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UK registry analysis of donor substance misuse and outcomes following pancreas transplantation

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Abstract

Substance abuse is unfortunately common in organ donors. Often, these organs are declined for transplant, not only because of concerns around blood-borne virus transmission but also because of perceived poor outcomes. In kidney transplantation, previous studies have demonstrated donor smoking status significantly impacts transplant outcome, but intravenous drug use or alcohol dependence does not. This study aims to clarify these issues in pancreas transplantation. Retrospective data on all UK solid organ pancreas transplants from 1994 to 2015 were obtained from the NHSBT UK Transplant Registry. The impact of illicit drug misuse, alcohol abuse, and smoking on graft and patient survival were analyzed using Kaplan-Meier plots and a Cox regression model. A total of 1175 of the 2317 (49.5%) donors were categorized as substance misusers. Univariate survival analysis revealed no significant impact of substance misuse on 10-year graft or patient survival. Multivariate analysis confirmed substance misuse was not associated with impaired graft or patient survival. A history of donor substance misuse does not negatively impact 10-year graft or patient survival following pancreas transplantation. This is a large national registry analysis with long-term follow-up data and should therefore provide clinicians with reassurance when considering pancreas grafts from substance misuse donors.

KEYWORDS
alcoholism and substance abuse, donors and donation, donors and donation: extended criteria

1 | INTRODUCTION

Pancreas transplantation is a definitive treatment for type 1 diabetes mellitus, having a 85% success rate of insulin independence at 1 year.[1]

Currently, the number of potential recipients for a pancreas transplant exceeds the number of ideal donors. It is well established that successful solid organ transplant outcomes are dependent on careful donor and recipient selection; however, there is increasing pressure to meet the needs of patients on growing waiting lists. To overcome this shortfall, considerable attempts have been made to increase the donor pool. A recent meta-analysis found that donors after circulatory death (DCD) had comparable graft and recipient outcomes to donor after brain death (DBD) pancreas transplantation,[2,3] but these are usually a highly selected cohort of often younger donors with minimal risk of a significant warm ischemic injury. Nevertheless, this suggests that pancreas transplants using carefully selected marginal donors may not have the morbidity often anticipated.

Donors who have misused substances, including alcohol, drugs (eg, cannabis, cocaine, heroin), and cigarette smoking are often considered suboptimal due to the potential effects of these substances on the pancreas. These donors are usually young and otherwise ideal, but their organs are often turned down due to uncertainty surrounding the implications of their substance misuse on transplant outcomes. This is reflected in the high decline rate with 13% of otherwise acceptable organs rejected due to "donor history".[4]

It is well established that the pancreas is particularly susceptible to damage from alcohol. Long-term alcohol abuse is the primary cause of chronic pancreatitis, accounting for approximately 70%-80% of cases, and a major cause of acute pancreatitis.[5] Clinicians have traditionally been wary of using organs from alcohol abuse donors as there is a perceived increased risk of reperfusion pancreatitis in the recipient. This complication is thought to be associated with increased patient morbidity and decreased pancreas graft survival.[6]

Donors who have engaged in illicit drug misuse, particularly intravenous drug use, raise concerns regarding their blood-borne virus status. Most donor-to-recipient disease transmissions are expected and as such pre-emptive therapy and prophylaxis can be used to minimize the impact of transmission.[7] However, despite screening, the transmission of certain diseases (including HIV and HCV) may occur unexpectedly.[8] This remains a rare complication; however, when it does occur the ramifications can be severe with high adverse media interest.[7]

The association between smoking and vascular disease is well established. Vascular thrombosis is the main cause of early graft loss following pancreas transplantation, and theoretically, the endothelial activation associated with smoking may be transferred with the organ. We have previously demonstrated that recipient smoking does not negatively impact pancreas transplant outcomes[9] but the impact of donor smoking on the graft has not been previously reported.

