

NHS BLOOD AND TRANSPLANT
CARDIOTHORACIC ADVISORY GROUP
CHANGES TO LUNG CUSUM MONITORING - SUMMARY

1. BACKGROUND

- 1.1. NHSBT monitors short-term patient outcomes following organ transplantation through centre specific cumulative sum (CUSUM) analyses. These are undertaken monthly for lung transplantation and enable prompt detection of any changes in 90-day mortality rates, provide external assurance and enable centres to compare current outcomes with their own past performance to assist in internal auditing.
- 1.2. CUSUM monitoring compares current outcome rates with an expected rate. Concern was raised at an Advisory Group for a different organ in 2016 regarding the lack of observed signals and it was agreed in November 2016 that the following CUSUM aspects should be reviewed for all organ-specific CUSUMs.
 - 1.2.1. Update the baseline period used to calculate the expected mortality rates so that more recent mortality rates are used for comparison.
 - 1.2.2. Review 'chart limit', and if thought desirable, update the trigger to improve the sensitivity of the monitoring system
- 1.3 This paper examines the impact of applying these changes to lung transplantation as the baseline period used for comparing outcomes has not been updated since 2012.

2. UPDATING THE EXPECTED BASELINE

- 2.1. The current expected rates are based on first, NHS group 1, deceased donor lung only transplants in the UK between 1 January 2008 and 31 December 2011. Retransplants and multi-organ transplants (e.g. heart-lung transplants) are excluded from the analysis.
- 2.2. The national baseline mortality rate for transplants performed during the current time period (2008-2011) was 9.8% for adult transplants and 11.5% for paediatric transplants. During a more recent time period (2013-2016), the national mortality rates were 10.5% for adult lung and 7.8% for paediatric lung transplants. The majority of the 95% confidence intervals for the centre-specific rates included the corresponding national rate, suggesting that individual centre specific rates may just be a manifestation of the inherent variability in outcomes. Thus, this time period (2013-2016) will be used as the baseline period in future CUSUM monitoring.

3. REVIEW THE CURRENT CHART LIMIT AND, IF THOUGHT DESIRABLE, UPDATE THE TRIGGER TO IMPROVE THE SENSITIVITY OF THE MONITORING SYSTEM

- 3.1. The threshold on the tabular CUSUM at which a centre is deemed to have had a significant increase in mortality requiring investigation (known as the *chart limit*) was set at 2.5 following statistical analysis in 2006. This limit has not changed since 2006, meaning that we have used the same levels of sensitivity of the charts since then.
- 3.2. **Figure 1** shows the impact of changing the chart limit from 2.5 to 2.0. This change would lead to more signals potentially arising earlier than had the chart limit remained as 2.5. Six adult lung transplant signals have been observed for three transplant centres observed since 1 January 2011 under the current baseline period (2008-2011) and chart limit (2.5). Retrospective analysis indicated that there would have been *five additional signals* at three adult lung transplant centres if the limit of 2.0 was used. For paediatric patients, there would have been no additional signals had the limit been 2.0.

RECOMMENDATIONS AND ADVICE REQUIRED

- 4.1 The **BASELINE PERIOD** used to calculate the expected mortality rates will be updated to transplants performed between *1 January 2013 and 31 December 2016* for both adult and paediatric lung transplants. Retrospective analysis of transplants since January 2017, using the revised mortality rates, indicated there would have been no additional signals for either adult or paediatric lung only transplants.
- 4.2 Members are asked to advise whether the **SENSITIVITY** of the lung CUSUM charts should increase through changing the chart limit from 2.5 to 2.0.

