The impact of patient ethnicity on HCT outcome – the UK experience

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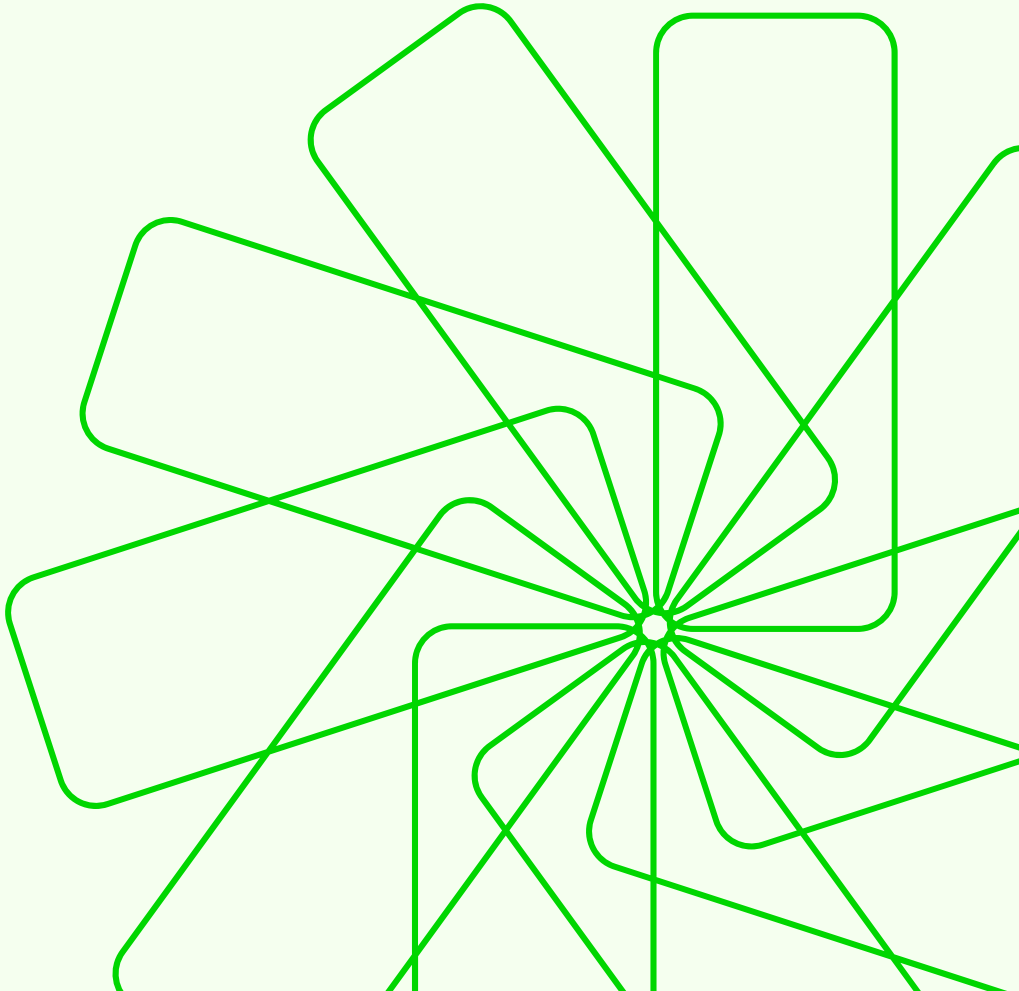
BSHI Conference, Manchester 2024



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Unlocking new ways to treat every patient

Initial piece of work to determine if inequities exist in HCT

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Ethnicity/race and patient outcomes studies

- Studies have shown that patients from minority ethnic backgrounds do worse post-HCT compared to those from White backgrounds – inconsistent findings

- Numerous reasons for differences in the studies:
  - Size of cohorts, type of transplant, donor type, era, data quality etc.

- Limitations of the data include self-defined ethnicity, inconsistent categorisation terminology

- Data predominantly from US cohorts – access & healthcare models are different to UK
  - Lack of primary care; health insurance vs NHS; transplant centre set up – crossing state borders for treatment; transplant protocols etc.

