NHS BLOOD AND TRANSPLANT
ORGAN DONATION AND TRANSPLANTATION DIRECTORATE

KIDNEY ADVISORY GROUP

EFFECT OF CIT ON OUTCOMES OF DBD AND DCD DONOR KIDNEY TRANSPLANTS

INTRODUCTION

1 It has previously been shown that cold ischaemia time (CIT) has a significant impact on transplant outcome in kidneys donated after circulatory death. Summers et al (Lancet 2010 and 2013) described a poorer graft survival with CIT >12 hours for DCD kidney transplants however this was not seen with DBD donor transplants.

2 Over recent years, CIT has been reduced through the efforts of multiple teams. UK transplant centres and teams work hard to transplant organs in a timely manner, however this raises issues of out-of-hours workload and long-term sustainability. A balance must be sought to ensure that transplants occur at the highest possible standard with the resources we have. Organisational restructuring with changing allocation schemes can affect the distance that organs travel, and advances in the use of machine perfusion technology also herald many changes. In addition, as median CITs drop, the perceived 'acceptability' of CITs may change (e.g. due to unfamiliarity with the outcomes of organs implanted with prolonged CITs), leading to potential decline of organs at the upper limits of biologically acceptable CITs.

3 This analysis was performed to update the Kidney Advisory Group (KAG) of the impact of CITs on DBD and DCD donor kidney transplant outcomes. Analyses were also performed to investigate the effect of prolonged CITs of kidneys of varying organ 'quality', as quantified using the new UKKDRI developed for the 2019 Kidney Offering Scheme.

DATA

4 Data were obtained from the UK Transplant Registry on deceased donor adult single kidney-only transplants between 1 January 2000 and 31 December 2017 in the UK. Only transplants from donors over the age of 18 into recipients over the age of 18 were included.

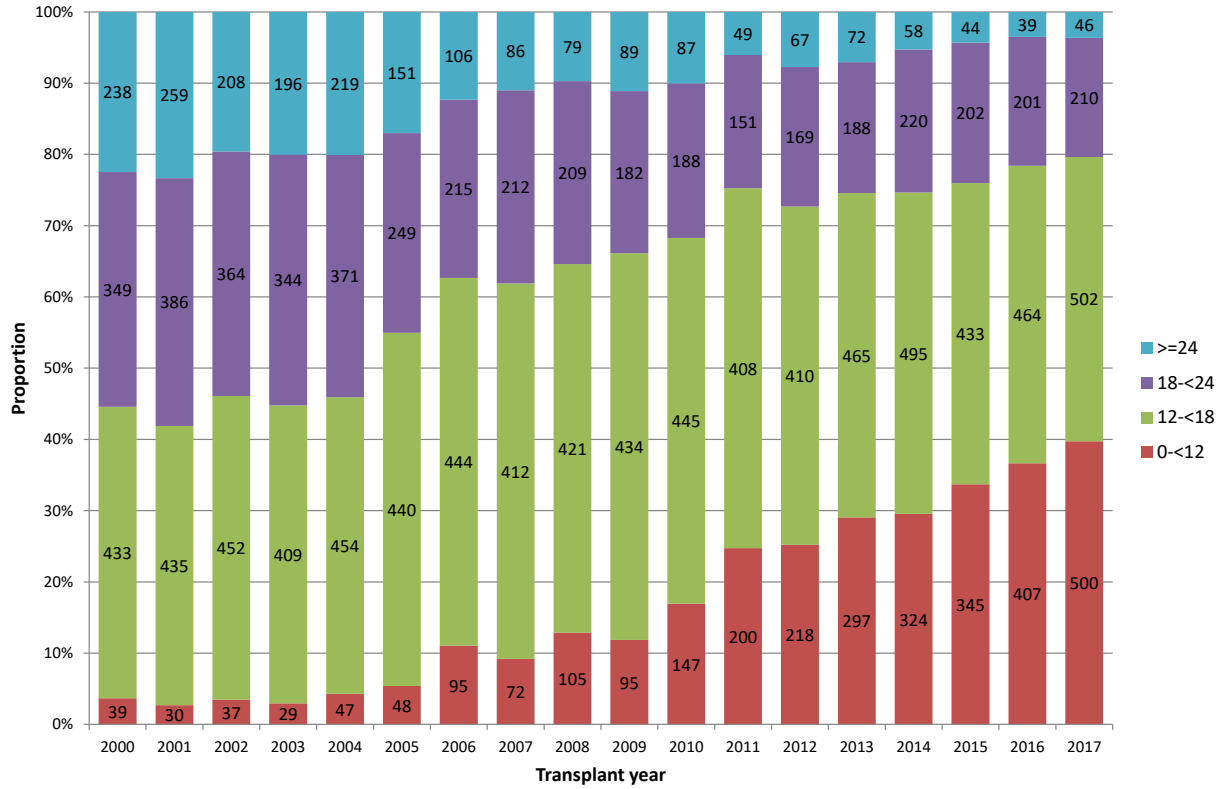
5 All kidneys that had undergone warm or cold machine perfusion were excluded from the analysis. An 'upper limit' for cold ischaemia time was set at 48 hours; any data outside this time period were excluded due to uncertainties with accuracy.

