NHS BLOOD AND TRANSPLANT

LIVER ADVISORY GROUP

NATIONAL LIVER OFFERING SCHEME - UPDATING THE ESTIMATES USED TO CALCULATE THE ESTIMATED TRANSPLANT BENEFIT SCORE

RESULTS

1. INTRODUCTION

1.1. In seeking to update cohorts and model parameter estimates for the Transplant Benefit Score used in the National Liver Offering Scheme (NLOS), some unexpected results occurred. Investigations led to investigating the impact of the choice of registration year for the baseline model and it was agreed at the Spring 2021 Liver Advisory Group (LAG) that the registration year included in the baseline model should be the latest group (2013-2016) rather than earliest individual registration year currently implemented.

1.2. This paper examines the impact of updating the post-transplant survival cohort as well as simplifying the models by only including the statistically significant factors.

2. BASELINE SURVIVOR FUNCTIONS

2.1. There was variation in the position of the M1 baseline survivor function (and resulting estimate of survival post listing (M1)), depending upon the registration year selected as the baseline. There was a lack of consistency within and between cancer and non-cancer trends, as shown in **Figures 1, 2 and 3**. Baselines were, as originally defined:

- **Non-cancer:** 51-year-old male with ALD registered in 2006 who was not on renal replacement therapy and was an outpatient with a bilirubin of 62, creatinine of 84, INR of 1.4, sodium of 136.
- **Cancer:** 57-year-old male registered in 2009 who was not on renal replacement therapy and was an outpatient with a bilirubin of 22, creatinine of 75, INR of 1.2 and sodium of 138. The cancer variable values were maximum AFP of 21, maximum tumour size of 2.6cm and only one tumour.

2.2. **Figure 4** shows the potential impact on the Transplant Benefit Score (TBS) for patients active on the waiting list, with different baseline registration years.

3. SIMULATION RESULTS

3.1. Simulations were run to explore the impact of choice of baseline registration year on resultant 'transplants' and the differing impacts on transplant patient demographics, estimated deaths on the list and estimated patient life years of the cohort. **Figures 5A and 5B** show the baseline survivor functions used for the first 10 simulations, using observed data from the UK Transplant Registry. There was a lack of events (deaths) beyond two years for both the cancer and non-cancer cohorts as the vast

majority of patients have reached an outcome (eg death, transplant, removal) within two years of being listed. This lack of data may lead to unreliable estimation of the survival on the list. Published data and data from other registries were thus used to derive the baseline survivor functions used in Simulations 11 to 14. Details of simulations are shown in **Table 1**. They are based on 559 liver donors and 1194 patient registrations,and generate 556 liver 'transplants' in each simulation. Note that Simulation 1 reflects the current scheme, against which other simulations can be compared.

3.2. **Table 2** shows key results from the Simulations. Key conclusions from Simulations 1-10 were:

- all simulations resulted in fewer estimated patient deaths / removals due to condition deterioration than actually occurred in 2018/2019.
- HCC patients appeared as the top named patient for less than 10% of donors in Simulations 1,2, 4 and 6. Given that 21% of the simulation waiting list were HCC, these were not considered appropriate as they under-prioritised HCC patients.
- Simulations 8 and 10 resulted in a higher proportion of HCC patients as the top named patient than the waiting list cohort. These were not considered appropriate as deemed to over prioritise HCC patients.
- Of remaining simulations based on real data for baseline survivor functions (Simulations 3, 5, 7 and 9), Simulations 3 and 7 resulted in a higher estimated number of deaths and Simulations 3 and 5 resulted in lower estimated patient life years. **Thus Simulation 9 was preferred.**

3.3. Concerns remained about Simulation 9, which despite giving good overall results, (counter-intuitively) used the earliest year group for the baseline (into which group new registrations are allocated). The baseline survivor functions were still not felt to reflect clinical experience and concerns remained about the paucity of reliable data beyond 2 years for M1. Simulated functions were therefore explored.

3.4. Simulated baseline survivor functions were developed as follows:

3.4.1. **CLD** survival was estimated for a 51-year old male with ArLD. The baseline was MELD 15 and UKELD 56. Mortality was applied daily according to published estimates of short-term mortality over the 5-year follow-up period at that disease severity (Barber et al, Transplantation 2011).

3.4.2. **Cancer** survival was estimated for a 57-year old male with HCC (single tumour measuring 2.6cm). Estimates of waiting list survival were made from published overall survival outcomes for persons with BCLC-A HCC who were considered potentially suitable for transplant but not eventually transplanted (Vitale et al, Lancet Oncology, 2011, https://doi.org/10.1016/S1470-2045(11)70144-9).

3.5. Simulations were run using the simulated baseline survivor functions with different cohorts as shown in **Table 1**. While M2 was unchanged from the currently used cohort and model in Simulations 1-12 so that M2 could be examined fully, clearly the intention is to update both cohorts to include more recent data, and thus Simulations 13 and 14 use an updated cohort for M2 (survival post-transplant) also, (ie 2006-2016 rather then 2006-2012).

3.6. The results in **Table 2** show little difference in results of Simulations 11-14. A similar number of expected deaths and patient life-years were seen, with priority for HCC patients dropping slightly when updating M2 to include latest data.

3.7. More detailed results of actual allocation and simulated allocation in Simulations 12-14 are shown in Appendix 1. **Table 3** and **Table 4** shows that among the few estimated deaths in the simulations, there is no pattern that causes any concern in terms of the patient characteristics these are associated with. They broadly reflect what has been seen in practice.

3.8. **Table 5** shows the characteristics of the patients selected for transplant in the same simulations while **Table 6** shows either the fishers exact p-value or the Wilcoxon p-value when comparing the demographics of each simulation with actual transplants. There were no statistically significant differences for most characteristics between the distribution of "transplants" in simulations 12, 13 and 14 compared with the actual transplants performed involving livers included in the donor cohort in 2018/2019. There were, however, statistically significant difference at a 10% significance level in

- age for all three simulations,
- creatinine and number of tumours when comparing simulation 12 versus actual
- HCV when comparing simulation 13 versus actual

3.9. **Figures 6A to 11** show these factors for each simulation.

3.10. For most characteristics, there are few changes in the distribution of 'transplants', although we know that in terms of aetiology, more HCC patients are the top-named patient in the simulation, compared with what has been happening in practice under the current iteration of the National Liver Offering Scheme. This change sees more equitable access to transplant for HCC patients (21% of the waiting list, 12% of actual transplants, 17% of transplants in Simulations 11 and 12 and 15% of transplants in Simulation 13 and 14), with a consequent impact on other patients (mostly PBC and AID). The grey shading in the table highlights the distribution of transplants across aetiology in the different scenarios.

3.11. The other noticeable difference is in terms of age of patients selected for transplant (also highlighted). There are fewer transplants allocated to younger patients compared with what is seen in practice and the composition of the waiting list. This reflects the older age of the HCC patients compared with others, and the increased priority afforded them compared with the current situation.

4. **SUMMARY**

4.1. The view of the FTWU considering the simulation results is that:

- Of simulations with real data baseline survivor functions, Simulation 9 was preferred but concerns remained about the clinical relevance of the baseline and the counter-intuitive choice of earliest year group as the baseline, to which new registrations are allocated.
- Simulated baselines seemed more clinically plausible and stable (Simulations 11-12).
- Simulations 13 and 14 gave good overall estimated results using the metrics of estimated deaths, allocation to HCC patients and estimated patient life-years acknowledging that more livers are allocated to older patients as a result of more equitable allocation to (older) HCC patients.

4.2. The FTWU recommend simulation 14 should be implemented which uses
   4.2.1. updated M1 and M2 cohorts (2006-2016/ 2009-2016)
   4.2.2. Simulated M1 baseline survivor functions for both non-cancer and cancer
   4.2.3. Only statistically factors in all models

ACTION: Members are asked to consider how the transplant benefit score should be updated.

