

# NHS BLOOD AND TRANSPLANT

## CARDIOTHORACIC ADVISORY GROUP

### CHANGES TO HEART 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 heart transplantation and enable prompt detection of any changes in 30-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 heart transplantation as the baseline period used for comparing outcomes has not been updated since 2012. This paper also examines the impact of including DCD heart transplantation.

#### 2. UPDATING THE BASELINE PERIOD

- 2.1. The current expected 30-day mortality rates are based on first, NHS Group 1, deceased donor heart only transplants in the UK between 1 January 2008 and 31 December 2011 (*baseline period*). Heart transplants involving organs from donors after circulatory death (DCD) are currently excluded from any analysis as are heterotopic heart transplants, retransplants or multi-organ transplants.
- 2.2. The national mortality rate for transplants performed during the current baseline time period (2008-2011) was 14.3% for adult transplants and 4.0% for paediatric transplants. During a more recent time period (2013-2016), the national 30-day mortality rates were 8.9% for adult heart and 6.0% for paediatric heart 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. INCLUSION OF DCD HEARTS

- 3.1 Fifty-seven UK adult DCD heart transplants have been performed at three transplant centres between February 2015 and February 2018. There has also been one paediatric DCD heart transplant in November 2013. Thirty-day outcome was known for all patients and all but one patient survived the first 30-days post-transplant.
- 3.2 Inclusion of DCD transplants in the CUSUM monitoring, would lead to a 1.1% reduction in the revised 30-day mortality rates for two adult transplant centres (Papworth and Harefield) and a 0.6% decrease in the adult national 30-day mortality rate (8.9% to 8.3%). The expected mortality rate for Papworth would decrease from 5.2% to 4.1% while the expected mortality rate for Harefield would decrease from 14.6% to 13.5%.
- 3.3 It is not clear whether DCD heart transplants should be included in the CUSUM monitoring.

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

- 4.1 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.
- 4.2 **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. Only one adult heart transplant signal 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 *two additional adult heart signals* if a 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

- 5.1 The **BASELINE PERIOD** used to calculate the expected mortality rates will be updated to *1 January 2013 to 31 December 2016* for both adult and paediatric heart 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 heart only transplants.
- 5.2 Members are asked to advise whether **DCD HEART TRANSPLANTS** should be included in the CUSUM monitoring now or whether they should be included later e.g. when established at more than three adult transplant centres.
- 5.3 Members are also asked to advise whether the **SENSITIVITY** of the heart CUSUM charts should increase through changing the chart limit from 2.5 to 2.0.

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April 2018

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**CARDIOTHORACIC ADVISORY GROUP**  
**CHANGES TO HEART 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 heart transplantation and enable prompt detection of any changes in 30-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 heart transplantation as the baseline period used for comparing outcomes has not been updated since 2012. This paper also examines the impact of including DCD heart transplantation.

## **2. UPDATING THE BASELINE PERIOD**

- 2.1. The current expected rates are based on first, NHS Group 1, deceased donor heart only transplants in the UK between 1 January 2008 and 31 December 2011. Heart transplants involving organs from donors after circulatory death (DCD) are excluded from any analysis as are heterotopic heart transplants, retransplants or multi-organ transplants.
- 2.2. **Table 1** shows the current centre specific 30-day mortality rates and confidence intervals for adult and paediatric heart only transplants along with the corresponding rate for a recent four-year time period (1 January 2013 – 31 December 2016). Under the current rates, three adult centres and one paediatric centre receive centre-specific mortality rate charts in addition to the national expected mortality rate charts. Under the revised rates, two adult centres and one paediatric centre would receive the centre-specific charts. It should, however, be noted that only one centre had confidence intervals which were outside the national confidence intervals.

**Table 1 Revised expected thirty day mortality rates based on DBD heart 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 (%)
<b>ADULT</b>						
Newcastle	16.2 (10.6, 21.8)	10.2 (6.3, 14.0)	-6.0	National	National	-5.4
Papworth	9.1 (5.7, 12.4)	5.2 (2.8, 7.5)	-3.9	Centre	Centre	-3.9
Harefield	23.8 (15.5, 32.1)	14.6 (9.9, 19.4)	-9.2	National	National	-5.4
Birmingham	12.1 (7.5, 16.7)	10.0 (6.4, 13.6)	-2.1	Centre	National	-3.2
Manchester	10.7 (5.4, 16.0)	5.2 (2.6, 7.8)	-5.5	Centre	Centre	-5.5
Glasgow	30.3 (19.9, 40.6)	14.0 (7.9, 20.2)	-16.3	National	National	-5.4
<b>National</b>	<b>14.3 (12.1, 16.5)</b>	<b>8.9 (7.5, 10.4)</b>	<b>-5.4</b>			
<b>PAEDIATRIC</b>						
Newcastle	2.5 (0.1, 4.9)	8.6 (4.4, 12.7)	6.1	Centre	National	3.5
GOSH	5.3 (2.1, 8.4)	3.2 (0.4, 5.9)	-2.1	National	Centre	-0.8
<b>National</b>	<b>4.0 (1.9, 6.0)</b>	<b>6.0 (3.4, 8.5)</b>	<b>2.0</b>			