6 When considering donor / organ 'quality', the new UKKDRI used for the 2019 Kidney Offering Scheme was used. This takes the following donor factors into consideration: donor height, history of hypertension, sex, CMV status, eGFR at retrieval, and days in hospital. Patients were stratified according to these variables and split into quartiles based on death-censored graft survival, with 'D1' having superior outcomes (see Appendix A).

RESULTS

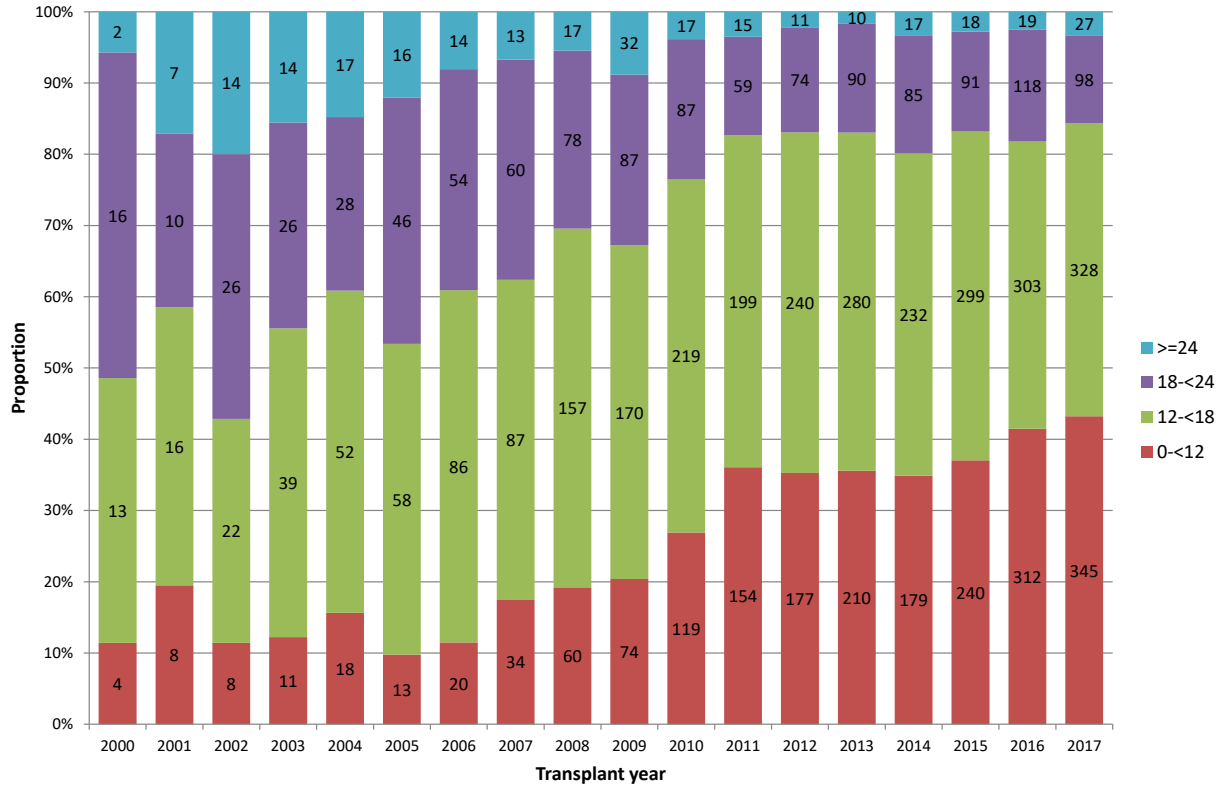
7 **Figure 1** shows the proportion of DBD donor kidney-only transplants by CIT group. Prior to the introduction of the 2006 Kidney Allocation Scheme on 3rd April 2006 at least half of all DBD kidney only transplants had a CIT of greater than 18 hours. Since the introduction, CIT has been reducing and in 2017 only 20% had a CIT greater than 18 hours with 40% having a CIT of less than 12 hours.