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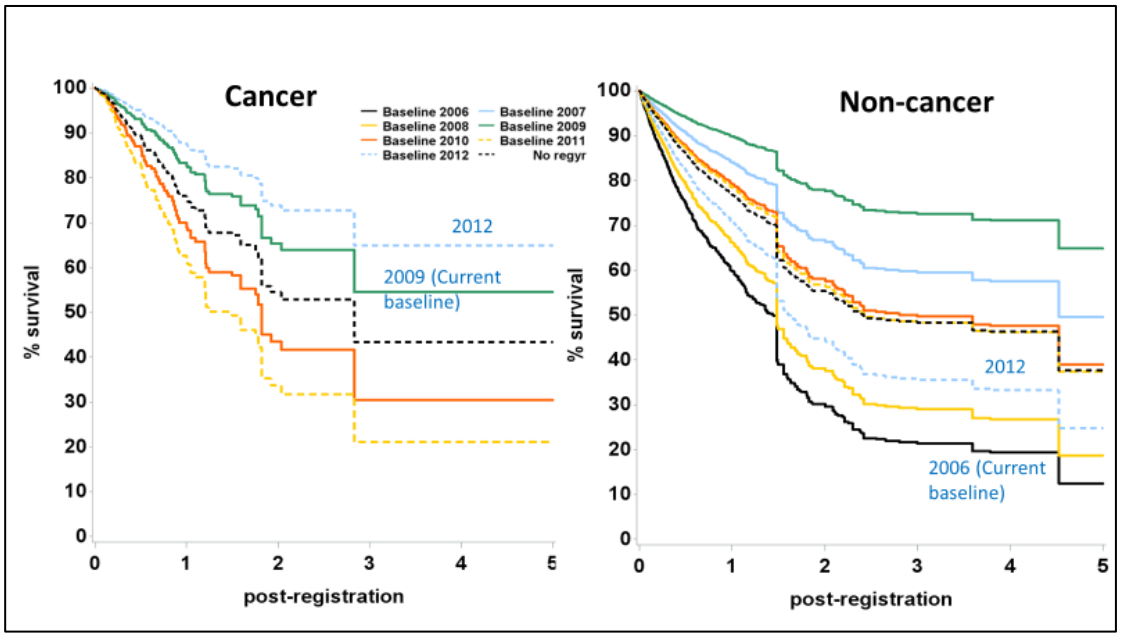

Figure 1 Baseline survivor functions by registration year for current cohorts (2006-2012 for non-cancer and 2009-2012 for cancer)

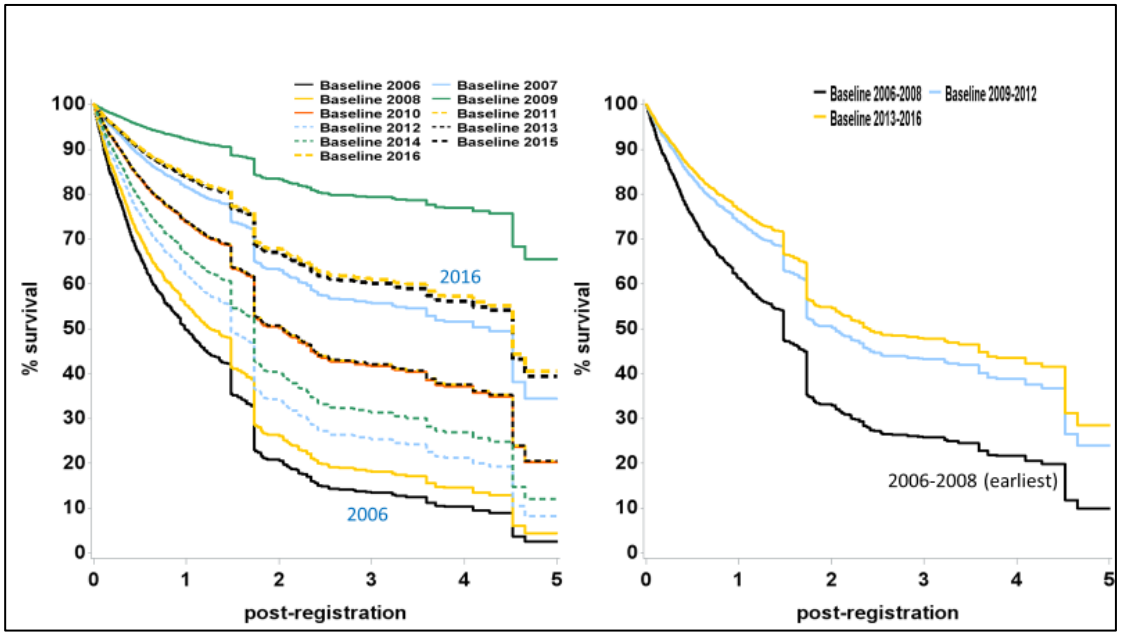

Figure 2 Baseline survivor functions by registration year and grouped registration year for updated non-cancer cohort (2006-2016)

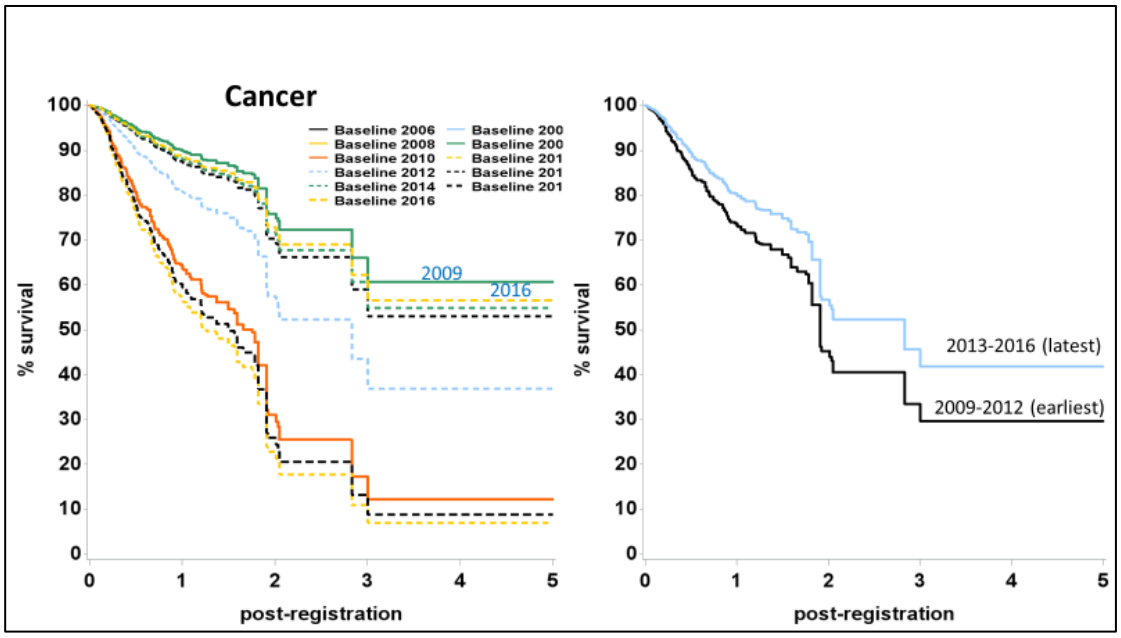

Figure 3 Baseline survivor functions by registration year and grouped registration year for updated cancer cohort (2009-2016)

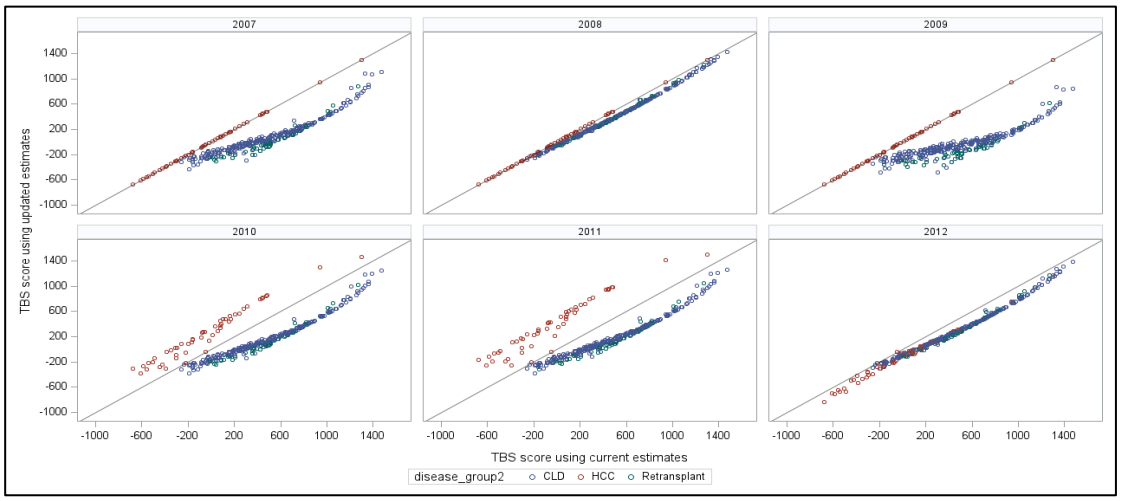

Figure 4 Potential TBS score for patients active on the waiting list using current (x-axis) and updated (y-axis) cohorts/estimates, by baseline registration year