2.5 The latest CUSUMs using the current expected mortality rates were run on 19 April 2018 for transplants performed between 1 January 2011 and 28 February 2018. Under the national mortality rates, there was one signal in February 2015 for adult heart only transplants.

2.6 Retrospective analysis of transplants performed since 1 January 2017, using the revised expected 30-day mortality rates (2013-2016), indicated there would have been no signals for either adult or paediatric transplant centres.

#### **CHANGES:**

2.7 The baseline time period used to calculate the expected mortality rates will be updated to 1 January 2013 to 31 December 2016 for both adult and paediatric heart only transplants.

### 3. DCD HEART TRANSPLANTATION

3.1. There have been 57 UK adult DCD heart transplants performed at 3 centres between February 2015 and February 2018. There has also been one paediatric DCD heart transplant in November 2013. Thirty-day outcome was known for all patients and all but one patient survived the first 30-days post-transplant.

3.2. **Table 2** shows the impact of including DCD heart transplantation on the current centre specific 30-day mortality rates for adult and paediatric heart only transplants along with the corresponding rates for the most recent four-year time period. The current expected mortality rate did not change as the first DCD heart transplant was not performed until 2013. The revised rates decreased by 1.1% for adult transplants at both Harefield (14.6% to 13.5%) and Papworth (5.2% to 4.1%) and 0.1% for paediatric transplants at Newcastle (8.6% to 8.5%).

	DBD only Expected mortality (%)			DBD and DCD Expected mortality (%)	
	Current rate (2008-2011)	Revised rate (2013-2016)	Centre rate change	Revised rate (2013-2016)	Centre revised rate change
<b>ADULT</b>					
Newcastle	16.2 (10.6, 21.8)	10.2 (6.3, 14.0)	-6.0	10.2 (6.3, 14.0)	0.0
Papworth	9.1 (5.7, 12.4)	5.2 (2.8, 7.5)	-3.9	4.1 (2.3, 6.0)	-1.1
Harefield	23.8 (15.5, 32.1)	14.6 (9.9, 19.4)	-9.2	13.5 (9.1, 17.9)	-1.1
Birmingham	12.1 (7.5, 16.7)	10.0 (6.4, 13.6)	-2.1	10.0 (6.4, 13.6)	0.0
Manchester	10.7 (5.4, 16.0)	5.2 (2.6, 7.8)	-5.5	5.2 (2.6, 7.8)	0.0
Glasgow	30.3 (19.9, 40.6)	14.0 (7.9, 20.2)	-16.3	14.0 (7.9, 20.2)	0.0
<b>National</b>	<b>14.3 (12.1, 16.5)</b>	<b>8.9 (7.5, 10.4)</b>	<b>-5.4</b>	<b>8.3 (7.0, 9.7)</b>	<b>-0.6</b>
<b>PAEDIATRIC</b>					
Newcastle	2.5 (0.1, 4.9)	8.6 (4.4, 12.7)	6.1	8.5 (4.4, 12.6)	-0.1
GOSH	5.3 (2.1, 8.4)	3.2 (0.4, 5.9)	-2.1	3.2 (0.4, 5.9)	0.0
<b>National</b>	<b>4.0 (1.9, 6.0)</b>	<b>6.0 (3.4, 8.5)</b>	<b>2.0</b>	<b>5.9 (3.4, 8.5)</b>	<b>-0.1</b>

3.3. Retrospective analysis indicated there would be no additional signals when DCD hearts were included regardless of whether the current or the revised rates were used.