Figure 1 Proportion of DBD kidney only transplants in the UK by CIT group, 1 January 2000 – 31 December 2017



8 **Figure 2** shows the proportion of DCD donor kidney-only transplants by CIT group. Following the publication of Summers et al in 2010 and 2013 CITs for DCD donor kidney transplants reduced, with fewer than 20% of transplants being performed within 12 hours prior to these dates to more than 40% in 2017.

Figure 2 **Proportion of DCD kidney only transplants in the UK by CIT group, 1 January 2000 – 31 December 2017**



9 **Figure 3** shows 5 year graft survival following adult DBD donor kidney-only transplantation in the UK between 1 January 2000 and 31 December 2017 by time period. Prior to the 2006 Kidney Allocation Scheme a significant difference was observed across the CIT groups (p=0.0006). In the period 2006-2017 no significant difference is observed (p=0.11). Similar outcomes were observed for DBD 'D4' kidney transplants only (Appendix B). Time periods were further separated into cohorts of 2006 – 2011 and 2012- 2017 for DBD kidney transplants but no differences were observed.

10 **Figure 4** shows 5 year graft survival following adult DCD donor kidney-only transplantation in the UK between 1 January 2006 and 31 December 2017. A significant difference was observed across the CIT groups (p=0.0003) with a CIT of 12 hours or more having inferior graft survival. DCD donor kidneys with CITs of 24 hours or more still have a 5-year graft survival of more than 80%. Similar outcomes were observed for DCD 'D4' kidney transplants only (Appendix B). A further analysis was conducted with CIT groups of 0-8 hours and 8-10 hours however no significant difference in graft survival was observed in these cohorts. In addition, time periods were further separated into cohorts of 2006 – 2010 and 2011- 2017 for DCD kidney transplants but no differences were observed.

Figure 3 5 year graft survival following adult DBD kidney only transplant in the UK, 1 January 2000 – 31 December 2017