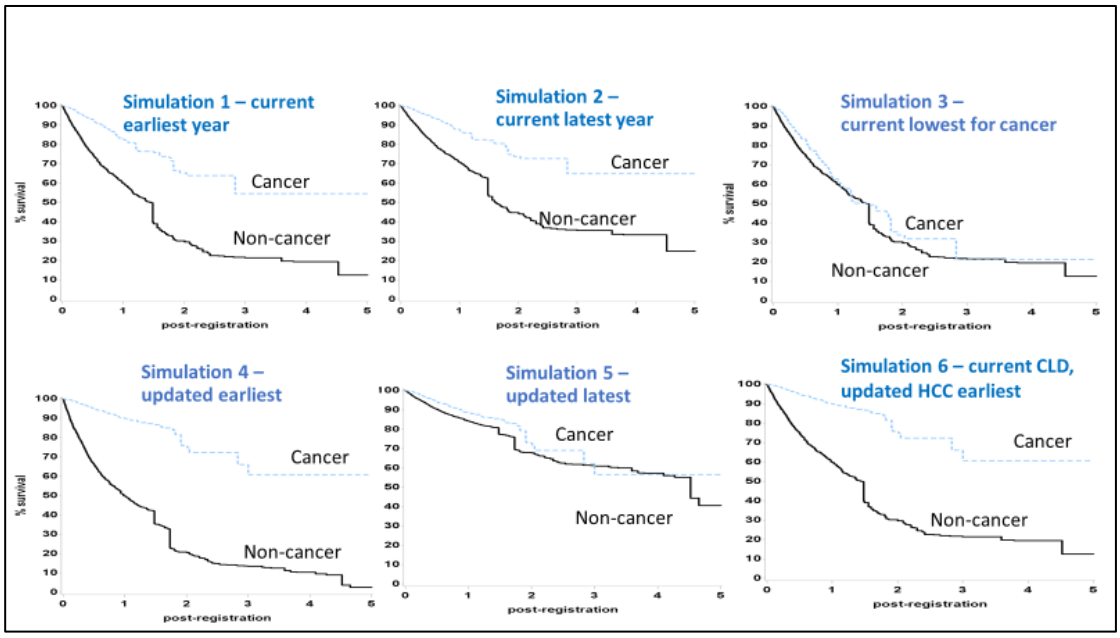

Figure 5A M1 Baseline survivor functions for simulations 1-6

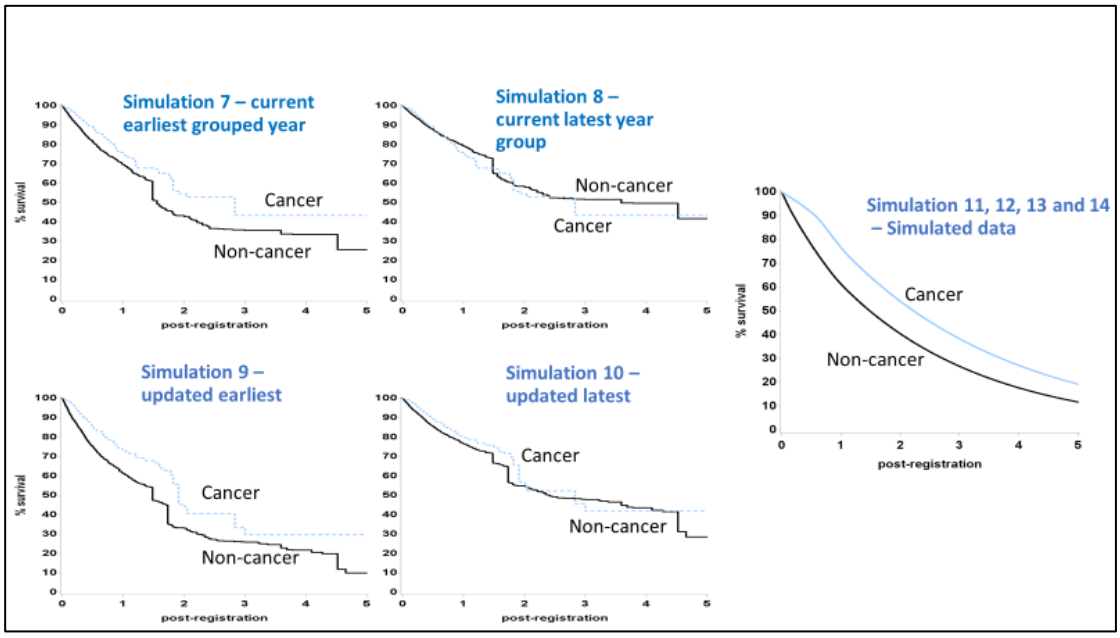

Figure 5B M1 Baseline survivor functions for simulations 7-14

Table 1 Simulations run

Simulation	Details (M2 as current for Sims 1 – 12)
S1	Current cohort (and models) with earliest baseline year (2006 or 2009)
S2	Current cohort with latest year as baseline (2012)
S3	Current cohort with earliest year (2006) for non-cancer and lowest baseline for cancer (2011)
S4	Updated cohort with earliest year as baseline (2006 or 2009)
S5	Updated cohort with latest year as baseline (2016)
S6	Current cohort with earliest year as baseline for non-cancer (2006) and updated cohort with earliest year as baseline for cancer (2009)
S7	Current cohort with earliest baseline year group for non-cancer (2006-2008) and no registration year for cancer
S8	Current cohort with latest baseline year group for non-cancer (2009-2012) and no registration year for cancer
S9	Updated cohort with earliest baseline year group (2006-2008 for non-cancer and 2009-2012 for cancer)
S10	Updated cohort with latest baseline year group (2013-2016 for both)
S11	Updated cohort with earliest baseline year group (2006-2008 for non-cancer and 2009-2012 for cancer) using **simulated** M1 baseline survivor functions for both cancer and non-cancer
S12	Updated cohort with latest baseline year group (2013-2016 for both) using **simulated** M1 baseline survivor functions for both cancer and non-cancer
S13	Updated cohorts for M1 and M2 with latest baseline year group for M1 (2013-2016) and **simulated** M1 baseline survivor functions for both cancer and non-cancer
S14	Updated cohorts for M1 and M2 with models containing only statistically significant factors with latest baseline year group for M1 (2013-2016) and **simulated** M1 baseline survivor functions for both cancer and non-cancer

Table 2 Mortality and patient-years associated with the current and simulated liver allocation scheme, for 1194 patient registrations between 1 April 2018 and 31 March 2019

	No (%) died/ removed[1]	No (%) HCC patient as top named patient	Patient-years using M1 from S12
Waiting list	-	256 (21)	-
Actual allocation	61 (5)	66 (12)	-
Simulation 1	49 (4)	26 (5)	4086
Simulation 2	49 (4)	30 (5)	4067
Simulation 3	50 (4)	104 (16)	3778
Simulation 4	51 (4)	15 (3)	4131
Simulation 5	45 (4)	116 (21)	3740
Simulation 6	49 (4)	13 (2)	4129
Simulation 7	51 (4)	82 (15)	3867
Simulation 8	52 (4)	131 (24)	3659
Simulation 9	47 (4)	98 (18)	3826
Simulation 10	42 (4)	126 (23)	3725
Simulated baselines:			
Simulation 11	49 (4)	96 (17)	3833
Simulation 12	46 (4)	97 (17)	3836
Simulation 13	47 (4)	81 (15)	3897
Simulation 14	48 (4)	82 (15)	3886