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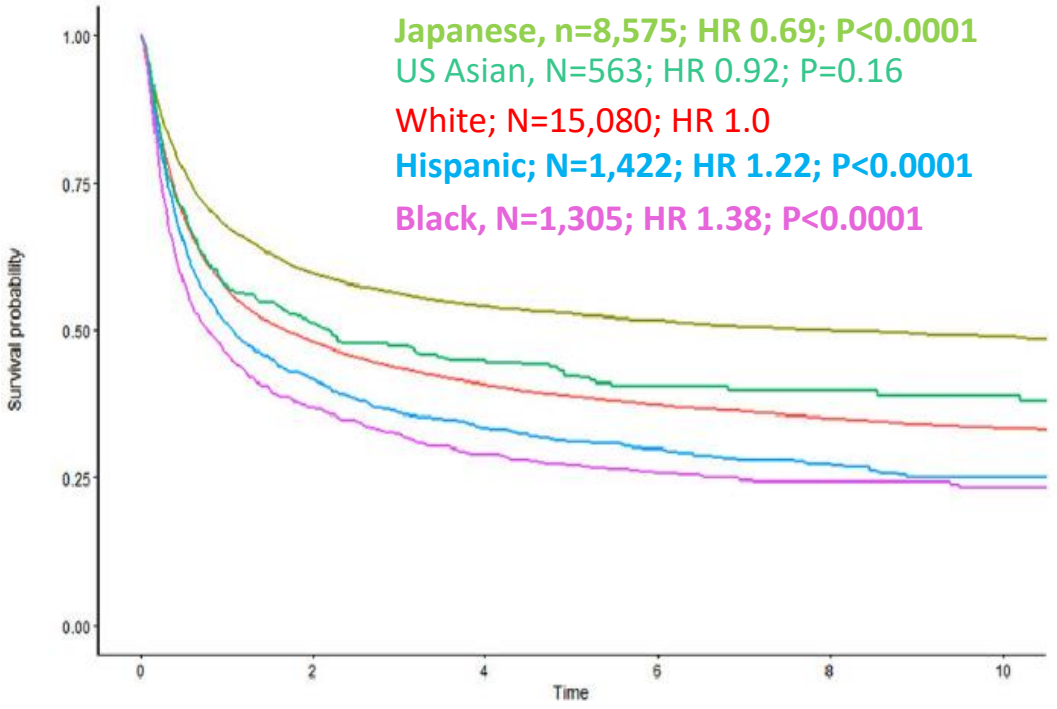
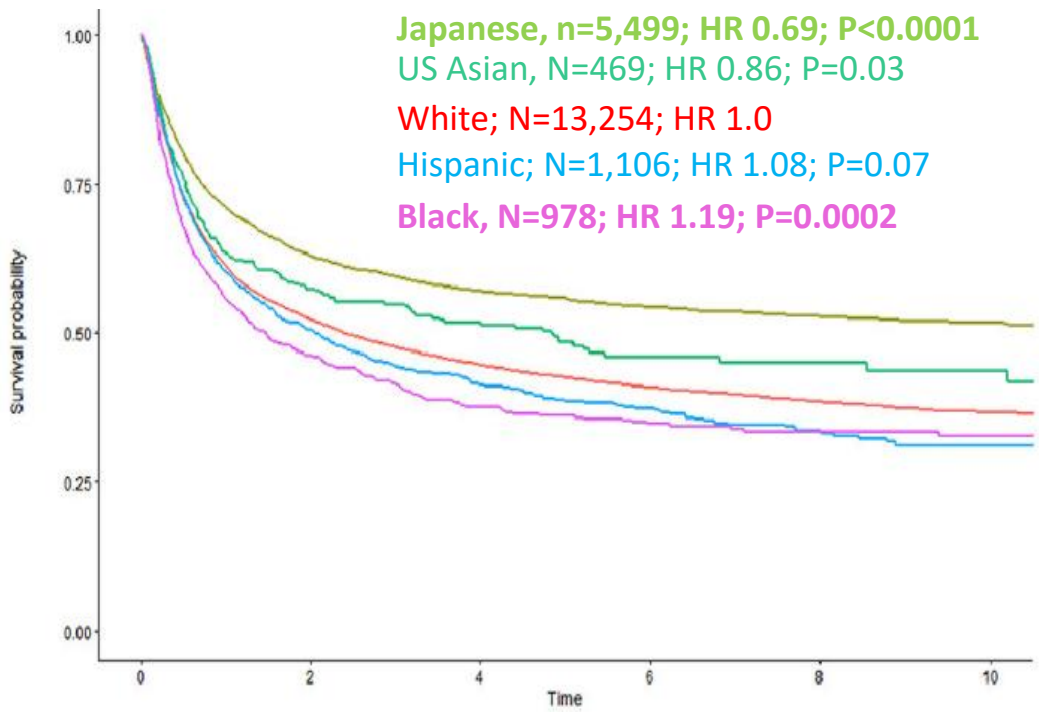
Largest study to date

- 26,945 Patients receiving a MUD HCT, North-America and Japan only.
- Concluded that *"mortality after HCT was strongly influenced by both race and HLA factors"*

UNADJUSTED FOR HLA



ADJUSTED FOR HLA



MORISHIMA *et al*. TCT (2022) 28:357.e1-357.e6

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Ethnicity data in the UK registry

- Ethnicity has been collected in the UK registry since 2009

- Self-defined ethnicity; reliant on third party to translate ethnicity from notes into records

- Ethnicity data categorisations based on US data from pre-2009:
  - Asian
  - Black
  - Hispanic
  - Native American
  - Native Hawaiian
  - Other ethnicity (inc. any other ethnicity and mixed heritage)
  - White

} Grouped into ‘Other’ category due to low numbers of cases

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Methods

Inclusion criteria

- Any patient (adult and paeds) undergoing first Auto-HCT or Allo-HCT from any donor source
- All disease types
- Transplant dates between 1st Jan 2009 and 31st December 2019
- Transplant received in England, Northern Ireland, Scotland or Wales

Exclusion Criteria

- Republic of Ireland centres
- Private treatment only centres (lack of long-term follow-up)
- Overseas patients (if known)

Primary Outcome

- Overall Survival

Secondary Outcomes

- aGvHD, Relapse, NRM, EFS

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Cohort characteristics – Autologous HCT (N=20,119)

Variable		N (%)
Ethnicity		919 (5)
Asian		727 (4)
	Black	612 (3)
	Other	17,861 (88)
	White	
Patient age	<30	1,776 (9)
	30-49	3,687 (18)
	≥ 50	14,656 (73)
Recipient Sex	Female	7,647 (38)
Disease		11,043 (55)
MM		1,486 (7)
	Hodgkin's Lymphoma	5,441 (27)
	NHL	668 (3)
	Other malignant	310 (1.5)
	Autoimmune	22 (<1)
	Other non-malignant	1,149 (6)
	Solid Tumours	

Variable		N (%)
Graft type		19,992 (>99)
PBSC		117 (<1)
	Bone Marrow	
HCT-CI	None	10,273 (51)
(0)		3,709 (18)
	Low (1 or 2)	2,184 (11)
	Intermediate/High (3+)	1,677 (8)
	Comorbid, HCT-CI unknown	2,276 (11)
	Unknown comorbidity	
EBMT Risk Score		675 (3)
0		476 (2)
	1	4,109 (21)
	2	14,859 (74)
	≥3	
Year of Transplant	2009 – 2011	4,601 (23)
	2012 – 2014	5,259 (26)
	2015 – 2017	6,075 (30)
	2018 - 2019	4,184 (21)