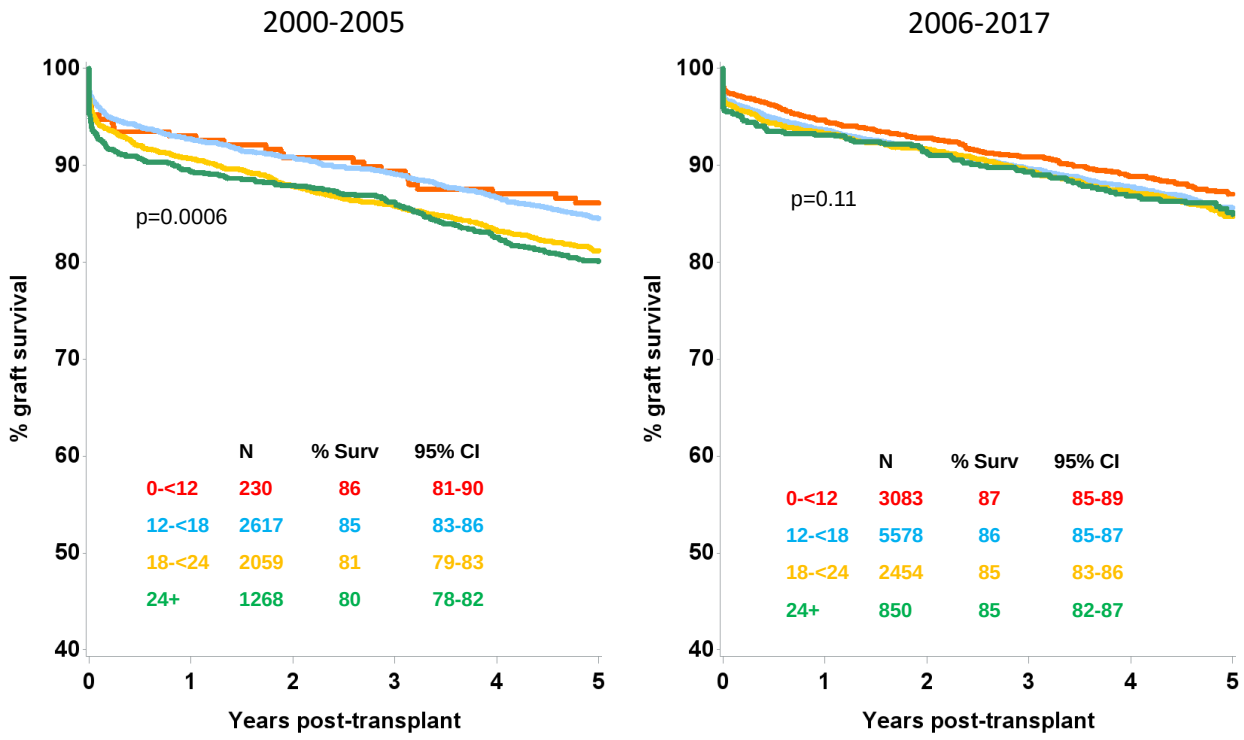
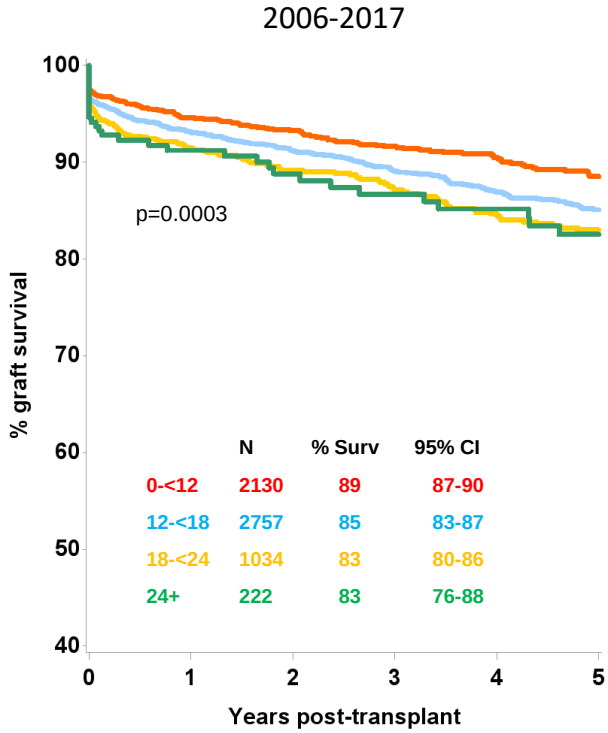


Figure 4 5 year graft survival following adult DCD kidney only transplant in the UK, 1 January 2000 – 31 December 2017



11 **Figure 5** shows the distribution of CITs by new UKKDRI quartiles for DBD and DCD donor kidney-only transplants between 1 January 2006 and 31 December 2017, separately. The proportion of transplants with a CIT of 18 hours or more when the donor was D4 compared with D1 was similar for both DBD (30% D1 v 26% D4) and DCD donor kidney transplants (22% D1 v 19% D4).

