

TABLE S1: CONCEPTS OF IMMUNE RISK AND HLA COMPATIBILITY

- Incompatible transplant
- Mismatched transplant
- Desensitization
- Acceptable mismatch program (of the Eurotransplant)
- Donor – recipient incompatibility
- High-risk transplant
- HLA mismatch
- (un)acceptable mismatch
- Repeat (antigen) mismatch
- HLA epitope mismatch
- HLA eplet mismatch
- Donor-specific antibody (DSA) positive transplant (Ig subclasses: IgM, IgG(s))
- Preformed / historic DSA
- Crossmatch (flow/cell-based) positive transplant
- XM (flow/cell-based/virtual) positive transplant
- Complement-dependent cytotoxic crossmatch
- B-cell crossmatch

- T-cell crossmatch
- “Highly Sensitized”
- PRA, panel reactive antibodies
- Calculated PRA, cPRA

TABLE S2: INDEPENDENT SEARCH STRATEGIES

SEARCH STRATEGY 1 (JOHNS HOPKINS UNIVERSITY):

Embase [embase.com] (August 22, 2019)

No.	Query	Results
#14	#12 NOT #13	3310
#13	#1 AND #9 AND [2000-2019]/py AND [humans]/lim AND [medline]/lim	3863
#12	#1 AND #9 AND [2000-2019]/py AND [humans]/lim	7173
#11	#1 AND #9 AND [2000-2019]/py	8221
#10	#1 AND #9	12309
#9	#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	784458
#8	'alloantibody'/exp	29640
#7	'antibody dependent cellular cytotoxicity'/exp	13110
#6	'histocompatibility test'/exp	4028
#5	'alloantigen'/exp	181482
#4	'b lymphocyte'/exp	188432
#3	't lymphocyte'/exp	520524
#2	'histocompatibility antigen'/exp	152342
#1	'kidney transplantation'/exp/mj	104142

Medline [Pubmed] (August 22, 2019)

Search	Query	Items found
#25	Search ((#6 OR #12 OR #18 OR #22) AND #4) Filters: Publication date from 2000/01/01 to 2019/12/31; Humans Sort by: Author	8086
#24	Search ((#6 OR #12 OR #18 OR #22) AND #4) Filters: Publication date from 2000/01/01 to 2019/12/31 Sort by: Author	8273
#23	Search ((#6 OR #12 OR #18 OR #22) AND #4) Sort by: Author	12208
#22	Search ("Living Donors"[Mesh]) OR "Antibody-Dependent Cell Cytotoxicity"[Mesh] Sort by: Author	21177
#20	Search "Living Donors"[Mesh] Sort by: Author	14574
#18	Search ("T-Lymphocytes/transplantation"[Mesh]) OR "B-Lymphocytes/transplantation"[Mesh] Sort by: Author	6227
#12	Search (("Allografts"[Mesh]) OR "Isoantibodies"[Mesh]) OR "Histocompatibility Testing"[Mesh] Sort by: Author	49149
#6	Search "Histocompatibility Antigens"[Mesh]AND (incompatib* or mismatch* or crossmatch* or cross-match*) Sort by: Author	5553
#4	Search ("Kidney Transplantation"[Majr]) OR "Kidney/transplantation"[Majr] Sort by: Author	76441

SEARCH STRATEGY 2 (MCGILL UNIVERSITY HEALTH CENTRE):

Medline [Ovid] (August 19, 2019)