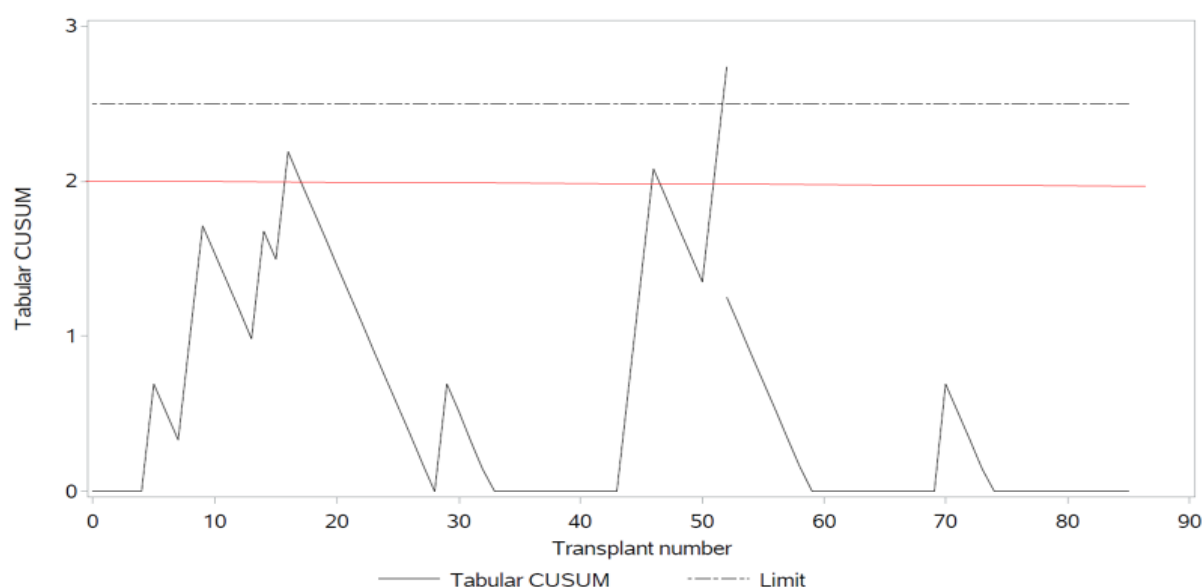
#### ADVICE REQUIRED

3.4 Members are asked to advise whether DCD heart transplants should be included in the CUSUM monitoring now or whether it should be included later, e.g. when established at more than three adult transplant centres.

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

- 4.1 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.
- 4.2 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.
- 4.3 **Figure 1** shows the tabular CUSUM chart for a heart 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 heart transplant centre, 1 January 2011 to 28 February 2018**



- 4.4 Only one adult heart transplant signal 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 *two additional adult heart signals* 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

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

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**April 2018**

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## APPENDIX A - REVIEW OF 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	0.121	1.5	0.182	191	58	0.242	80	20
		2.0		424	87		145	27
		2.5		793	115		280	35
		3.0		1468	144		508	45
		3.5		2551	178		881	53
Paediatric	0.056	1.5	0.084	452	131	0.112	171	43
		2.0		950	195		339	61
		2.5		1875	268		645	80
		3.0		3381	341		1166	101
		3.5		5991	416		2060	121

- 5 **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 12.1% in the original time period to 8.9% in the

revised baseline period. This decrease in mortality rates has seen an increase in the  $ARL_0$  (280 to 389) leading to a potential delay in a genuine signal arising.

- 6 The corresponding national mortality rates for paediatric transplants was 5.6% in the original time period and 6.0% 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.**

Transplant type	p0	Limit	Odds ratio=1.5			Odds ratio=2.0		
			p1	$ARL_0$	$ARL_1$	p1	$ARL_0$	$ARL_1$
Adult	0.143	1.5	0.215	157	48	0.286	62	16
		2.0		347	72		116	22
		2.5		663	93		226	29
		3.0		1194	119		411	36
		3.5		2110	148		743	43
Paediatric	0.040	1.5	0.060	649	187	0.080	241	61
		2.0		1379	281		490	85
		2.5		2617	380		932	113
		3.0		4849	488		1685	143
		3.5		8458	589		2892	172

Transplant type	p0	Limit	Odds ratio=1.5			Odds ratio=2.0		
			p1	$ARL_0$	$ARL_1$	p1	$ARL_0$	$ARL_1$
Adult	0.089	1.5	0.134	276	81	0.178	107	27
		2.0		594	120		208	38
		2.5		1137	160		389	48
		3.0		2054	208		717	60
		3.5		3586	256		1241	72
Paediatric	0.060	1.5	0.089	416	124	0.119	161	41
		2.0		901	184		316	57
		2.5		1731	250		602	75
		3.0		3196	315		1092	94
		3.5		5445	387		1913	113