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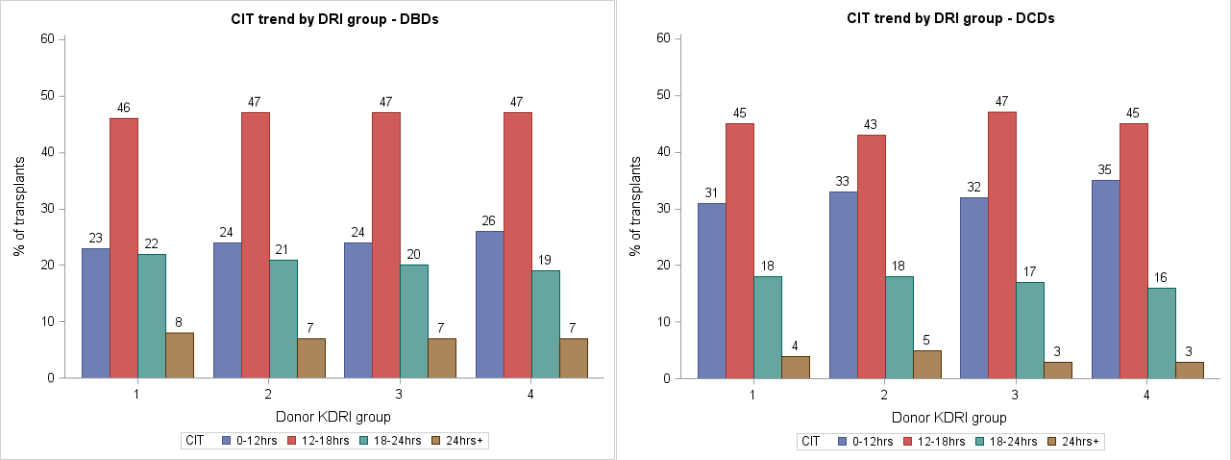
Figure 4 Proportion of adult DBD and DCD kidney only transplant in the UK by CIT and UKKDRI, 1 January 2000 – 31 December 2017



13 A multivariable Cox-proportional hazards model was fitted, adjusting for donor age, donor cause of death, recipient age, waiting time to transplant, primary renal disease, HLA mismatch level, recipient ethnicity, and year of transplant. **Table 1** shows the hazard ratios for CIT group after it was added to the model for DBD and DCD donor kidney transplants separately.

Table 1 Cox-proportional hazards model

CIT Group	Hazard Ratio	95% CI	p-value
DBD			
0-<12	1.00	-	-
12-<18	1.04	0.88 – 1.18	0.6
18-<24	1.11	0.91 – 1.30	0.3
24+	1.14	0.90 – 1.43	0.3
DCD			
0-<12	1.00	-	-
12-<18	1.28	1.04 – 1.56	0.02
18-<24	1.63	1.24 – 1.99	0.0002
24+	1.73	1.08 – 2.39	0.02

Adjusted for donor age, donor cause of death, recipient age, waiting time to transplant, primary renal disease, HLA mismatch level, recipient ethnicity, year of transplant

SUMMARY

14 Over the past decade, CITs have decreased significantly likely due to multiple factors. Univariate analysis of DCD donor kidney transplants shows a statistically significant decreasing graft survival when CITs exceed 12 hours. There is no CIT threshold effect for DBD donor kidney transplants for the more recent time period, although 80% of DBD transplants now have a CIT of less than 18 hours.

15 This trend is also true when known significant risk factors are adjusted for using a multivariable Cox Proportional Hazards Model.