[1] Removed due to condition deteriorated

APPENDIX 1

Table 3 Characteristics of transplant list deaths/removals

Variable	Levels	All regs (n=1194)	Actual N (n=61)	Actual % of deaths	Actual % of all reg	Simulation 12 N (n=46)	Simulation 12 % of deaths	Simulation 12 % of all reg	Simulation 13 N (n=47)	Simulation 13 % of deaths	Simulation 13 % of all reg	Simulation 14 N (n=48)	Simulation 14 % of deaths	Simulation 14 % of all reg
Age	Median (IQR)	55 (45, 62)	59 (51, 65)			57.5 (46, 65)			58 (50, 65)			58 (50.5, 65)		
Age group														
	0-16	15 (1)	0	0	0	0	0	0	0	0	0	0	0	0
	17-29	96 (8)	1	2	1	1	2	1	1	2	1	1	2	1
	30-39	109 (9)	7	11	6	8	17	7	7	15	6	6	13	6
	40-49	171 (14)	4	7	2	3	7	2	3	6	2	3	6	2
	50-59	409 (34)	21	34	5	15	33	4	15	32	4	17	35	4
	60-69	379 (32)	26	43	7	18	39	5	19	40	5	19	40	5
	70+	15 (1)	2	3	13	1	2	7	2	4	13	2	4	13
Gender	Male	788 (66)	44	72	6	31	67	4	31	66	4	31	65	4
	Female	406 (34)	17	28	4	15	33	4	16	34	4	17	35	4
Blood group	O	567 (47)	33	54	6	25	54	4	24	51	4	25	52	4
	A	447 (37)	21	34	5	16	35	4	17	36	4	17	35	4
	B	136 (11)	6	10	4	5	11	4	6	13	4	6	13	4
	AB	44 (4)	1	2	2	0	0	0	0	0	0	0	0	0
Aetiology	Cancer	256 (21)	18	30	7	9	20	4	12	26	5	12	25	5
	HCV	35 (3)	1	2	3	0	0	0	0	0	0	1	2	3
	ALD	320 (27)	11	18	3	9	20	3	8	17	3	8	17	3
	HBV	15 (1)	0	0	0	0	0	0	0	0	0	0	0	0
	PSC	111 (9)	1	2	1	1	2	1	1	2	1	1	2	1
	PBC	79 (7)	1	2	1	1	2	1	1	2	1	1	2	1
	AID	93 (8)	3	5	3	3	7	3	3	6	3	3	6	3
	Metabolic liver disease	131 (11)	12	20	9	11	24	8	10	21	8	11	23	8
	Other liver disease	61 (5)	5	8	8	4	9	7	5	11	8	5	10	8
	≥ 1 previous tx	93 (8)	9	15	10	8	17	9	7	15	8	6	12	6
HCV	Yes	117	3	5	3	2	4	2	2	4	2	3	6	3
	No	1077	58	95	5	44	96	4	45	96	4	45	94	4
Creatinine	Median (IQR)	73 (60, 89)	80 (65, 106)			79 (63, 106)			80 (65, 108)			78.5 (63, 107)		
Bilirubin	Median (IQR)	40 (23, 81)	33 (17, 57)			36 (18, 115)			33 (13, 115)			33 (18, 121)		
INR	Median (IQR)	1.3 (1.2, 1.6)	1.3 (1.2, 1.6)			1.3 (1.2, 1.8)			1.3 (1.1, 1.8)			1.3 (1.1, 1.8)		
Sodium	Median (IQR)	137 (134, 140)	136 (133, 139)			135 (132, 138)			136 (133, 140)			136 (133, 140)		

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Table 3 Characteristics of transplant list deaths/removals

Variable	Levels	All regs (n=1194)	Actual N (n=61)	Actual % of deaths	Actual % of all reg	Simulation 12 N (n=46)	Simulation 12 % of deaths	Simulation 12 % of all reg	Simulation 13 N (n=47)	Simulation 13 % of deaths	Simulation 13 % of all reg	Simulation 14 N (n=48)	Simulation 14 % of deaths	Simulation 14 % of all reg
Potassium	Median (IQR)	4.2 (3.9, 4.5)	4.2 (3,9, 4.6)			4.2 (3.9, 4.6)			4.2 (3.9, 4.6)			4.3 (4.0, 4.7)		
Albumin	Median (IQR)	32 (28, 37)	32 (26, 35)			31 (24, 35)			32 (26, 36)			32 (26, 36)		
Renal replacement therapy	Yes	16 (1)	3	5	19	3	7	19	4	9	25	4	8	25
	No	1178 (99)	58	95	5	43	93	4	43	91	4	44	92	4
Patient location	Inpatient	122 (10)	15	25	12	17	37	14	16	34	13	17	35	14
	Outpatient	1072 (90)	46	75	4	29	63	3	31	66	3	31	65	3
Registration year	2014	4 (0)	0	0	0	0	0	0	0	0	0	0	0	0
	2015	8 (1)	1	2	13	0	0	0	1	2	13	1	2	13
	2016	31 (3)	2	3	6	0	0	0	1	2	3	1	2	3
	2017	119 (10)	7	11	6	7	15	6	7	15	6	6	13	5
	2018	804 (67)	47	77	6	35	76	4	34	72	4	36	75	4
	2019	228 (19)	4	7	2	4	9	2	4	9	2	4	8	2
Previous abdominal surgery	Yes	278 (23)	22	36	8	17	37	6	17	36	6	16	33	6
	No	916 (77)	39	64	4	29	63	3	30	64	3	32	67	3
Encephalopathy	Yes	408 (34)	26	43	6	22	48	5	19	40	5	21	44	8
	No	786 (66)	35	57	4	24	52	3	28	60	4	27	56	3
Ascites	Yes	661 (55)	39	64	6	33	72	5	31	66	5	33	69	6
	No	533 (45)	22	36	4	13	28	2	16	34	3	15	31	3
Diabetes	Yes	315 (26)	24	39	8	15	33	5	14	30	4	14	29	4
	No	879 (74)	37	61	4	31	67	4	33	70	4	34	71	4
Of the patients with cancer (N)		**256**	**18**			**9**			**12**			**12**		
Maximum AFP	Median (IQR)	8 (5, 20)	8 (4, 20)			5 (4, 7)			6.5 (4, 15)			8 (4, 36.5)		
Max tumour size	Median (IQR)	2.5 (1.9, 3.2)	2.6 (1.8, 2.9)			2.6 (2.2, 2.9)			2.6 (2.2, 3.1)			2.6 (2.2, 2.9)		
Number of tumours	1	178 (69)	12	67	7	7	78	4	9	75	5	8	67	4
	2	48 (19)	5	28	10	2	22	4	3	25	6	4	33	8
	3	22 (9)	0	0	0	0	0	0	0	0	0	0	0	0
	4	4 (2)	0	0	0	0	0	0	0	0	0	0	0	0
	5	4 (2)	1	6	25	0	0	0	0	0	0	0	0	0

Table 4 p-values[1] for characteristics of deaths/removals from transplant list (simulation versus actual allocation)

		S12 v actual	S13 v actual	S14 v actual
Registration age	continuous	0.5	0.8	0.9
	Grouped	0.97	>0.99	>0.99
Gender		0.7	0.5	0.4
Blood group		>0.99	0.94	0.98
Aetiology		0.98	>0.99	>0.99
HCV		>0.99	>0.99	>0.99
Creatinine	continuous	0.7	0.91	0.7
Bilirubin	continuous	0.6	0.9	0.9
INR	continuous	0.5	0.9	0.7
Sodium	continuous	0.5	0.7	0.97
Potassium	Continuous	0.8	0.7	0.5
Albumin	continuous	0.4	0.91	0.91
Renal replacement therapy		>0.99	0.5	0.7
Patient location		0.2	0.3	0.3
Registration year		0.8	0.95	0.99
Previous abdominal surgery		>0.99	>0.99	0.8
Encephalopathy		0.7	0.8	>0.99
Ascites		0.4	0.8	0.7
Diabetes		0.5	0.3	0.3
Of the patients with cancer				
Maximum AFP	continuous	0.2	0.7	0.93
Maximum tumour size	continuous	0.8	0.6	0.7
Number of tumours		>0.99	>0.99	>0.99

[1] chi-squared p-values for categorical data and Wilcoxon p-values for continuous data