Most prior work into the effect of substance abuse on transplant outcomes have focused on the impact of recipient's smoking, illicit drug misuse, and alcohol dependency status, not the donor's history of substance misuse.[10,11] In kidney transplantation, the outcomes following donor substance misuse have been better outlined. A large retrospective study found that in kidney transplants, a donor history of cigarette smoking had a significant negative impact on both graft and recipient survival,[12] whereas donor IV drug use and donor alcohol dependency were not found to have any significant adverse impact. As smoking,[13] illicit drug misuse,[14] and alcohol abuse[15] are common within the general population, it is important to understand the potential impact this may confer on transplantation outcomes.

The aim of this study was to evaluate whether donor substance misuse has any effect on pancreas transplant outcomes, allowing optimization of donor selection and providing clinicians with the confidence to scientifically assess the risk.

2 | MATERIALS AND METHODS

The UK transplant registry is maintained by the National Health Service Blood and Transplant (NHSBT). Donor next of kin and recipients give informed consent for continuing data collection and subsequent analyses. There are eight centers in the UK that routinely perform pancreas transplantation. Data on all UK solid organ pancreas transplants from 1984 to 2015 were obtained from NHSBT UK transplant registry, n = 2618. Information on substance misuse was only available on those transplants performed from 1994 onwards. Those patients for which there was no available information on substance misuse were removed from the analysis, resulting in a final cohort of 2317. Substance misuse included those donors with a history of alcohol abuse, history of illicit drug misuse, or current/past cigarette smoker as identified and recorded by Specialist Nurses in Organ Donation during the donor screening process. Sources of this information include the next of kin and the donor's GP medical records. Data were also gathered on other donor variables included the following: age, sex, BMI, ethnic group, DBD/DCD, cause of death, warm ischemic time, cold ischemic time, smoking status, and alcohol history. The donor cause of death was coded as per NHSBT core donor forms and for the purpose of this analysis was grouped into common codes, CVA, trauma, or other. CVA refers to cerebrovascular accident including ischemic stroke, intracerebral hemorrhage, and intracranial event unspecified. Recipient variables included the following: age, sex, BMI, ethnicity, sensitization, dialysis modality, previous transplant, mismatch grade, and immunosuppression regimes. Information on recipient survival and death-censored graft survival was extracted from the UK Transplant Registry.

To standardize terminology, we have grouped commonly used terms for different types of substance misuse under three headings. This is with an aim to be consistent with commonly used nomenclature on the NHSBT Core Donor Form. Any documented history of donor alcoholism, alcohol abuse, or alcohol dependence has been termed "Alcohol Abuse." Any reported illicit drug misuse, including intravenous drug misuse, cannabis, cocaine, has been termed "drug misuse." The term "smoker" incorporates any history of regular cigarette or pipe smoking as recorded on the core donor forms. The umbrella term "substance misuser" incorporates all three of these categories.

2.1 | Statistical analysis

Follow-up analysis of the entire cohort was submitted to NHSBT by December 2015. All patients included had a minimum of 12 months follow-up. Donor and recipient characteristics categorized by substance misuse status were reported as percentages or mean ± SD where appropriate. Univariate analysis was carried out using one-way analysis of variance (ANOVA) with a Dunnett's post hoc multiple comparisons correction for continuous data. The donors with no history of substance abuse were used as the control group for the Dunnett's test. Categorical data were analyzed using chi-squared tests. Graft and patient survival was censored at 10 years. Unadjusted graft and patient survival was calculated using Kaplan-Meier (K-M) plots and p-values derived from the univariate log-rank test. Given the heterogeneity of the recipients within the UK pancreas transplant registry, a sensitivity analysis was performed to ensure validity of these findings when