Ovid MEDLINE and epub ahead of print, in-process and other nonindexed citations and daily <1946 to August 16, 2019>		
#	Searches	Results
1	kidney transplantation/	92564
2	exp kidney/tr	74
3	((kidney* or renal) adj3 (allotransplant* or transplant* or allograft* or graft* or donor* or recipient*)).tw,kf.	96250
4	1 or 2 or 3	115699
5	exp Histocompatibility Antigens/ and (incompatib* or mismatch* or mis-match* or crossmatch* or cross-match* or xm).tw,kf.	5225
6	((antigen* or anti-gen* or hla* or histocompatib*) adj6 (incompatib* or mismatch* or mis-match* or crossmatch* or cross-match* or xm or test*)).tw,kf.	38280
7	(exp T-Lymphocytes/ or exp B-Lymphocytes/) and (incompatib* or mismatch* or mis-match* or crossmatch* or cross-match* or xm).tw,kf.	3442
8	((t-cell* or t-lymphocyte* or b-cell* or b-lymphocyte* or positive) adj5 (incompatib* or mismatch* or mis-match* or crossmatch* or cross-match* or xm)).tw,kf.	2118
9	Isoantibodies/	13038
10	(allo?antibod* or iso?antibod* or ((donor-specific* or panel-reactive*) adj3 antibod*)).tw,kf.	7540
11	((Donor* or recipient* or transplant* or acceptab* or unacceptab* or repeat*) adj4 (mismatch* or mis-match*)).tw,kf.	5189
12	((Donor* or recipient* or transplant* or candidate*) adj8 incompatib*).tw,kf.	2985
13	((DSA or PRA or cPRA or (high* adj2 risk)) and transplant*).tw,kf.	19048
14	exp Histocompatibility Testing/	31143
15	Antibody-Dependent Cell Cytotoxicity/ and (test* or crossmatch* or cross-match* or xm).tw,kf.	1038
16	(cytotoxic* adj3 (crossmatch* or cross-match* or xm or test*)).tw,kf.	7700
17	((sensiti* or desensiti*) adj5 (patient* or recipient* or candidate*)).tw,kf.	46736
18	or/5-17	153965
19	4 and 18	14992

20	((Animals/ or Models, animal/ or Disease models, animal/) not Humans/) or ((animal or animals or canine* or cat or cats or dog or dogs or feline or hamster* or lamb or lambs or mice or monkey or monkeys or mouse or murine or pig or pigs or piglet* or porcine or primate* or rabbit* or rats or rat or rodent* or sheep* or veterinar* or non-human) not (human* or patient*)).ti,kf,jw.	4961893
21	19 not 20	14223
22	limit 21 to yr="2000 -Current"	9233

Embase [Ovid] (August 19, 2019)

Embase <1996 to 2019 August 16>		
#	Searches	Results
1	exp kidney transplantation/	115017
2	kidney transplant*.hw.	83315
3	((kidney* or renal) adj3 (allotransplant* or transplant* or allograft* or graft* or donor* or recipient*)).tw,kw.	114754
4	1 or 2 or 3	134215
5	exp histocompatibility antigen/	111501
6	histocompatibility antigen.hw.	40003
7	5 or 6	111580
8	(incompatib* or mismatch* or mis-match* or crossmatch* or cross-match* or xm).tw,kw.	98380
9	7 and 8	5586
10	((antigen* or anti-gen* or hla* or histocompatib*) adj6 (incompatib* or mismatch* or mis-match* or crossmatch* or cross-match* or xm or test*)).tw,kw.	40949
11	(exp T-Lymphocytes/ or exp B-Lymphocytes/) and (incompatib* or mismatch* or mis-match* or crossmatch* or cross-match* or xm).tw,kw.	8089
12	((t-cell* or t-lymphocyte* or b-cell* or b-lymphocyte* or positive) adj5 (incompatib* or mismatch* or mis-match* or crossmatch* or cross-match* or xm)).tw,kw.	3859
13	exp alloantibody/	19775
14	(isoantibod* or alloantibod*).hw.	4656
15	13 or 14	19779
16	(allo?antibod* or iso?antibod* or ((donor-specific* or panel-reactive*) adj3 antibod*)).tw,kw.	13457
17	((Donor* or recipient* or transplant* or acceptab* or unacceptab* or repeat*) adj4 (mismatch* or mis-match*)).tw,kw.	9596
18	((Donor* or recipient* or transplant* or candidate*) adj8 incompatib*).tw,kw.	4710
19	((DSA or PRA or cPRA or (high* adj2 risk)) and transplant*).tw,kw.	43184
20	exp histocompatibility test/	1378
21	histocompatib* test*.hw.	1379
22	20 or 21	1379

23	exp antibody dependent cellular cytotoxicity/	9382
24	antibody dependent cell* cytotoxic*.hw.	7033
25	23 or 24	9384
26	(test* or crossmatch* or cross-match* or xm).tw,kw.	3416004
27	25 and 26	2082
28	(cytotoxic* adj3 (crossmatch* or cross-match* or xm or test*)).tw,kw.	8215
29	((sensiti* or desensiti*) adj5 (patient* or recipient* or candidate*)).tw,kw.	63827
30	9 or 10 or 11 or 12 or 15 or 16 or 17 or 18 or 19 or 22 or 27 or 28 or 29	176642
31	4 and 30	21771
32	limit 31 to (conference abstract or conference paper or "conference review")	11826
33	(animal or animals or canine* or cat or cats or dog or dogs or feline or hamster* or lamb or lambs or mice or monkey or monkeys or mouse or murine or pig or pigs or piglet* or porcine or primate* or rabbit* or rats or rat or rodent* or sheep* or veterinar*).ti,kw,dq,jx. not (human* or patient*).mp.	1160009
34	32 not 33	11736
35	31 not 32	9945
36	(exp animal/ or exp juvenile animal/ or adult animal/ or animal cell/ or animal tissue/ or nonhuman/ or animal experiment/ or animal model/) not human/	4073584
37	35 not (33 or 36)	9633
38	limit 37 to yr="2000 -Current"	8913