Table 5 Characteristics of transplanted patients

Variable	Levels	All regs (n=1194)	Actual allocation N (n=559)	Actual allocation % of txs	Actual allocation % of all reg	Simulation 12 N (n=556)	Simulation 12 % of txs	Simulation 12 % of all reg	Simulation 13 N (n=554)	Simulation 13 % of txs	Simulation 13 % of all reg	Simulation 14 N (n=556)	Simulation 14 % of txs	Simulation 14 % of all reg
Age	Median (IQR)	55 (45, 62)	57 (47, 63)			59 (50, 64)			58 (50, 64)			58.5 (50, 64)		
Age group	<16	15 (1)	7	1	47	4	1	27	4	1	27	4	1	27
	17-29	96 (8)	49	9	51	34	6	35	35	6	36	37	7	39
	30-39	109 (9)	42	8	39	36	6	33	40	7	37	41	7	38
	40-49	171 (14)	65	12	38	51	9	30	56	10	33	53	10	31
	50-59	409 (34)	183	33	45	172	31	42	171	31	42	169	30	41
	60-69	379 (32)	208	37	55	247	44	65	236	43	62	240	43	63
	70+	15 (1)	5	1	33	12	2	80	12	2	80	12	2	80
Gender	Male	788 (66)	366	65	46	369	66	47	360	65	46	367	66	47
	Female	406 (34)	193	35	48	187	34	46	194	35	48	189	34	47
Blood group	O	567 (47)	258	46	46	258	46	46	258	47	46	258	46	46
	A	447 (37)	217	39	49	217	39	49	212	38	47	215	39	48
	B	136 (11)	51	9	38	49	9	36	48	9	35	49	9	36
	AB	44 (4)	33	6	75	32	6	73	36	6	82	34	6	77
Aetiology	Cancer	256 (21)	66	12	26	97	17	38	81	15	32	82	15	32
	HCV	35 (3)	14	3	40	13	2	37	13	2	37	15	3	43
	ALD	320 (27)	168	30	53	166	30	52	167	30	52	171	31	53
	HBV	15 (1)	14	3	93	10	2	67	10	2	67	10	2	67
	PSC	111 (9)	55	10	50	55	10	50	58	10	52	55	10	50
	PBC	79 (7)	46	8	58	35	6	44	38	7	48	37	7	47
	AID	93 (8)	57	10	61	37	7	40	37	7	40	38	7	41
	Metabolic LD	131 (11)	76	14	58	82	15	63	85	15	65	83	15	63
	Other LD	61 (5)	12	2	20	11	2	18	10	2	16	10	2	16
	≥1 previous tx	93 (8)	51	9	55	50	9	54	55	10	59	55	10	59
HCV	Yes	117 (10)	34	6	29	28	5	24	20	4	17	29	5	25
	No	1077 (90)	525	94	49	528	95	49	534	96	50	527	95	49
Creatinine	Median (IQR)	72.5 (60, 89)	76 (63, 94)			78 (64. 97)			77 (64, 97)			77.5 (64, 97)		
Bilirubin	Median (IQR)	40 (23, 81)	55 (31,114)			56 (33, 119)			60 (35, 122)			59 (35, 120)		
INR	Median (IQR)	1.3 (1.2, 1.6)	1.4 (1.2, 1.6)			1.4 (1.2, 1.7)			1.4 (1.2, 1,7)			1.4 (1.2, 1.7)		
Sodium	Median (IQR)	137 (134, 140)	136 (133, 139)			136 (133, 139)			136 (133, 139)			136 (133, 138)		
Potassium	Median (IQR)	4.2 (3.9, 4.5)	4.2 (3.9, 4.5)			4.2 (3.9, 4.6)			4.2 (3.9, 4.5)			4.2 (3.9, 4.6)		
Albumin	Median (IQR)	32 (28, 37)	31 (26, 35)			31 (27, 35)			31 (26, 35)			31 (26, 35)		
Renal replacement therapy	Yes	16 (1)	4	1	25	7	1	44	6	1	38	6	1	38
	No	1178 (99)	555	99	47	549	99	47	548	99	47	550	99	47

Table 5 Characteristics of transplanted patients

Variable	Levels		Actual allocation			Simulation 12			Simulation 13			Simulation 14		
		All regs (n=1194)	N (n=559)	% of txs	% of all reg	N (n=556)	% of txs	% of all reg	N (n=554)	% of txs	% of all reg	N (n=556)	% of txs	% of all reg
Patient location	Inpatient	122 (10)	66	12	54	58	10	48	62	11	51	64	12	52
	Outpatient	1072 (90)	493	88	46	498	90	46	492	89	46	492	88	46
Registration year	2014	4 (0)	2	0	50	2	0	50	2	0	50	2	0	50
	2015	8 (1)	0	0	0	2	0	25	1	0	13	1	0	13
	2016	31 (3)	10	2	32	10	2	32	9	2	29	9	2	29
	2017	119 (10)	60	11	50	44	8	37	43	8	36	46	8	39
	2018	804 (67)	422	75	52	417	75	52	415	75	52	418	75	52
	2019	228 (19)	65	12	29	81	15	36	84	15	37	80	14	35
Previous abdominal surgery	Yes	278 (23)	135	24	49	140	25	53	142	26	51	142	26	51
	No	916 (77)	424	76	46	416	75	45	412	74	45	414	74	45
Encephalopathy	Yes	408 (34)	213	38	52	201	36	49	208	38	51	212	38	52
	No	786 (66)	346	62	44	355	64	45	346	62	44	344	62	44
Ascites	Yes	661 (55)	349	62	53	340	61	51	345	62	52	351	63	53
	No	533 (45)	210	38	39	216	39	41	209	38	39	205	37	38
Diabetes	Yes	315 (26)	149	27	47	165	30	52	166	30	53	164	30	52
	No	879 (74)	410	73	47	391	70	44	388	70	44	392	70	41
Of the patients with cancer (N)		**256**	**66**			**97**			**81**			**82**		
AFP	Median (IQR)	8 (4.5, 20)	7 (4, 17)			8 (5, 20)			8 (4, 20)			7.5 (4, 20)		
Max tumour size	Median (IQR)	2.5 (1.9, 3.2)	2.3 (2.0, 3.0)			2.2 (1.8, 2.7)			2.2 (1.8, 2.9)			2.2 (1.7, 2.9)		
Number of tumours	1	178 (70)	52	77	29	57	59	33	52	64	29	56	68	31
	2	48 (19)	10	15	21	20	21	42	15	19	31	15	18	31
	3	22 (9)	4	6	18	16	16	73	10	12	45	8	10	36
	4	4 (2)	0	0	0	2	2	50	2	2	50	1	1	25
	5	4 (2)	1	2	25	2	2	50	2	2	50	2	2	50

Table 6 p-values[1] for characteristics of transplanted patients (simulation versus actual allocation)

		S12 v actual	S13 v actual	S14 v actual
Registration age	continuous	**0.0007**	**0.005**	**0.006**
	Grouped	**0.06**	0.18	0.15
Gender		0.8	0.9	0.9
Blood group		>0.99	0.97	>0.99
Aetiology		0.18	0.5	0.5
HCV		0.5	**0.07**	0.6
Creatinine	continuous	**0.06**	0.3	0.16
Bilirubin	continuous	0.8	0.2	0.2
INR	continuous	0.7	0.5	0.5
Sodium	continuous	0.7	0.3	0.2
Potassium	Continuous	0.7	0.9	0.7
Albumin	continuous	0.4	0.7	0.5
Renal replacement therapy		0.4	0.5	0.5
Patient location		0.5	0.8	0.93
Registration year		0.3	0.2	0.5
Previous abdominal surgery		0.7	0.6	0.6
Encephalopathy		0.5	0.85	>0.99
Ascites		0.7	>0.99	0.9
Diabetes		0.3	0.2	0.3
Of the patients with cancer				
AFP	continuous	0.3	0.5	0.7
Maximum tumour size	continuous	0.14	0.5	0.3
Number of tumours		**0.07**	0.4	0.7

[1] chi-squared p-values for categorical data and Wilcoxon p-values for continuous data