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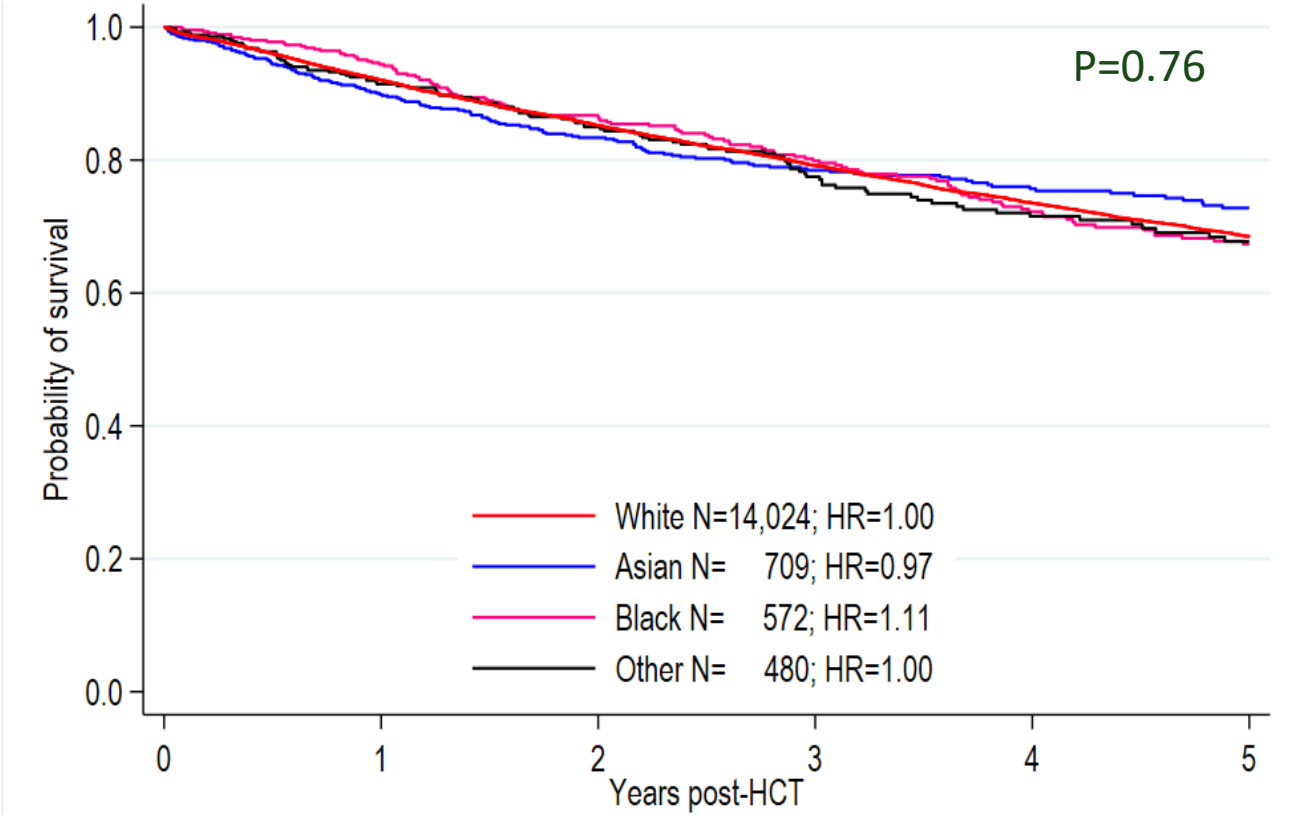
Autologous HCT – 5y OS MV analysis

- Patient ethnicity not associated with significant differences in 5y OS in:
  - Full cohort
  - Malignant disease only
  - Non-malignant disease only
  - Different disease subcategories



Cox Regression models adjusted for: Karnofsky/Lansky status at Tx, HCT-CI, patient age, patient sex at birth, diagnosis, EBMT risk score, source of stem cells

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Cohort characteristics – Allogeneic HCT (N=13, 978)

Variable		N (%)
Ethnicity		1,081 (8)
Asian		441 (3)
	Black	751 (5)
	Other	11,705 (84)
	White	
Patient age		3,968 (29)
<30		3,490 (25)
	30-49	6,520 (46)
	≥ 50	
Disease		342 (2)
MM		542 (4)
	Hodgkin's Lymphoma	1,347 (10)
	NHL	2,047 (15)
	MDS/MPN	4,801 (34)
	AML	1,795 (13)
	ALL	1,284 (8.5)
	Other malignant	806 (6)
	Bone Marrow Aplasia	1,014 (7)
	Other non-malignant	

Variable		N (%)
Sex at birth	Recipient F	5,441 (39)
	Donor F	4,671 (33)
Type of donor	Related	4,268 (30)
	Unrelated	8,540 (61)
	Cord	683 (5)
	MMRD/Haploidentical	487 (4)
T cell depletion	None	3,620 (26)
	Alemtuzumab	8,181 (58)
	ATG or ALG	2,177 (16)
Conditioning regimen	RIC	8,995 (64)
	Myeloablative	4,808 (34)
	Missing	175 (1)
Year of Transplant.	2009 – 2011	3,221 (23)
	2012 – 2014	3,939 (28)
	2015 – 2017	4,094 (29)
	2018 - 2019	2,724 (20)

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HLA matching challenges

- Adjusting for impact of HLA matching was vital for Allo-HCT cases
- HLA matching data was insufficiently reported; significant bioinformatic analysis was required to determine match status
- Donor type is not descriptive
  - MMRD proxy for Haplo?
- Matching status did not always correlate with donor type
  - 10/10 marked as MMRD/Haplo?

	RD	UD	Cord	Haplo
10/10	4,152	5,744	86	0
9/10	29	1,410	41	38
8/10	6	169	57	183
7/10	4	27	34	24
6/10	10	14	19	61
5/10 or lower	28	8	7	157
Indeterminable	19	47	57	24
Missing	20	1,121	382	0

Orange shading denotes unexpected HLA typing vs. donor type, or high numbers of missing data