Rhiannon Taylor
Statistics and Clinical Studies, NHSBT

April 2018

NHS BLOOD AND TRANSPLANT
CARDIOTHORACIC ADVISORY GROUP
CHANGES TO LUNG CUSUM MONITORING

1. BACKGROUND

- 1.1. NHSBT monitors short-term patient outcomes following organ transplantation through centre specific cumulative sum (CUSUM) analyses. These are undertaken monthly for lung transplantation and enable prompt detection of any changes in 90-day mortality rates, provide external assurance and enable centres to compare current outcomes with their own past performance to assist in internal auditing.
- 1.2. CUSUM monitoring compares current outcome rates with an expected rate. Concern was raised at an Advisory Group for a different organ in 2016 regarding the lack of observed signals and it was agreed in November 2016 that the following CUSUM aspects should be reviewed for all organ-specific CUSUMs.
 - 1.2.1 Update the baseline period used to calculate the expected mortality rates so that more recent mortality rates are used for comparison.
 - 1.2.2 Review 'chart limit', and if thought desirable, update the trigger to improve the sensitivity of the monitoring system
- 1.2. This paper examines whether these changes should be made when monitoring lung transplantation as the baseline period used for comparing outcomes has not been updated since 2012.

2. UPDATING THE EXPECTED BASELINE

- 2.1. The current expected rates are based on first, NHS group 1, deceased donor lung only transplants in the UK between 1 January 2008 and 31 December 2011. Retransplants and multi-organ transplants (e.g. heart-lung transplants) are excluded from the analysis.
- 2.2. **Table 1** shows the current centre specific 90-day mortality rates and confidence intervals for adult and paediatric lung only transplants along with the corresponding rate for a recent four-year time period (1 January 2013 – 31 December 2016) Under the current rates, two adult centres receive centre-specific mortality rate charts in addition to the national expected mortality rate charts. Under the revised rates, three adult centres would receive the centre-specific charts.
- 2.3. **Table 1** also shows that the mortality rates at all but one transplant centres is higher in the revised period than in the current baseline period. It should, however, be noted that only one centre had confidence intervals which were outside the national confidence intervals. It should also be noted that the 90-day mortality rate at Newcastle paediatric was 0% both the current and revised time periods.

Table 1 Revised expected ninety day mortality rates based on deceased lung only transplants performed between 1 January 2008 and 31 December 2016

	Expected mortality (%)			Baseline comparison		
	Current rate (2008-2011)	Revised rate (2013-2016)	Centre rate change (%)	Current	Revised	Revised rate change (%)
ADULT						
Newcastle	13.1 (10.0, 16.3)	13.8 (10.5, 17.1)	0.7	National	National	0.6
Papworth	10.2 (6.7, 13.6)	7.5 (4.8, 10.2)	-2.6	National	Centre	-2.3
Harefield	7.7 (5.3, 10.1)	9.0 (6.4, 11.6)	1.3	Centre	Centre	1.3
Birmingham	16.1 (9.3, 22.9)	16.9 (11.8, 22.0)	0.8	National	National	0.6
Manchester	4.7 (2.0, 7.4)	7.1 (4.0, 10.2)	2.4	Centre	Centre	2.4
National	9.8 (8.3, 11.3)	10.5 (9.0, 11.9)	0.6			
PAEDIATRIC						
Newcastle	13.0 (3.3, 22.8) ¹	10.0 (2.4, 17.6) ¹	-3.0	National	National	0.0
GOSH	13.0 (3.3, 22.8)	10.0 (2.4, 17.6)	-3.0	National	National	-3.7
National	11.5 (2.9, 20.2)	7.8 (1.8, 13.8)	-3.7			

¹ Actual mortality rate is 0% so the lowest centre specific expected mortality rate is presented and used in practice

2.5 The latest CUSUMs using the current expected mortality rates were run on the 19th April 2018 for transplants performed between 1 January 2011 and 30 November 2017. Under the national mortality rates, there were six signals for three adult lung only transplant centres.

2.6 Retrospective analysis of transplants performed since 1 January 2017, using the revised expected 90-day mortality rates (2013-2016), indicated there would have been no signals for either adult or paediatric transplant centres.