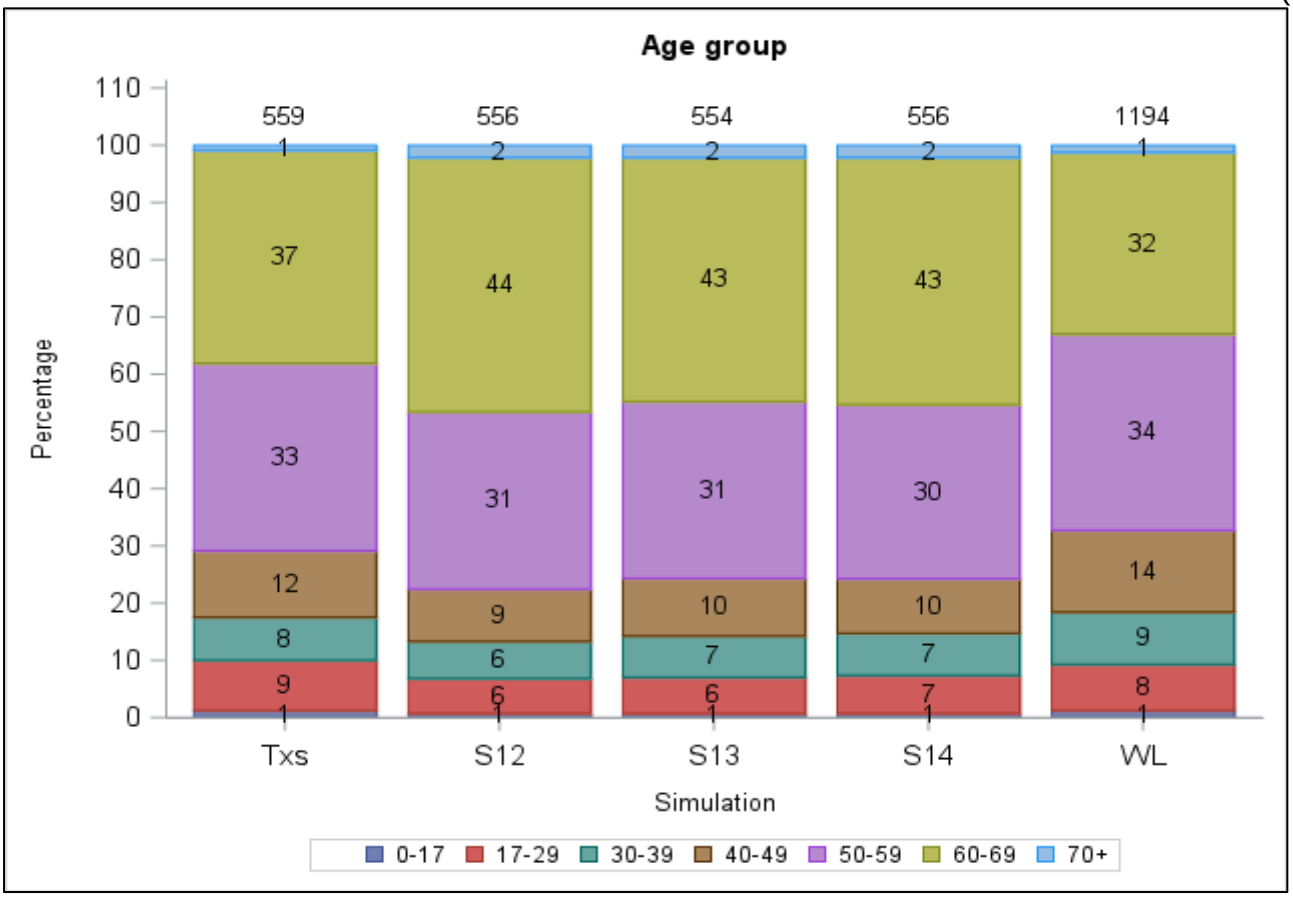

Figure 6A Age group for actual transplants, waiting list and top named patients in simulations 12, 13 and 14

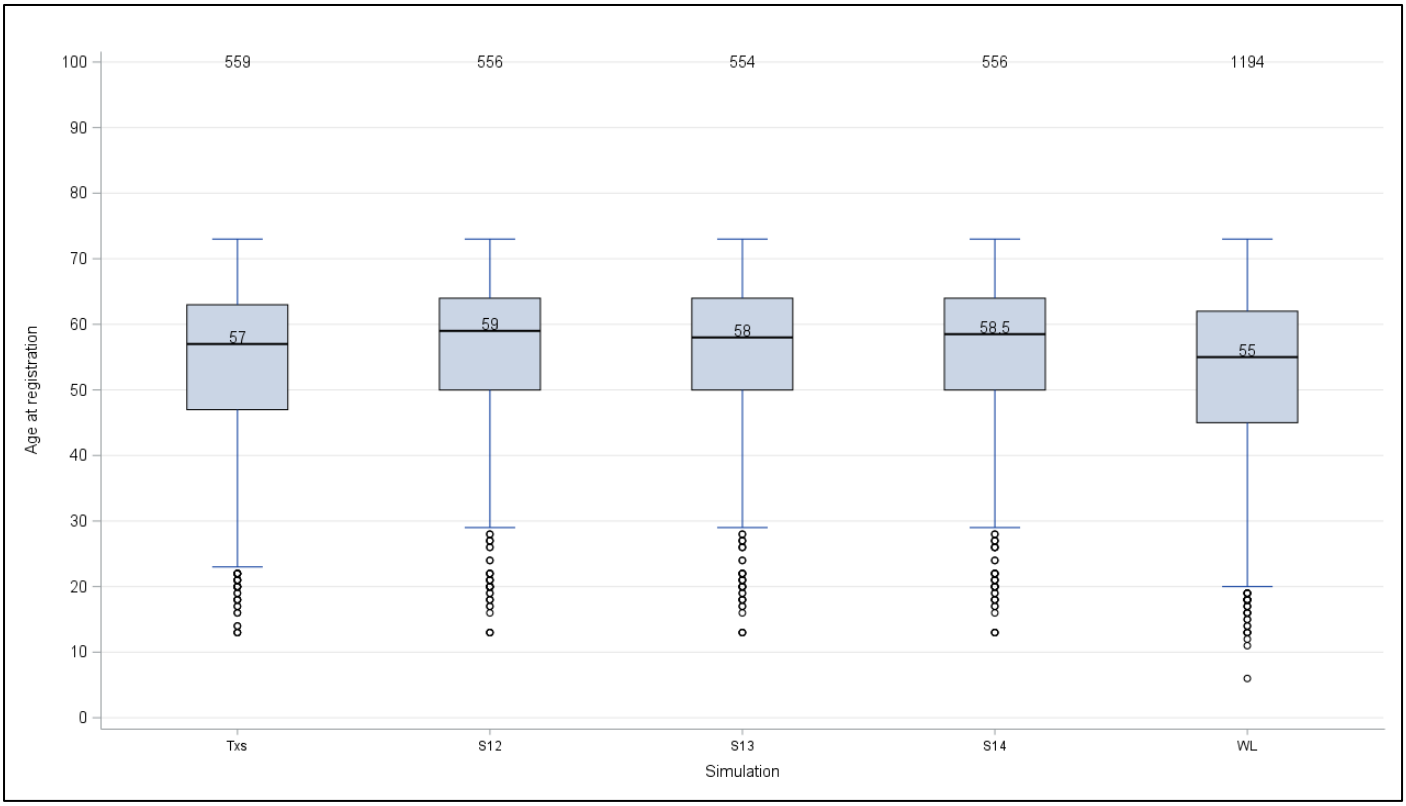

Figure 6B Age at registration for actual transplants, waiting list and top named patients in simulations 12, 13 and 14