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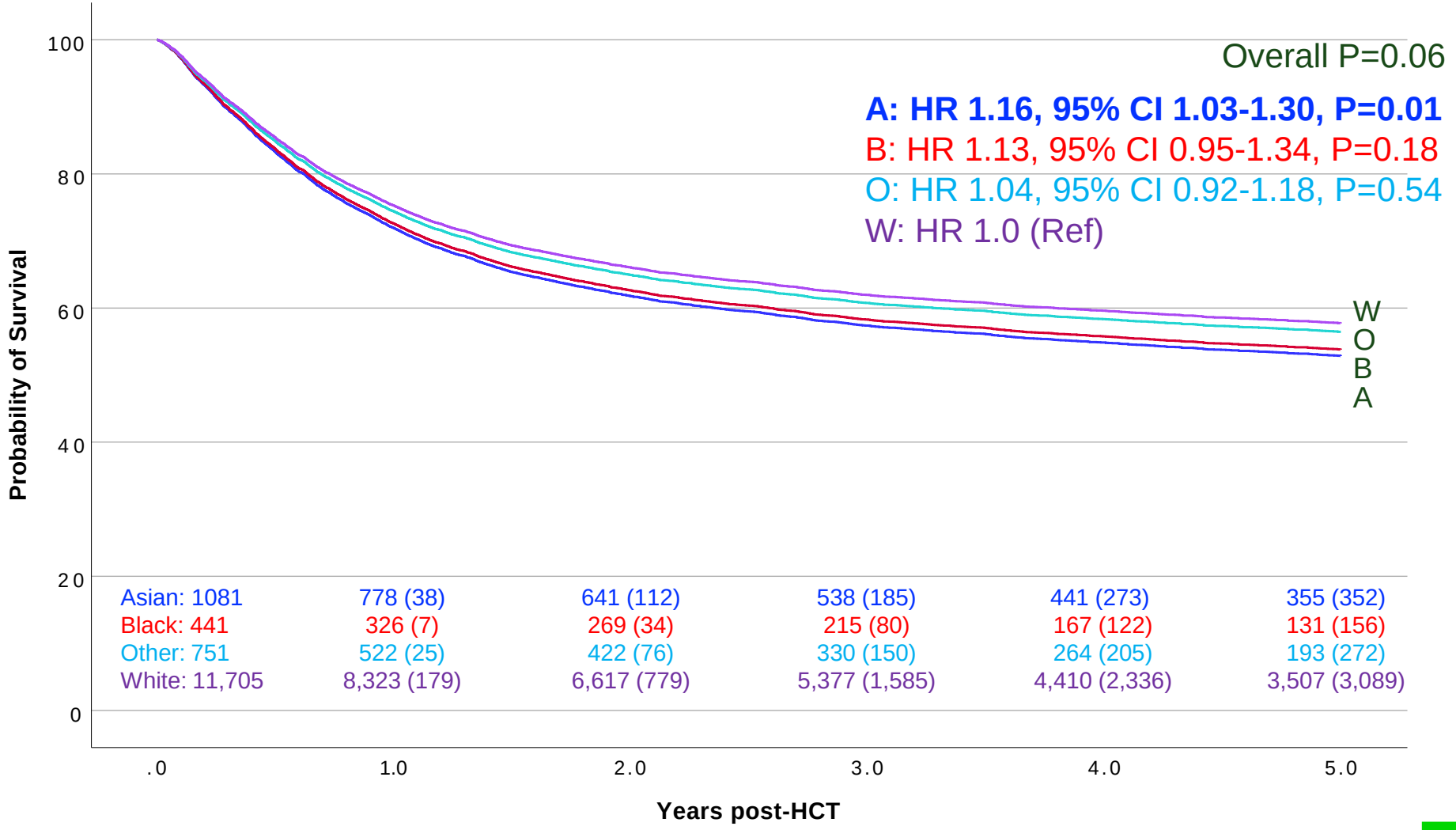
5y OS in the allo-HCT cohort (N=13,978)



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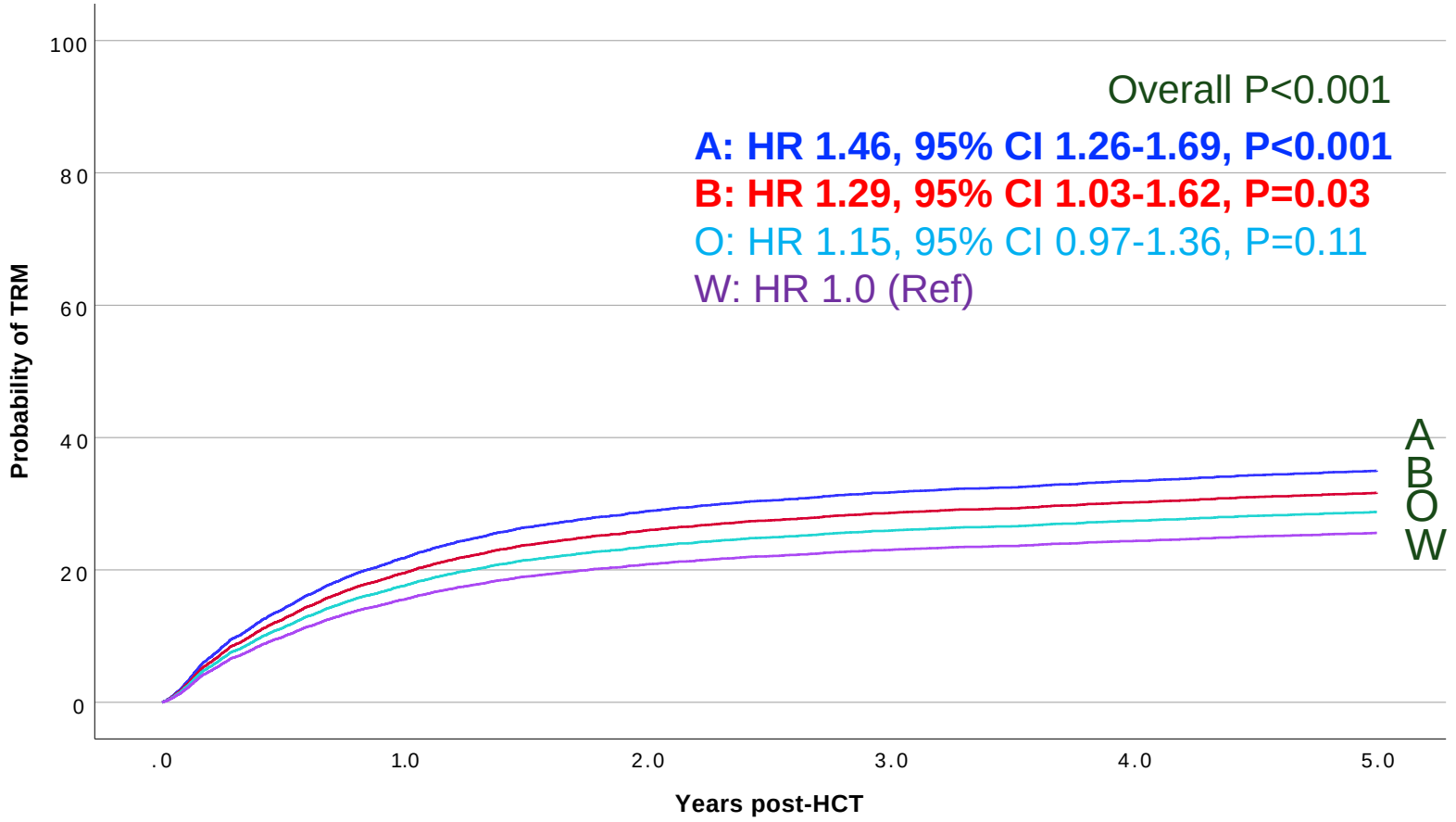
5y TRM in the allo-HCT cohort (N=13,978)