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Appendix A

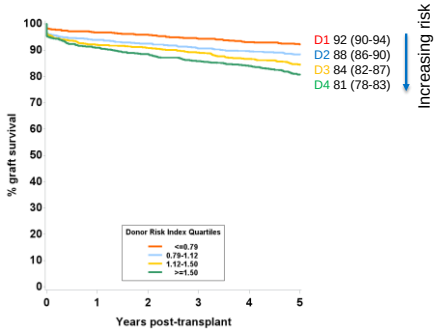
Donor Risk Index (DRI)

Validation dataset

NHS Blood and Transplant

Donor Factor	Hazard Ratio	p-value
Age	1.02	<0.0001
Height	0.86	0.0005
Hypertension	1.15	0.1
CMV	1.20	0.02
Hospital stay	1.02	0.006
eGFR	0.98	0.02
Female	0.83	0.04

C-statistic = 0.64

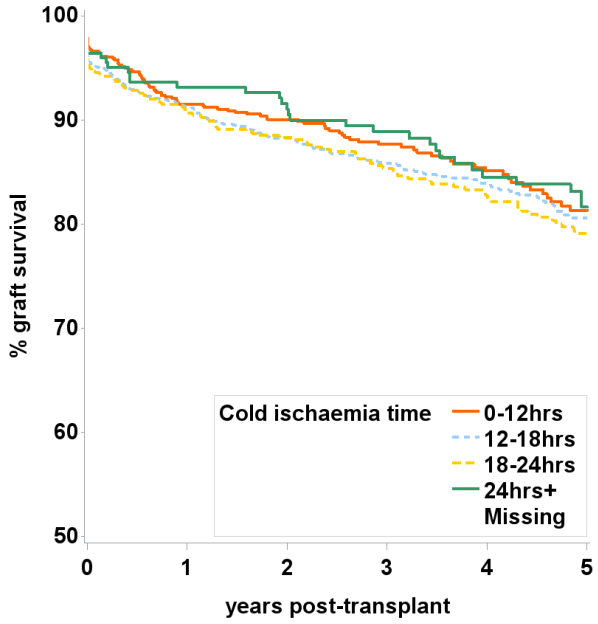


Slide courtesy of presentation ‘A new deceased donor kidney offering scheme in the UK’, Lisa Mumford, NHSBT

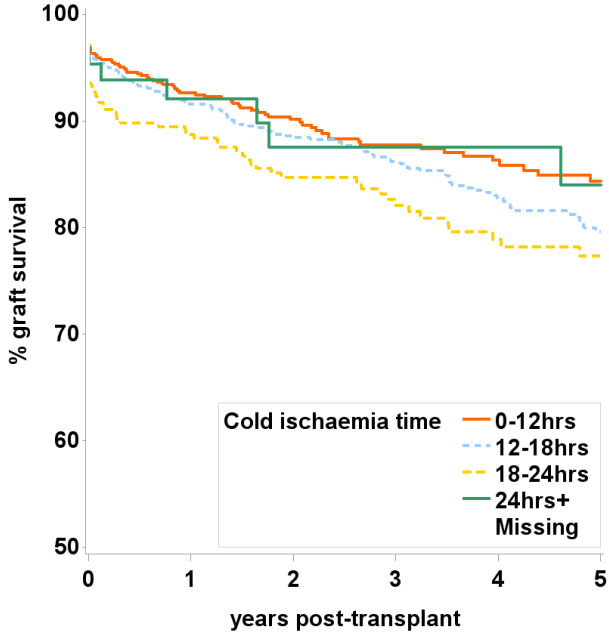
Appendix B

Kaplan Meier survival graphs to show 5 year unadjusted DCGS for DBD and DCD 'DR4' kidneys.

DBD DR4 2006 – 2011, p=0.60



DCD DR4 2006 – 2011, p=0.048



CIT (hrs)	Frequency	%	Survival	Lcl	UCL
0-12	890	26	81.1	77.2	84.4
12-18	1636	47	80.5	78	82.7
18-24	660	19	79.1	75.1	82.5
24+	226	7	81.9	75.4	86.8
Missing	40	1	77	60.4	87.4

CIT (hrs)	Frequency	%	Survival	Lcl	UCL
0-12	741	35	83.8	79.8	87
12-18	960	45	79.4	75.8	82.5
18-24	339	16	77	71	82
24+	65	3	84.2	69.8	92.1
Missing	15	1	70	37.2	87.9