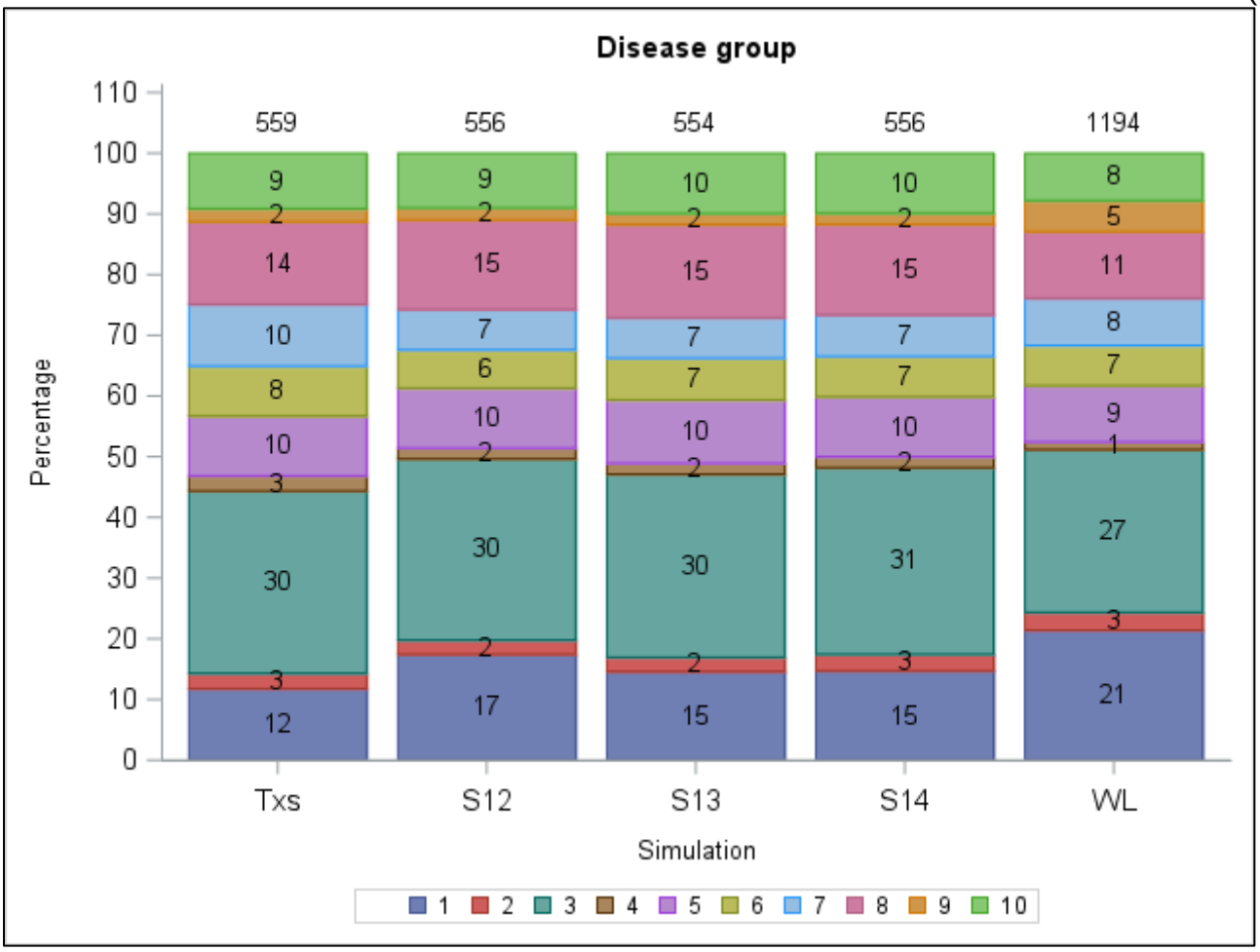

Figure 7 Aetiology (1=cancer, 2=HCV, 3=ALD, 4=HBV, 5=PSC, 6=PBC, 7=AID, 8=Metabolic, 9=other, 10=retransplants) for actual transplants, waiting list and top named patients in simulations 12, 13 and 14

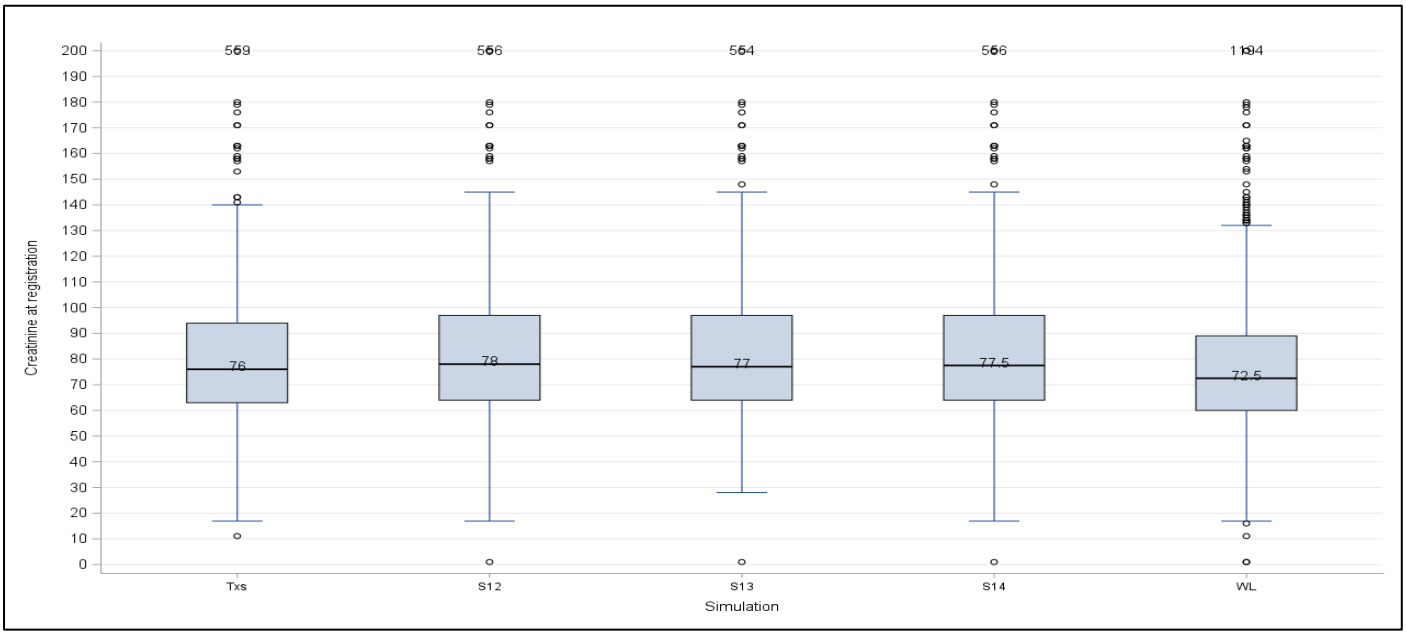

Figure 8 Serum creatinine at registration for actual transplants, waiting list and top named patients in simulations 12, 13 and 14

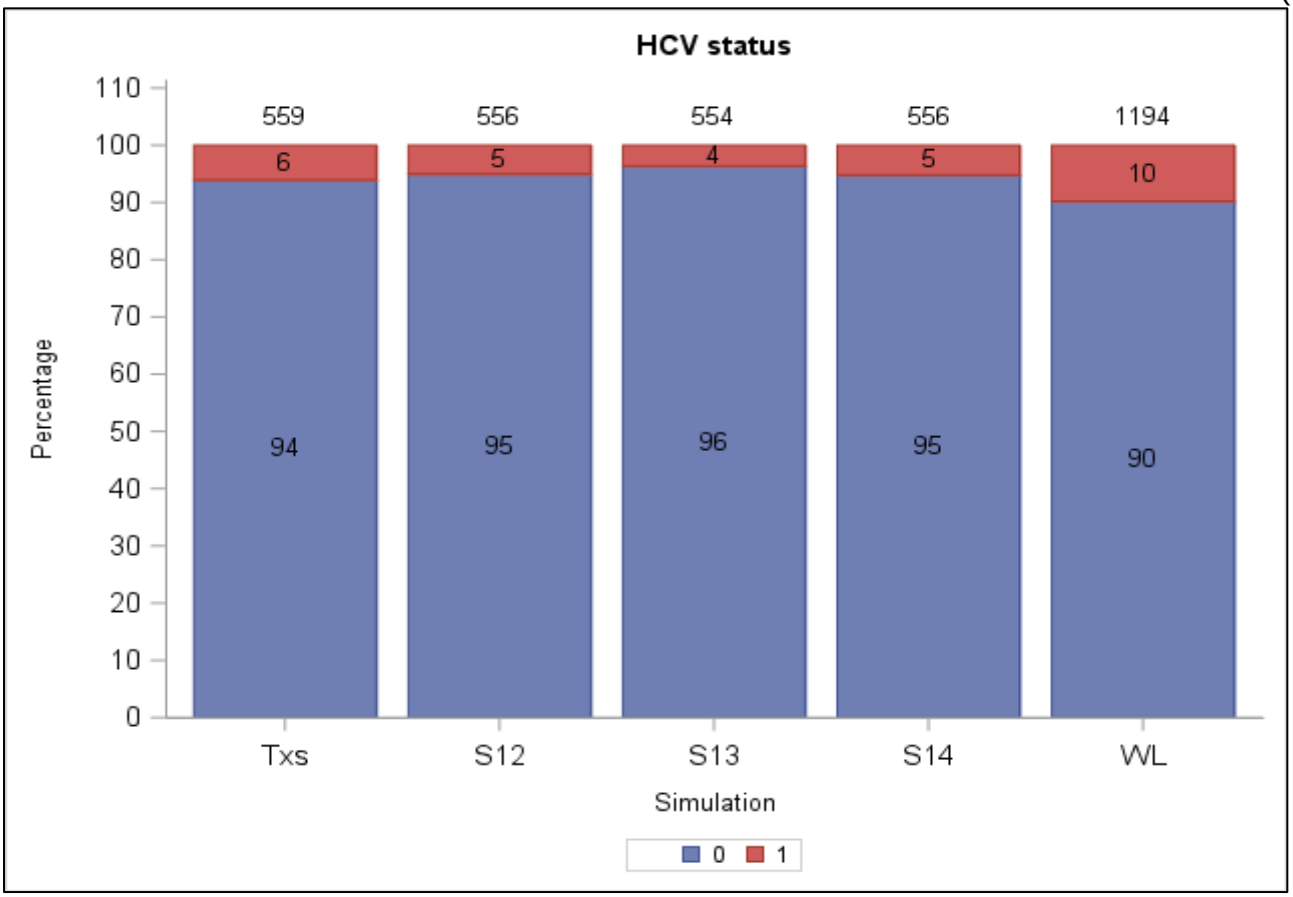

Figure 9 HCV status (0=No, 1=Yes) for actual transplants, waiting list and top named patients in simulations 12, 13 and 14