Asian: 1,074	717 (162)	590 (260)	502 (335)	409 (425)	311 (517)
Black: 436	301 (57)	255 (93)	204 (140)	157 (184)	120 (221)
Other: 737	469 (141)	376 (214)	286 (294)	225 (348)	165 (407)
White: 11,562	7,339 (2,376)	5,772 (3,446)	4,634 (4,411)	3,803 (5,157)	3,011 (5,879)

Lower PFS:
Asian HR 1.14, P=0.02

Increased TRM at 100d & 1y

Relapse – N/S

aGvHD – N/S

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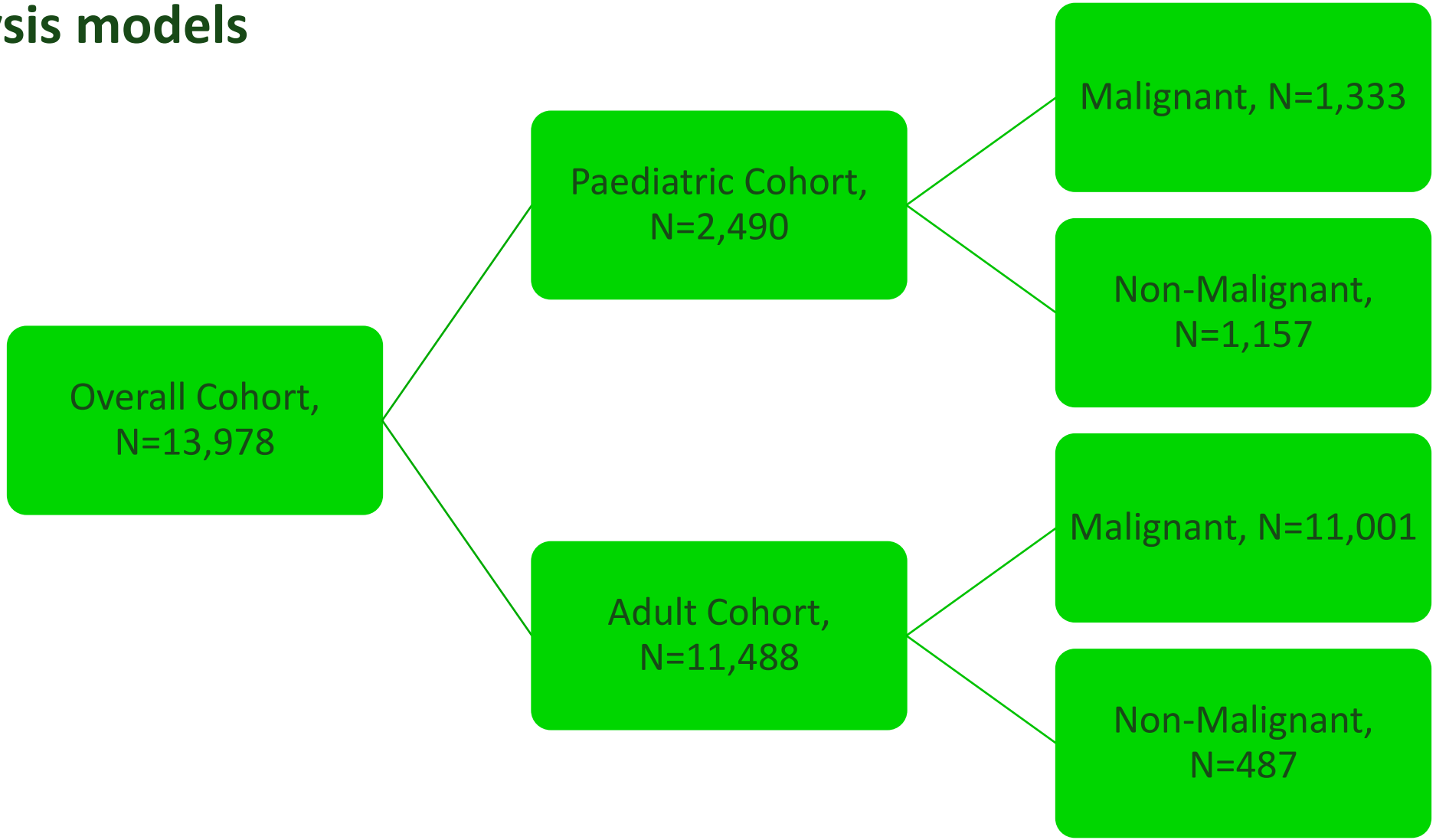
Analysis models