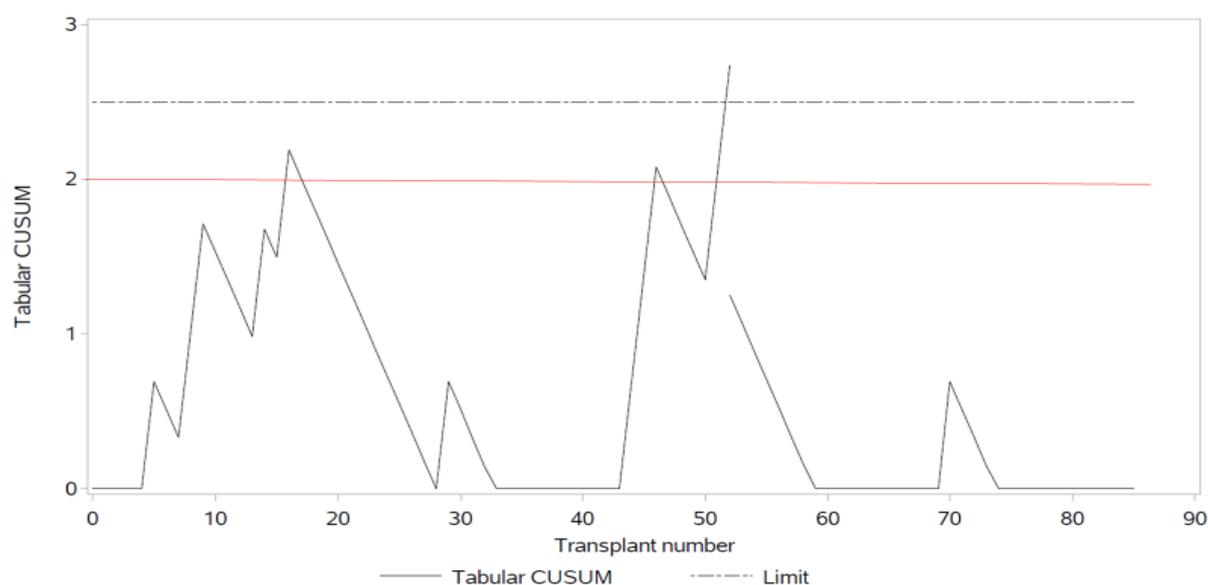
CHANGES:

2.7 The expected baseline will be updated to transplants performed between *1 January 2013 and 31 December 2016* for both adult and paediatric lung only transplants.

3. REVIEW THE CURRENT CHART LIMIT AND, IF THOUGHT DESIRABLE, UPDATE THE TRIGGER TO IMPROVE THE SENSITIVITY OF THE MONITORING SYSTEM

- 3.1 The threshold on the tabular CUSUM at which a centre is deemed to have had a significant increase in mortality requiring investigation (known as the *chart limit*) was set at 2.5 following statistical analysis in 2006. This limit has not changed since 2006.
- 3.2 The position of the limit on the tabular CUSUM was evaluated using Average Run Length (ARL) methodology to evaluate the charts performance. Further details are provided in the **APPENDIX A** regarding the ARLs for different chart limits for the current and revised national mortality rates.
- 3.3 **Figure 1** shows the tabular CUSUM chart for a cardiothoracic transplant centre using the current baseline time period. The dotted line is the current chart limit (2.5) while the red line is 2.0. This transplant centre actually signalled when the limit was 2.5 but would have signalled after 5 deaths within 18 transplants had the limit of been 2.0.

Figure 1 Tabular CUSUM chart for an adult cardiothoracic transplant centre, 1 January 2011 to 28 February 2018



- 3.4 Six adult lung transplant signals were observed at three transplant centres has been observed since 1 January 2011 under the current baseline period (2008-2011) and chart limit (2.5). Retrospective analysis indicated that there would have been *five additional adult lung signals* at three transplant centres if a limit of 2.0 was used. For paediatric patients, there would have been no additional signals had the limit been 2.0.

ADVICE REQUIRED

- 3.5 Members are asked to advise whether the sensitivity of the CUSUM charts should increase or whether the chart limit should remain as 2.5.

