens P, Wilcox A. Why do small twins have a lower mortality rate than small singletons? *American Journal of Obstetrics and Gynecology*. 1993; 168(3): 937-41.
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- Kiely JL. What is the population-based risk of preterm birth among twins and other multiples? *Clinical obstetrics and gynecology*. 1998; 41(1): 3-11.