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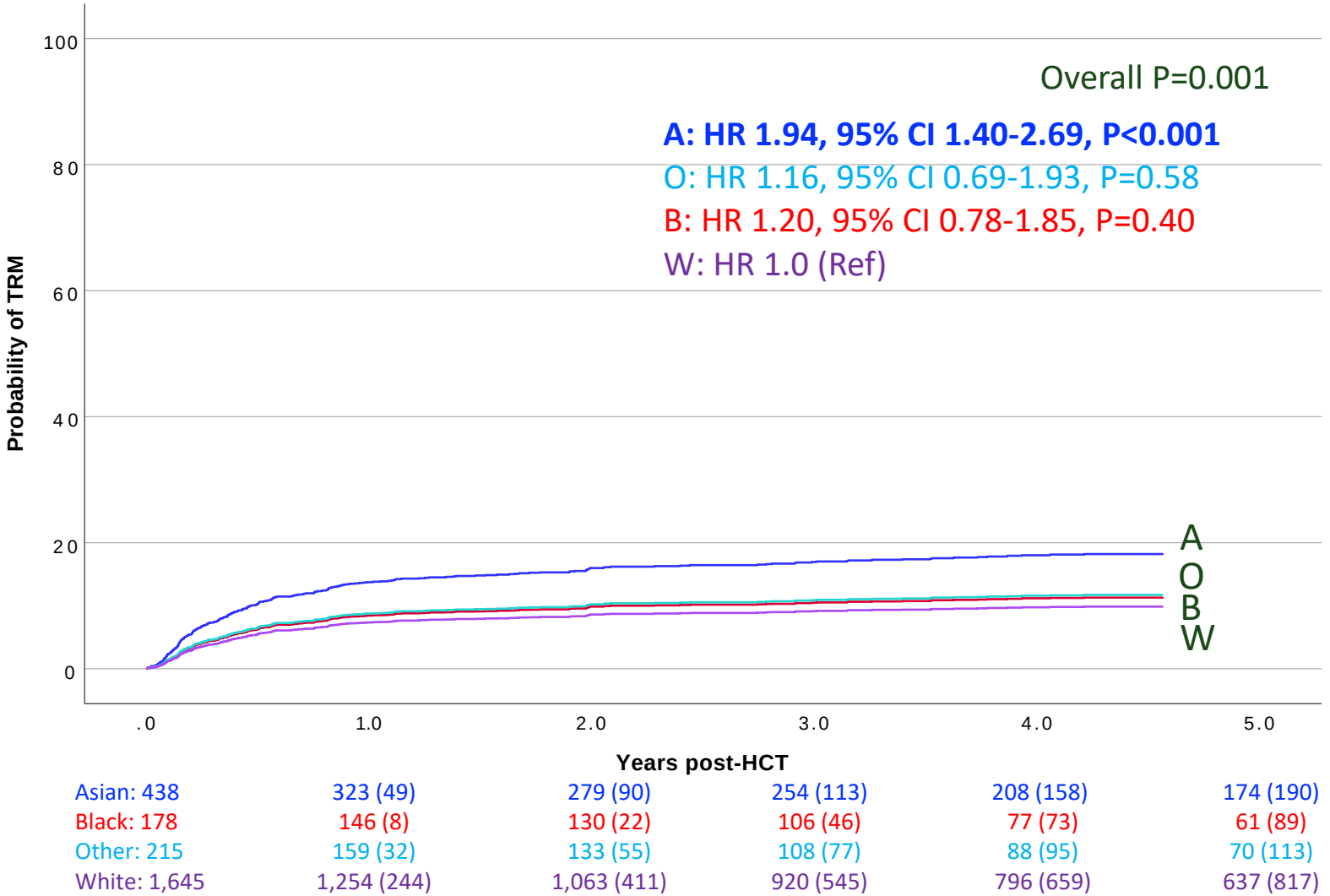
5y TRM in the paediatric allo-HCT cohort (N=2,490)



Asian: 438	323 (49)	279 (90)	254 (113)	208 (158)	174 (190)
Black: 178	146 (8)	130 (22)	106 (46)	77 (73)	61 (89)
Other: 215	159 (32)	133 (55)	108 (77)	88 (95)	70 (113)
White: 1,645	1,254 (244)	1,063 (411)	920 (545)	796 (659)	637 (817)

Lower OS:
Asian HR 1.67, P=<0.01

Lower PFS:
Asian HR 1.44, P=<0.01

Increased TRM at 100d & 1y

Relapse – N/S

aGvHD – N/S

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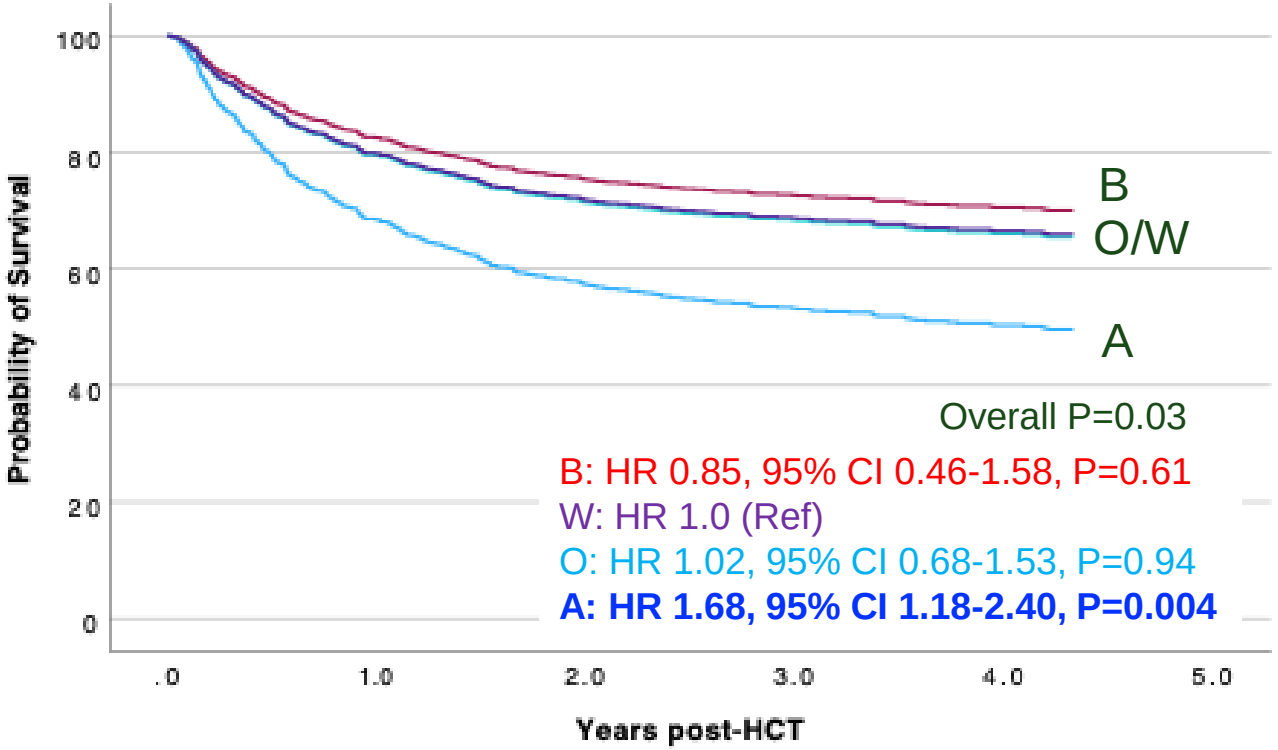
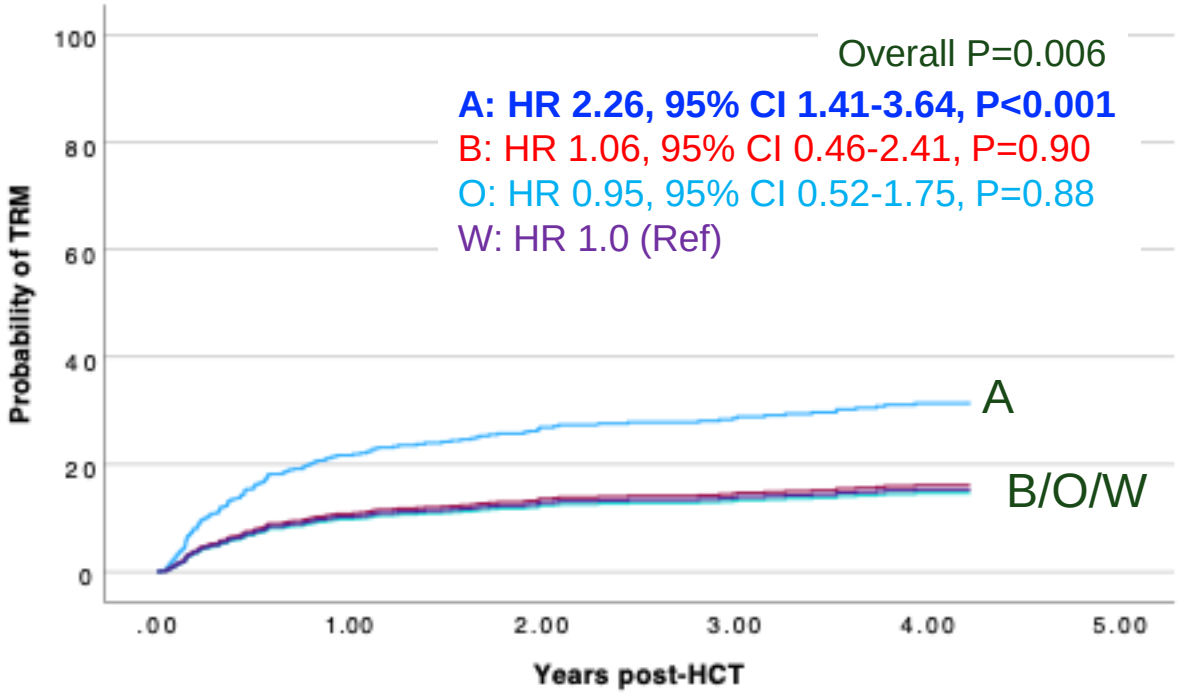
5y OS & TRM in the malignant paediatric allo-HCT cohort