TABLE 1 Donor characteristics

Donor characteristic	No substance misuse, n = 1144	Donor smoking, n = 1129	Donor alcohol abuse, n = 163	Donor drug misuse, n = 203	*P* value
Age (y)	32.7 ± 14.4	36.3 (±11.7)*	34.3 ± 13.4	30.0 ± 9.5*	<0.001*
Sex (%)					
Men	552 (48.2%)	566 (50.1%)	106 (65%)	146 (71.9%)	
Women	592 (51.7%)	562 (49.8%)	57 (35%)*	57 (28.1%)*	<0.001*
Ethnic group (%)					
White	1040 (90.8%)	1056 (93.5%)*	153 (93.9%)*	185 (91.1%)	
Other	104 (9.2%)	66 (5.8%)	10 (6.1%)	18 (8.9%)	0.025*
BMI (kg/m^2)	23.3 ± 3.7	23.8 ± 3.4	23.8 ± 3.6	23.4 ± 3.4	0.87
Donor type (%)					
DBD	968 (84.5%)	983 (87.1%)	135 (82.8%)	164 (80.8%)	0.62
DCD	176 (15.4%)	146 (12.9%)	28 (17.2%)	39 (19.2%)	
Donor cause of death (%)					
CVA	589 (51.5%)	721 (63.9%)*	92 (56.4%)	93 (45.8%)	<0.001*
Trauma	235 (20.5%)	174 (15.4%)	29 (17.8%)	35 (17.2%)	
Other	320 (28.0%)	234 (20.7%)	43 (25.8%)	75 (36.9%)*	

BMI, Body Mass Index; CVA, Cerebrovascular Accident; DBD, Donation after Brainstem Death; DCD, Donation after Circulatory Death.
Data shown as mean ± SD or percentage.
*, highlights significant finding.

applied to sub-populations within the whole pancreas transplant cohort, for example SPK only, DCD only, and re-transplant recipients. Multivariate analysis was performed using a Cox proportional hazards regression model to analyze the combined effect of selected factors on all-cause graft and patient survival. Log cumulative hazard plots were also analyzed and showed no evidence of non-proportionality of hazards. All tests were two-sided and p-values of less than 0.05 were deemed statistically significant. Analyses were performed using GraphPad Prism 7.0 and IBM SPSS Statistics version 22.

3 | RESULTS

Of the 2317 analyzed transplants, 1175 were categorized as substance misusers. Within this cohort, there were 1129 (48.7%) donors with a history of smoking, 163 (7%) donors with a history of alcohol abuse, and 203 (8.7%) donors with a history of drug abuse, Table 1. There were 327 donors who fell into more than one category of substance misuse.

3.1 | Clinical characteristics of donors with a history of substance misuse

Donors with a history of substance abuse represented a distinct population when compared to the normal donor population. The majority of donors who smoked were older (36.3 ± 11.7 vs 32.7 ± 14.4 years, $P < 0.001$), whereas those donors with a history of drug abuse were more likely to be younger (30.0 ± 9.5 vs 32.7 ± 14.4 years $P < 0.001$) when compared with non-substance-misusing donors. There was a higher proportion of male donors with a history of alcohol abuse (M:F, 65%:35%) and drug abuse (71.9%:28.1%), $P < 0.001$. Those donors with a history of any substance misuse were also significantly more likely to be of White, Caucasian ethnic origin, $P = 0.02$. There was no difference in the type of donation, DBD vs DCD. There was significant variation in donor's cause of death; the donors that smoked were more likely to die from a cerebrovascular accident (63.9% vs 51.5%, $P < 0.001$) and donors with a history of drug abuse were more likely to die from "other" causes (36.9% vs 28.0%, $P < 0.001$) examples include out of hospital cardiac arrest, meningitis, or suicide.

3.2 | Clinical characteristics of pancreas transplant recipients

With regard to the pancreas transplant recipient population, there were very few differences between the cohorts, Table 2. The groups were well matched for age, ethnicity, BMI, mismatch grade, dialysis status, type of pancreas transplant, warm and cold ischemic times. Recipients with their own history of substance misuse (ie, smokers) were not any more likely to be allocated organs from donors with a history of substance abuse. Interestingly, men were significantly more likely to receive a pancreas graft from a donor with a history of drug or alcohol abuse than women, (alcohol abuse—59.5% vs 40.5%; drug abuse—61.6% vs 38.4%, $P < 0.001$).