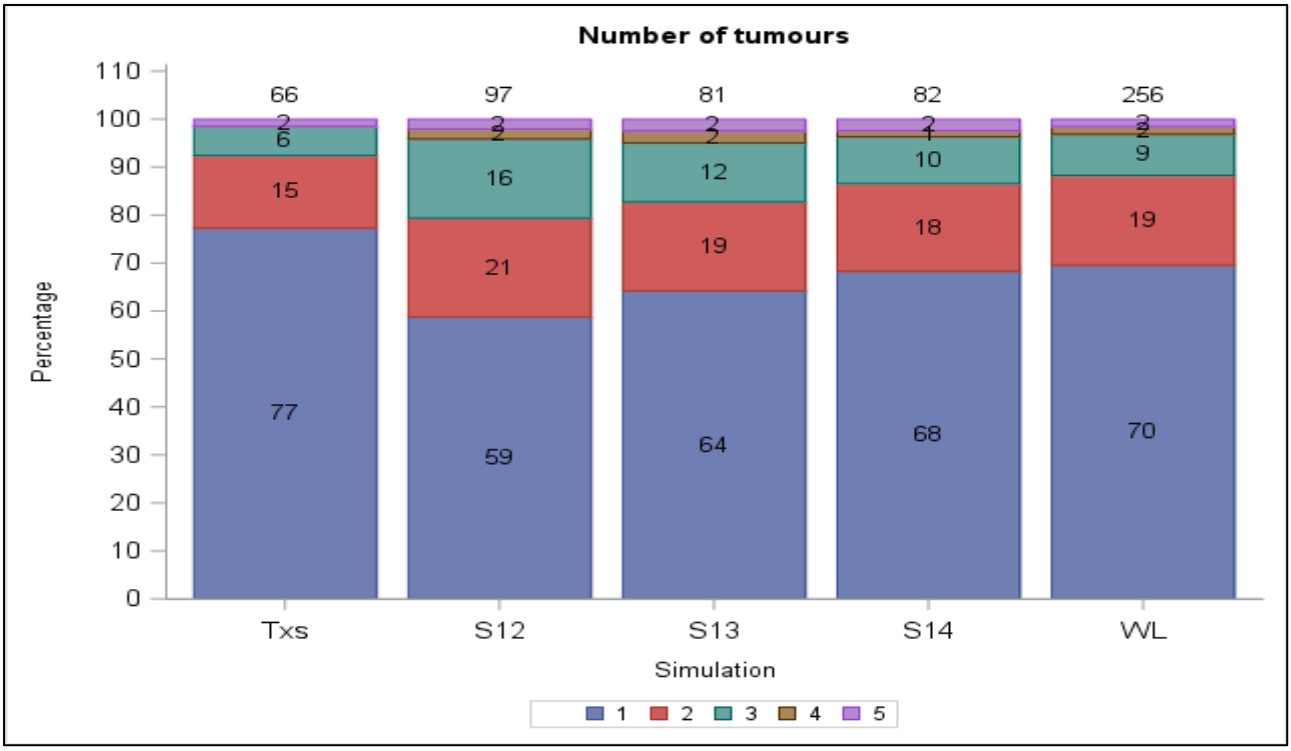

Figure 10 Number of tumours for actual transplants, waiting list and top named patients in simulations 12, 13 and 14

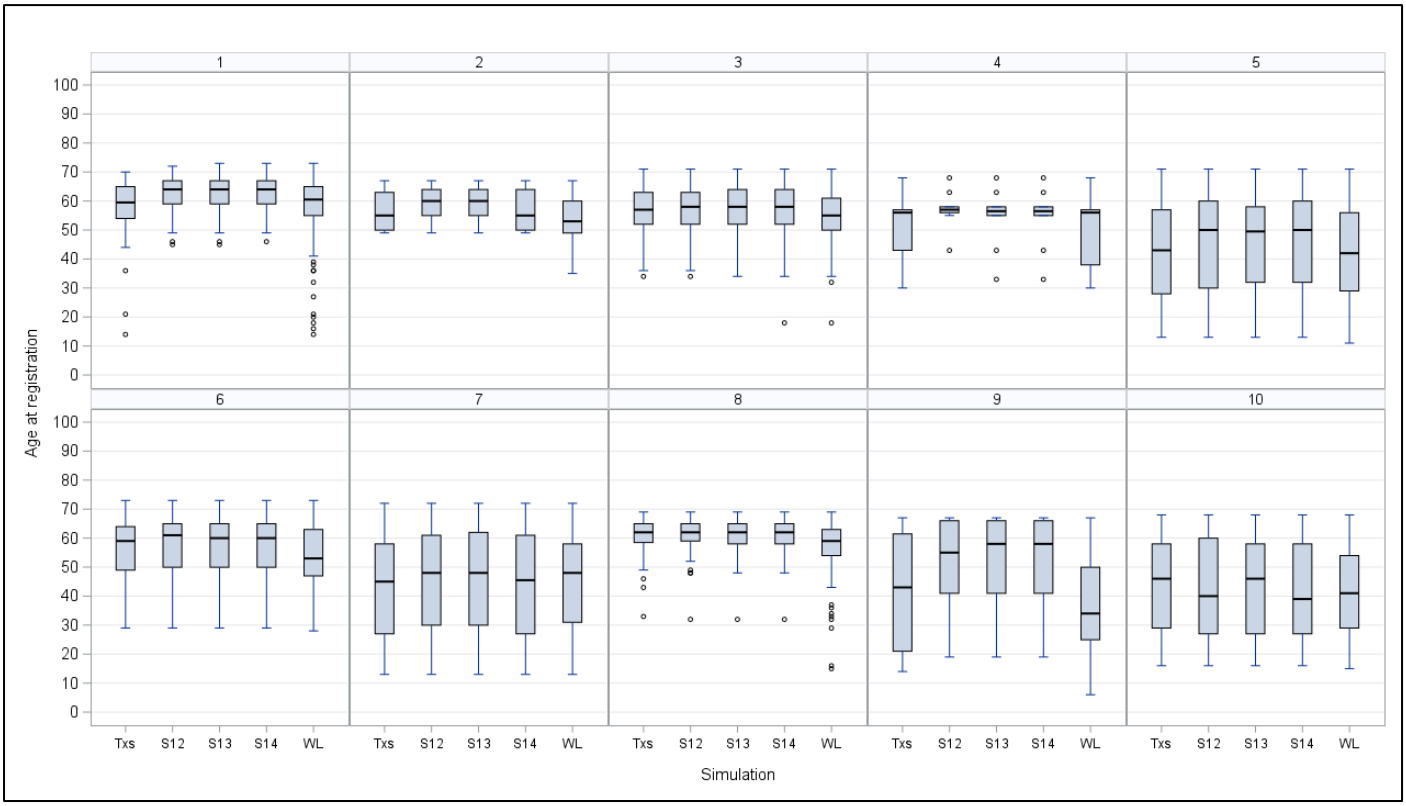

Figure 11 Age at registration by aetiology (1=cancer, 2=HCV, 3=ALD, 4=HBV, 5=PSC, 6=PBC, 7=AID, 8=Metabolic, 9=other, 10=retransplants) for actual transplants, waiting list and top named patients in simulations 12, 13 and 14