Similar effects for paediatric patients with non-malignant disease

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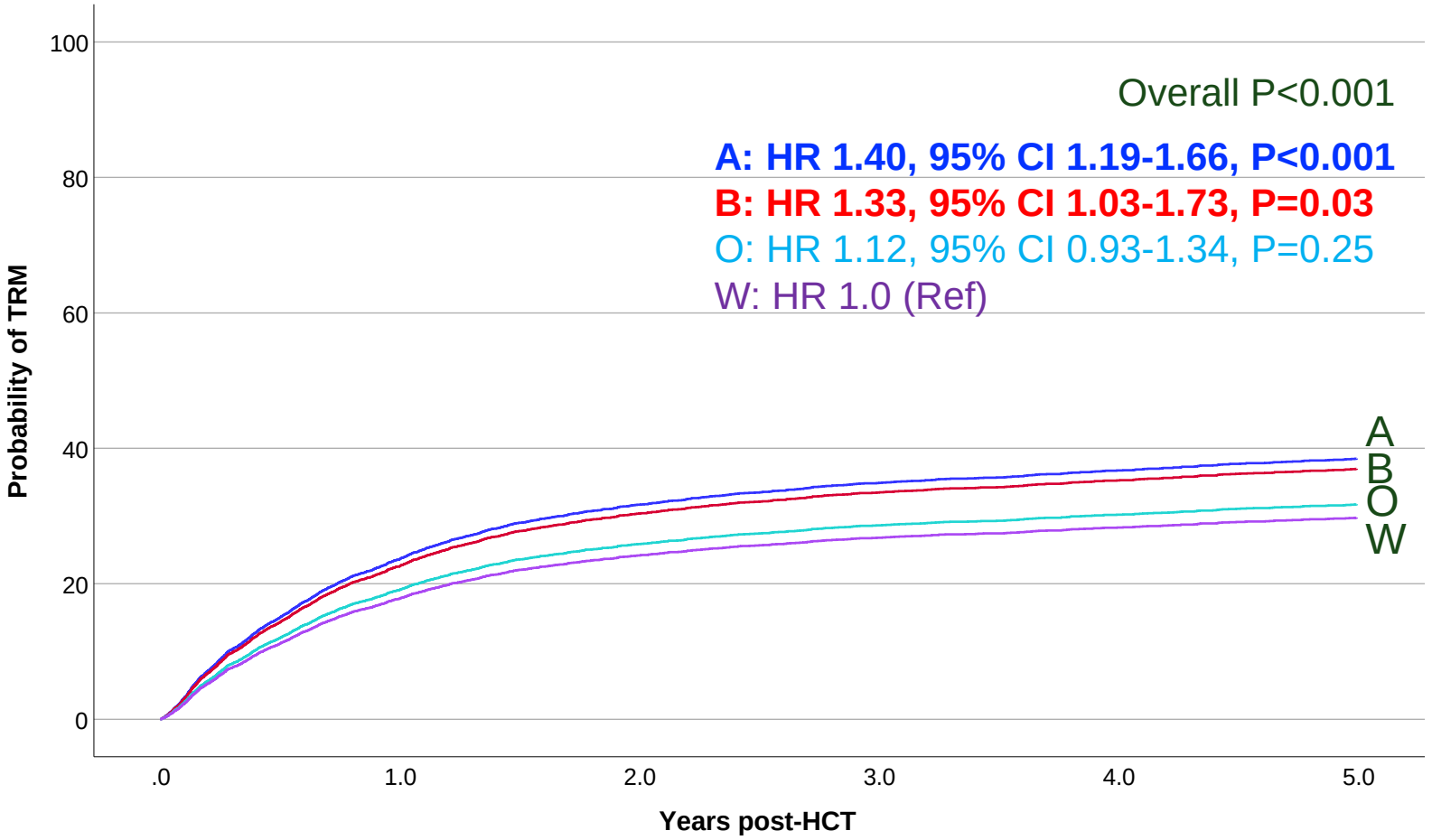
5y TRM in the adult allo-HCT cohort (N=11,488)