3.3 | Univariate analysis of the impact of donor substance misuse on graft & patient survival

Data on graft and patient survival were available for 2073 recipients. Survival analysis using Kaplan-Meier plots revealed a donor history of

TABLE 2 Recipient characteristics

Recipient characteristic	No substance misuse, n = 1144	Donor smoking, n = 1129	Donor alcohol abuse, n = 163	Donor drug misuse, n = 203	*P* value
Age (y)	41.45 ± 8.4	41.9 ± 8.5	41.6 ± 8.4	41.3 ± 8.6	0.58
Sex (%)					
Men	517 (45.2%)	466 (41.3%)	97 (59.5%)*	125 (61.6%)*	
Women	627 (54.8%)	663 (58.7%)	66 (40.5%)	78 (38.4%)	<0.001*
Ethnic group (%)					
White	1047 (91.4%)	1028 (91.1%)	146 (89.6%)	184 (90.6%)	
Other	97 (8.5%)	101 (8.9%)	17 (10.4%)	19 (9.4%)	0.86
BMI (kg/m^2)	24.5 ± 4.4	24.39 ± 4.3	24.5 ± 4.4	24.5 ± 3.8	0.94
Mismatch grade (%)					
000 mismatch	11 (1%)	10 (0.9%)	1 (0.6%)	0	
Favorable MM	66 (5.8%)	49 (4.3%)	10 (6.1%)	8 (3.9%)	
Non-favorable MM	1063 (92.8%)	1070(94.8%)	152 (93.3%)	195 (96.1%)	0.67
Dialysis status (%)					
Hemodialysis	287 (25.1%)	316 (28%)	39 (23.9%)	61 (30.0%)	
Peritoneal	227 (19.8%)	240 (21.3%)	40 (24.5%)	46 (22.7%)	
Not on dialysis	540 (47.2%)	502 (44.5%)	74 (45.5%)	86 (42.4%)	0.39
Warm ischemic time (min)	54.9 ± 108.5	49.4 ± 78.2	50.8 ± 105.2	38.2 ± 17.3	0.31
Cold ischemic time (min)	747.9 ± 321.3	758.8 ± 427.5	762.4 ± 653.3	755.25 ± 436.9	0.95
Type of transplant (%)					
PAK	111 (9.7%)	108 (9.6%)	14 (8.6%)	13 (6.4%)	
PTA	95 (8.3%)	81 (7.2%)	14 (8.6%)	18 (8.9%)	
SPK	938 (81.9%)	940 (83.3%)	135 (82.8%)	172 (84.7%)	0.71
Recipient smokers	128 (11.2%)	135 (11.4%)	19 (11.7%)	30 (14.8%)	0.36

BMI, Body Mass Index; PAK, Pancreas After Kidney transplant; PTA, Pancreas Transplant Alone; SPK Simultaneous Kidney-Pancreas Transplant.
Data shown as mean ± SD or percentage.
*, highlights significant finding.

substance misuse had no significant impact on 10-year graft survival (GS) or patient survival (PS), Figure 1, (alcohol abuse GS $P = 0.45$; PS $P = 0.65$, drug misuse GS $P = 0.93$; PS $P = 0.08$ and smoking GS $P = 0.93$; PS $P = 0.51$). Survival analysis was also performed examining the effect that donors with a history of multiple substance misuse (n = 327) may have on outcomes. This again revealed there was no significant impact on graft survival ($P = 0.69$) or PS ($P = 0.12$). A sensitivity analysis was performed to evaluate the impact of donor substance misuse on different sub-categories within the pancreas transplant population, for example. transplant type (SPK, PAK, PTA), donor type (DCD vs DBD), and re-transplants. This analysis revealed no effect of donor history of substance misuse on these sub-populations (data not shown).

3.4 | Multivariate analysis of the impact of donor substance misuse on graft & patient survival

To understand the impact of donor substance misuse, within the context of the multiple confounding risk factors present in a large retrospective registry analysis, a multivariate analysis was performed. This confirmed that any history of donor substance misuse was not associated with impaired graft of patient survival in pancreas transplantation. Only traditional markers of poor outcome that is cold ischemic time ($P < 0.0001$, HR 1.001 95% CI 1.001, 1.002), increasing donor age ($P = 0.02$, HR 1.014 95% CI 1.002, 1.026), pancreas transplant alone ($P < 0.0001$, HR 2.71 95% CI 1.69,4.3), pancreas after kidney ($P<0.001$, HR 2.24 95% CI 1.41, 3.55), and increasing recipient BMI ($P = 0.03$, HR 1.042 95% CI 1.003, 1.082) were found to have a significant negative impact on graft survival, Table 3. Interestingly, a donor history of alcohol abuse was a significant covariate in the cox regression model; however, the HR was <1 indicating this is not associated with a negative effect on graft survival but a positive effect ($P = 0.02$, HR 0.54 95% CI 0.32, 0.92).