Cochrane [Wiley] (August 19, 2019)

Cochrane Central Register of Controlled Trials - Issue 8 of 12, August 2019

Cochrane Database of Systematic Reviews - Issue 8 of 12, August 2019

ID	Search	Hits
#1	((kidney* or renal) NEAR/3 (allotransplant* or transplant* or allograft* or graft* or donor* or recipient*)):TI,AB,KW	11121
#2	((antigen* or anti gen* or hla* or histocompatib*) NEAR/6 (incompatib* or mismatch* or mis match* or crossmatch* or cross match* or xm or test*)):TI,AB,KW	15740
#3	((t cell* or t lymphocyte* or b cell* or b lymphocyte* or positive) NEAR/5 (incompatib* or mismatch* or mis match* or mis match* or cross match* or xm)):TI,AB,KW	2017
#4	(alloantibod* or isoantibod* or allo antibod* or iso antibod* or ((donor specific* or panel reactive*) NEAR/3 antibod*)):TI,AB,KW	3282
#5	((Donor* or recipient* or transplant* or acceptab* or unacceptab* or repeat*) NEAR/4 (mismatch* or mis match*)):TI,AB,KW	1255
#6	((Donor* or recipient* or transplant* or candidate*) NEAR/8 incompatib*):TI,AB,KW	89
#7	((DSA or PRA or cPRA or (high* NEAR/2 risk)) and transplant*):TI,AB,KW	3094
#8	(histocompatibility test* or blood group* and crossmatch* or lymphocyte culture test*):TI,AB,KW	656
#9	(cytotoxic* NEAR/3 (crossmatch* or cross match* or xm or test*)):TI,AB,KW	141
#10	((sensiti* or desensiti*) NEAR/5 (patient* or recipient* or candidate*)):TI,AB,KW	6354
#11	#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10	29646
#12	#1 AND #11	1556

NOTE S1: ACCESS DATABASE TEMPLATE FOR STUDY SELECTION AND DATA COLLECTION

The Access Database used for study selection and data collection is available upon request from the corresponded author.

TABLE S3: RISK OF BIAS BY THE PROBABST TOOL FOR PREDICTION MODEL

STUDIES

Author	Year	DOMAIN 1: PARTICIPANTS	DOMAIN 2: PREDICTORS	DOMAIN 4: ANALYSIS	OVERALL ASSESSMENT
Louis et al.	2019	High	Unclear	High	High
Meneghini et al.	2018	High	High	High	High
Michielsen et al.	2019	High	High	Unclear	High
Molina et al.	2017	High	High	Unclear	High
Passamonti et al.	2019	High	High	Unclear	High
Senev et al.	2019	High	Low	High	High
Uffing et al.	2019	High	High	High	High
Wehmeier et al.	2017	High	High	High	High
Zecher et al.	2017	High	High	High	High
Johnson et al.	2016	High	High	High	High
Khovanova et al.	2015	High	High	High	High
Kamburova et al.	2018	High	High	Unclear	High
Geneugelijck et al.	2018	High	High	High	High

Justification for overall risk of bias assessment by study:

Louis et al.	DOMAIN 1: PARTICIPANTS	KTR selected based on availability of posttransplant biopsy samples
	DOMAIN 2: PREDICTORS	Insufficient detail on HLA typing
	DOMAIN 4: ANALYSIS	Considered univariable analyses results to inform model specification and applied forward selection of covariates; conducted landmark analysis from posttransplant biopsy dates conducted at various intervals from transplantation in a subset with remaining tissue samples.
Meneghini et al.	DOMAIN 1: PARTICIPANTS	Included primarily White KTR; excluded HLA-identical
	DOMAIN 2: PREDICTORS	C3d assays conducted only among DSA positive KTR; missing HLA C, DRB3/4/5/, DQA1, DPA1 and DPB1 types
	DOMAIN 4: ANALYSIS	Multivariable models included posttransplant variables and potentially correlated variables. Models were likely overfitted.
Michielsen et al.	DOMAIN 1: PARTICIPANTS	Included primarily White KTR. To address confounding related to transplant era and donor characteristics, only subset of KTRs with DSA vs. nDSA paired by donor were analyzed excluding 50% of the cohort.
	DOMAIN 2: PREDICTORS	DSA status assignment varied by HLA locus
	DOMAIN 4: ANALYSIS	Not all pertinent confounders (e.g., KTRs' sex) were adjusted for in multivariable models
Molina et al.	DOMAIN 1: PARTICIPANTS	Included retransplant recipients; excluded KTR missing serum samples
	DOMAIN 2: PREDICTORS	Incomplete molecular (SSO) HLA typing
	DOMAIN 4: ANALYSIS	Model specification and handling of missing variables unclear
Passamonti et al.	DOMAIN 1: PARTICIPANTS	Included retransplant recipients; excluded KTR missing serum samples
	DOMAIN 2: PREDICTORS	HLA typing at split antigen level

	DOMAIN 4: ANALYSIS	Multiple potentially correlated variables informing immune risk were included in the model
Senev et al.	DOMAIN 1: PARTICIPANTS	Primarily White participants; included retransplant recipients
	DOMAIN 2: PREDICTORS	N/A
	DOMAIN 4: ANALYSIS	Considered univariable analyses results to inform model specification. Multivariable models included DSA and its effect mediator (AMR) in the same model
Uffing et al.	DOMAIN 1: PARTICIPANTS	Included retransplant recipients; excluded KTR with DSA class I/II
	DOMAIN 2: PREDICTORS	Serologic HLA types
	DOMAIN 4: ANALYSIS	Considered univariable analyses results to inform model specification
Wehmeier et al.	DOMAIN 1: PARTICIPANTS	Excluded KTR with HLA-identical donors and assumed husband/child to wife/mother to represent high immune risk
	DOMAIN 2: PREDICTORS	Incomplete typing and unclear method. Some DSA (by SAB) may have been missed
	DOMAIN 4: ANALYSIS	
Zecher et al.	DOMAIN 1: PARTICIPANTS	Excluded KTR receiving T-cell depleting induction agents, mTORi maintenance immunosuppression and missing pretransplant serum
	DOMAIN 2: PREDICTORS	Inconsistent DSA assignment across HLA loci
	DOMAIN 4: ANALYSIS	Considered bivariable analyses results to inform model specification. Included DSA effect mediator of DSA (AMR) among model covariates
Johnson et al.	DOMAIN 1: PARTICIPANTS	Included retransplant recipients; included KTR with negative virtual crossmatch to compare flow XM + vs. -
	DOMAIN 2: PREDICTORS	Incomplete HLA typing (included HLA-A,B, Cw, DRB1, and DQB1) for KTR and donors; HLA-DPB1 available after January 2008; HLA-DQA1 available after 009.
	DOMAIN 4: ANALYSIS	Considered univariable analyses results to inform model specification and included potentially correlated variables
Khovanova et al.	DOMAIN 1: PARTICIPANTS	Included KTR of HLAi transplants defined by CDC or flow XM + and treated with Double Filtration Plasmapheresis
	DOMAIN 2: PREDICTORS	Variable definitions for HLAi (by CDC/flow XM)
	DOMAIN 4: ANALYSIS	Sample underpowered for analysis and models likely overfitted
Kamburova et al.	DOMAIN 1: PARTICIPANTS	Included primarily White KTR and retransplant recipients
	DOMAIN 2: PREDICTORS	Inconsistent DSA assignment in KTR (mitigating factor: sensitivity analysis demonstrates similar results)
	DOMAIN 4: ANALYSIS	Multiple potentially correlated variables considered in the same model included (Ag MM and DSA as well as PRA). Mitigating circumstances: correlations were evaluated prior to model specification.
Geneugeljk et al.	DOMAIN 1: PARTICIPANTS	Excluded KTR with >5/6 HLA antigen mismatches, treated with nonstandard protocols per Eurotransplant, 0/10 HLA antigen mismatches, and 0-1 PIRCHE-II mismatches
	DOMAIN 2: PREDICTORS	Allele-level HLA types imputed to infer molecular compatibility
	DOMAIN 4: ANALYSIS	Considered univariable analyses results to inform model specification and multiple potentially correlated variables included in the same model