Rhiannon Taylor
Statistics and Clinical Studies, NHSBT

April 2018

APPENDIX A: REVIEW THE CURRENT CHART LIMIT AND, IF THOUGHT DESIRABLE, UPDATE THE TRIGGER TO IMPROVE THE SENSITIVITY OF THE MONITORING SYSTEM

- 1 The Average Run Length (ARL) is evaluated under the assumption that the mortality rate has remained the same (ARL_0) and under the assumption that it has increased to given level (ARL_1), for example that it has doubled. The best choice of a limit is one that gives a large ARL if the mortality rate has not changed, since in this case a signal would be a *false alarm*, and a small ARL if the mortality rate has increased, since in this case a signal would be a *correct detection of an increase*. A large ARL_0 requires a relatively high limit, while a small ARL_1 requires a relatively low limit and a compromise should be reached. If ARL_0 and ARL_1 are similar then the chart cannot distinguish between a centre whose mortality rate is consistent with the national average and a centre whose mortality rate is higher than the national average.
- 2 An added complication in this case is that the charts are produced for several centres and transplant types simultaneously. The choice of limit should be such that the number of false alarms seen out of all signals (false detection rate) is minimised, while maximising the number of genuine signals (true detection rate).
- 3 **Table A1** shows the original ARL_0 and ARL_1 for various limits, assuming that the mortality was 1.5 times ($OR=1.5$) or twice the national mortality ($OR=2.0$). This assessed the performance of the charts when optimised for detection of a 50% increase or a doubling of the mortality rate. The original time period included transplants performed between 1 July 1995 to March 2005 and it was agreed in 2006 that the limit should be 2.5 and with an OR of 2.0 ($p_1=2*p_0$).

Transplant type	p_0	Limit	Odds ratio=1.5			Odds ratio=2.0		
			p_1	ARL_0	ARL_1	p_1	ARL_0	ARL_1
Adult	0.127	1.5	0.191	182	57	0.254	73	19
		2.0		395	82		140	26
		2.5		760	110		261	33
		3.0		1383	138		481	42
		3.5		2462	169		820	49
Paediatric	0.115	1.5	0.173	212	63	0.230	76	20
		2.0		446	92		157	28
		2.5		839	121		313	38
		3.0		1552	156		521	46
		3.5		2726	190		967	57

- 4 **Table A2** and **Table A3** show the equivalent information presented in **Table A1** for the current (2008-2011) and revised national mortality rates (2013-2016) respectively. For adult transplants, the national mortality rate has decreased from 12.7% in the original time period to 10.5% in the revised baseline period. This decrease in mortality rates has seen an increase in the ARL_0 (261 to 327) leading to a potential delay in a genuine signal arising.

- 5 The corresponding national mortality rates for paediatric transplants was 11.5% in the original time period and 7.8% in the revised baseline period.

FINDING: Decrease in adult transplant national mortality rates has seen an increase in Average Run Lengths before a signal for a limit of 2.5 and OR of 2.0.

Table A2 Lung only transplant simulations using the CURRENT national mortality average (2008-2011) as the expected mortality; p0 is the national average and p1=Odds ratio (OR) x p0

Transplant type	p0	Limit	Odds ratio=1.5			Odds ratio=2.0		
			p1	ARL ₀	ARL ₁	p1	ARL ₀	ARL ₁
Adult	0.098	1.5	0.147	245	73	0.196	89	24
		2.0		535	108		195	34
		2.5		1036	145		351	43
		3.0		1862	183		603	53
		3.5		3216	227		1182	66
Paediatric	0.115	1.5	0.173	213	63	0.230	76	20
		2.0		441	91		159	28
		2.5		822	120		310	38
		3.0		1559	156		519	46
		3.5		2689	188		951	56

Table A3 Lung only transplant simulations using the REVISED national mortality average (2013-2016) as the expected mortality; p0 is the national average and p1=Odds ratio (OR) x p0

Transplant type	p0	Limit	Odds ratio=1.5			Odds ratio=2.0		
			p1	ARL ₀	ARL ₁	p1	ARL ₀	ARL ₁
Adult	0.105	1.5	0.157	232	68	0.210	89	23
		2.0		495	101		178	31
		2.5		946	135		327	42
		3.0		1740	171		603	51
		3.5		3035	213		1057	61
Paediatric	0.078	1.5	0.117	317	94	0.156	123	31
		2.0		677	139		244	43
		2.5		1295	189		453	56
		3.0		2365	247		802	70
		3.5		4257	291		1402	84