Recipient age ($P = 0.01$, HR 1.037 95% CI 1.008, 1.067) and PTA graft ($P = 0.006$, HR 2.952 95% CI 1.36, 6.41) correlated with poor patient survival, Table 4.

3.5 | Postoperative complications

To evaluate the impact of donor substance misuse on the recipient's postoperative course, the rate of a number of common complications was compared between groups. These data were taken from the 3-month follow-up report submitted to NHSBT by transplant coordinators. Follow-up data were not routinely collected for the early cohort of

transplants (prior to 2006) so the overall figures for these complication rates are lower when compared with other reported series. However, interestingly, this revealed that recipients who received a graft from a donor with a history of smoking were significantly more likely to develop an anastomotic leak (34 in smoking cohort vs 15 in control cohort, $P = 0.006$) than in grafts from non-substance misuse donors.

4 | DISCUSSION

The findings of this paper demonstrate that a history of donor substance misuse does not negatively impact on either 10-year pancreas graft or patient survival following pancreas transplantation. This is contrary to evidence in renal transplantation and the widely

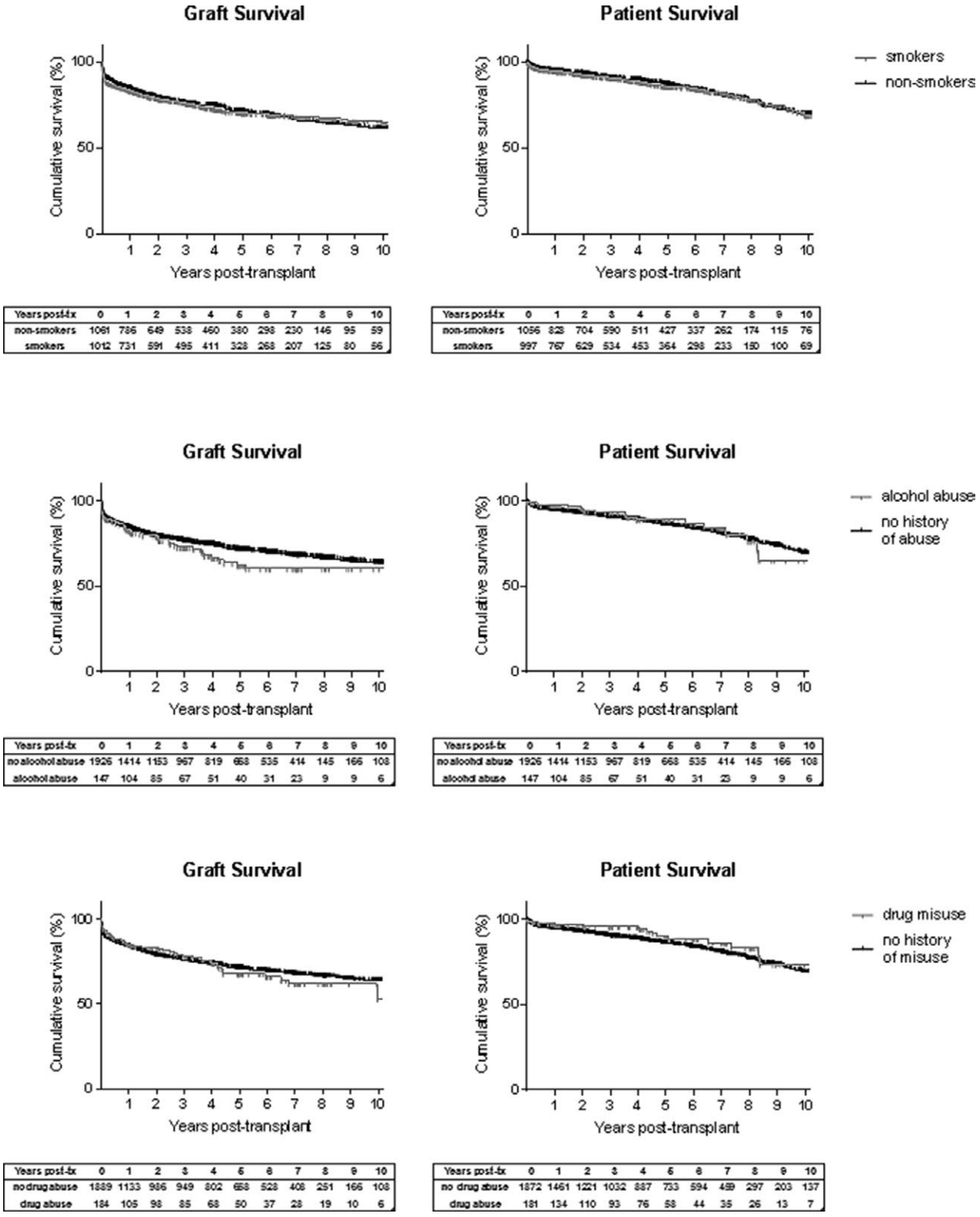

FIGURE 1 Kaplan-Meier survival plots demonstrate donor history of substance misuse does not impact 10-y graft or patient survival

TABLE 3 Multivariate analysis of graft survival

Variable	Hazards ratio	95.0% CI	*P* value
Donor Type (DCD vs DBD)	0.953	(0.63,1.45)	0.82
Donor age	1.014*	(1.00, 1.03)	0.02*
Donor BMI	0.982	(0.94, 1.03)	0.44
Donor history of alcohol abuse	0.541*	(0.32, 0.92)	0.02*
Donor history of drug misuse	0.988	(0.56, 1.73)	0.96
Donor history of smoking	1.337	(0.98, 1.83)	0.07
Recipient age	0.993	(0.97, 1.01)	0.43
Recipient BMI	1.042*	(1.00, 1.08)	0.03*
Sensitization pre-transplant	1.003	(0.99, 1.01)	0.29
Hemodialysis pre-transplant	1.160	(0.79, 1.71)	0.46
Peritoneal dialysis pre-transplant	1.166	(0.76, 1.78)	0.48
Transplant type—Pancreas transplant alone	2.711	(1.68, 4.33)	<0.0001*
Transplant type—Pancreas after kidney	2.236	(1.41, 3.55)	0.001*
Transplant year	1.064	(0.97, 1.16)	0.17
Warm ischemic time	1.000	(0.99, 1.01)	0.298
Cold ischemic time	1.010*	(1.01, 1.02)	<0.0001*

BMI, Body Mass Index; DBD, Donation after Brainstem Death; DCD, Donation after Circulatory Death.
*, highlights significant finding.

TABLE 4 Multivariate analysis of patient survival

Variable	Hazards ratio	95.0% CI	*P* value
Donor type (DCD vs DBD)	0.794	(0.40, 1.59)	0.59
Donor age	1.006	(0.97, 1.03)	0.55
Donor BMI	0.988	(0.92, 1.07)	0.75
Donor history of alcohol abuse	0.573	(0.24, 1.40)	0.22
Donor history of drug misuse	1.353	(0.46, 3.96)	0.58
Donor history of smoking	1.261	(0.76, 2.09)	0.37
Recipient age	1.037*	1.01, 1.07)	0.01*
Recipient BMI	0.999	(0.94, 1.06)	0.97
Sensitization pre-transplant	1.006	(0.99, 1.01)	0.16
Hemodialysis pre-transplant	1.827	(0.99, 3.37)	0.06
Peritoneal dialysis pre-transplant	1.289	(0.63, 2.64)	0.49
Transplant type—Pancreas transplant alone	2.952	(1.36, 6.41)	0.01*
Transplant type—Pancreas after kidney	0.731	(0.22, 2.40)	0.61
Transplant year	1.064	(0.97, 1.16)	0.17
Warm ischemic time	1.001	(0.99, 1.01)	0.71
Cold ischemic time	1.001	(0.99, 1.00)	0.37

BMI, Body Mass Index; DBD, Donation after Brainstem Death; DCD, Donation after Circulatory Death.
*, highlights significant finding.

held beliefs amongst transplant clinicians. This analysis therefore provides scope to widen the donor pool, utilizing marginal donors more readily. Clinicians should be confident in accepting a pancreas from a substance-misusing donor if all other factors are favorable.

This retrospective data analysis is limited by a degree of selection bias. With previous uncertainty, as to outcomes following donor substance misuse it is likely that clinicians would only choose to transplant pancreas allografts from the healthiest of these donors, skewing our results in a positive light. Information regarding donor substance misuse is often provided by the donor's next of kin or friend. This collateral information may be inaccurate as family members may not be aware of all risk-taking behaviors. Another difficulty associated with data capture in this circumstance is the confusing terminology. By using an inclusive, "broad-brush" approach to incorporate the entire spectrum of substance misuse and standardizing terminology to cover all variations, this may have resulted in a dilution of the actual effect size. For example, when comparing intravenous drug abuse versus casual cannabis misuse it might be assumed that one risk-taking behavior is likely to have a more significant impact on a donor's health than the other. However, in our analysis these two situations were both coded as the same variable. Nonetheless, this approach was necessary to facilitate the analysis and is a standard methodology when dealing with large retrospective datasets. Also, the likelihood is, these two opposing difficulties with data collection have negated each other, and therefore, we feel these findings can be reflected as an accurate representation of the donor population. The sensitivity analysis also confirmed these findings were consistent when focussing on specific sub-populations within the whole registry analysis.

This account is verified by the multivariate analysis which suggested that cold ischemic time, increasing donor age, increasing recipient BMI, PTA, and PAK pancreas grafts had a significant impact, with decreased graft survival. Increased recipient age and PTA grafts had a negative correlation with patient survival. These findings are well documented in previous literature.[16]

The primary concern many clinicians will have with accepting organs from substance misuse donors; particularly, IVDU donors are the

TABLE 5 Post-op complications and length of stay

Complication at 3 mo follow-up	No substance misuse, n = 1144	Donor smoking, n = 1129	Donor alcohol abuse, n = 163	Donor drug abuse, n = 203	*P* value
Median length of stay (d)	17 (0-742)	17 (0-759)	17 (6-406)	15 (6-118)	0.23
Myocardial infarction	4	5	0	0	0.66
Cerebrovascular accident	4	4	1	1	0.95
Anastomotic leak	15	34*	0	3	0.006*
Urinary tract infection	57	41	5	6	0.26
Intra-abdominal abscess	29	35	4	5	0.84
Pancreatic infection	9	7	1	2	0.93
Viral systemic infection	4	8	3	1	0.13
Bacterial systemic infection	32	33	3	6	0.89
Fungal systemic infection	7	4	0	1	0.65
Pancreatitis	16	24	5	3	0.35
Episode of acute rejection	64	77	9	14	0.62

*, highlights significant finding.

increased risk of viral transmission. A previous study published by one of our authors has investigated this aspect in significant detail using this same UK registry cohort of pancreas recipients but also including recipients of the other solid organs from the same donor. The study investigated outcomes from 1091 donors with a reported history of "increased risk-taking behavior" for example current use or history of IVDU, current or previous imprisonment, men who have sex with men, sex in exchange for money or drugs, or a high-risk sexual partner.[17] This comprehensive study revealed there have been no reported incidences of viral transmission to pancreas graft recipients. In other solid organ transplants, there has been one case of unexpected transmission of HCV from a single donor affecting one liver and two kidney recipients infected. This particular donor had a history of recent IVDU and had negative HCV antibody titers at the time of donation. The liver recipient was known to be HCV positive prior to transplant; however, the predominant HCV genotype changed after transplant from genotype 1 to 3. There were no reported HIV, HBV, or HTLV transmissions from any of these "increased risk taking" donors.[17] Currently, there are no nationwide guidelines on screening for seroconversion following transplantation in high-risk donors and this is left to the individual clinician's discretion. The protocol in our center advocates testing for seroconversion if the donor was considered high risk for blood-borne virus transmission.

Historical data suggest that Hepatitis C has a negative impact on both patient and graft survival.[18] Rapid advancements in direct-acting antivirals (DAAs) means interferon-free therapy with higher cure rates and less adverse side effects are now available. These have been used to enable kidney organ transplantation from HCV positive donors to HCV negative recipients who were treated with DAAs, preventing disease transmission.[19] These affiliated lines of research could mean donor IVDU is no longer a barrier to transplantation.

Currently in the UK, blood-borne virus screening of deceased donors relies on serology rather than nucleic acid testing (NAT). Uncertainty regarding the donor's serology may contribute to clinicians' apprehension to utilize functionally good pancreata from donors with a history of drug misuse. NAT can significantly reduce the "window period" from infection to detection and decrease the risk of transmitting disease from a serologically negative donor.[20] However, NAT is costly and can be logistically challenging.[21] A change in policy that advocates funding for routine NAT in high-risk donors may increase the utilization of organs.[22]

Interestingly, the recipients who received a graft from a donor with a history of smoking were significantly more likely to go on to develop an anastomotic leak. Fortunately, this is did not impair long-term graft or patient survival. The underlying reason for more leaks may be explained by the well-established effect that smoking has on wound healing and the microvasculature, resulting in the donor duodenum being more susceptible to dehiscence. This is a well-reported phenomenon in colorectal surgery.[23]

We have also shown that donors with a history of smoking were likely to be older but this did not have a compounding effect on graft or patient survival. When adding the variables into the multivariate model, donor age represented a significant hazard impairing graft survival, whereas smoking status did not. This demonstrates that the negative impact of donor age holds true in the model irrespective of donor smoking status and other potentially confounding variables. Equally, the nonsignificant impact of donor smoking status holds true when all other potentially confounding variables (donor age included) remain constant. The interaction term between donor age and smoking status was also nonsignificant revealing there is no compounding effect on graft survival when both of these variables are present.

The overall reported incidence of postoperative complications (Table 5) was significantly lower than other reported series. This likely represents a large amount of missing follow-up data not being reported back to NHSBT post-transplant. However, this is a frequent problem when dealing with large retrospective databases[24] and is

difficult to account for without considering statistical methods of imputation which were not undertaken for this study.

An unusual finding from this study has been that men were more likely than women to receive pancreas grafts from "risky" donors with a history of alcohol abuse or drug misuse. This phenomenon is difficult to understand but may be the result of a subconscious gender bias. There have been previous studies that reported clinician's decisions regarding organ allocation and listing for transplant are subject to socioeconomic and racial bias[25,26]; however, there is very limited data about the effect of recipient's gender on these decisions.

Our findings are consistent with those of a previous, much smaller study, which found no impact of donor substance misuse on early pancreas graft failure.[27] Whilst this is reassuring, the other study was based on a single center experience, with a cohort of 62 donors and no long-term follow-up. Having used data from the UK registry, our findings have greater statistical power, wider applicability, and the potential for greater clinical impact.

The majority of patients receiving a pancreas transplant had a simultaneous kidney transplant. However, our findings are contrary to those found in kidney transplants, with donor smoking having a significant effect on patient outcomes in kidney allografts.[12] It is unclear why this difference exists; however, that study utilized the American UNOS registry for analysis with donors from prior to 1999, whilst our study is a more contemporaneous UK registry analysis. Therefore, differences in the donor population groups may account for this discrepancy.

This study has been conducted using data from a large registry series, with long-term follow-up of 10 years. Consequently, it is very reassuring and convincing to see such positive outcomes. Decisions will still have to be taken on an organ-by-organ basis, weighing up risks and benefits for that particular recipient and collectively considering other donor factors. It is important that these decisions are taken during a process of shared decision making, with the patient fully informed of the risks and benefits of the individual grafts. Our study provides clinicians and surgeons with the ability to explain the evidence base regarding these allocation decisions and more confidence in the utility of this group of marginal donors.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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