Asian: 636	394 (113)	311 (170)	248 (222)	202 (266)	158 (306)
Black: 258	155 (49)	125 (71)	98 (94)	80 (111)	59 (132)
Other: 552	310 (109)	242 (160)	178 (217)	137 (253)	94 (295)
White: 11,333	6,085 (2,132)	4,709 (3,035)	3,714 (3,866)	3,007 (4,498)	2,373 (5,063)

OS – N/S

PFS – N/S

Increased TRM at 100d & 1y for all ethnicities

Relapse – N/S

aGvHD – N/S

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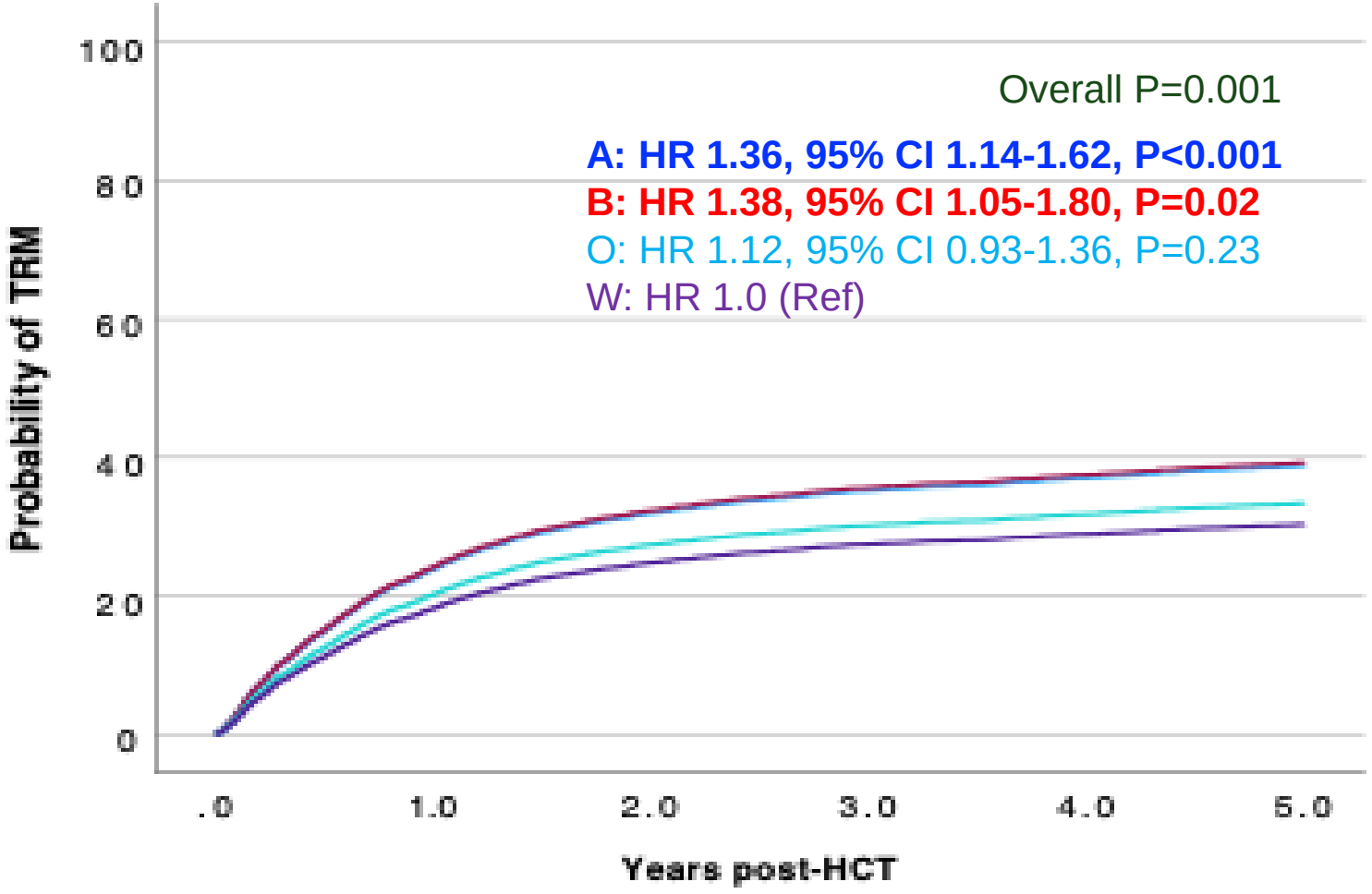
5y TRM in the adult malignant allo-HCT cohort (N=11,001)



No other significant effects on any other outcome tested

No effect of ethnicity in non-malignant cohort

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Conclusions

Ethnicity does affect HCT outcome, can lead to differences in OS, OFS and TRM

Confirms observations from previous studies BUT differences in cohort, data coding, demographics, etc. makes interpretation difficult

Why?

- Cause of death analysis didn’t identify cause
- HLA?
- Different genetic associations for drug metabolism?
- Other social, clinical or demographic factors, e.g. Socioeconomic status?

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Conclusions

Important to remember:

- Ethnicity coding was not optimal
- Study focused on those individuals that had a HCT
- Does not consider access to, or the experience of HCT

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Acknowledgements

Anthony Nolan:
Richard M Szydlo
Yasmin Sheikh
Caitlin Farrow
Michaela Agapiou
Steven GE Marsh

BSBMTCT:
Julia Lee
Rachel M Pearce
Kanchan Rao
Kim Orchard
Eduardo Olavarria
John A Snowden

Study performed by Anthony Nolan and BSBMTCT on behalf of the UK HCT community

The authors wish to acknowledge the participation of the patients and the allogeneic HCT donors who were part of these analyses

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Variable		Allogeneic, n (%)
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Ethnicity	Asian	1,081 (8)
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	White	11,705 (84)
Patient age	<30	3,968 (29)
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Disease	MM	342 (2)
	Hodgkin's Lymphoma	542 (4)
	NHL	1,347 (10)
	MDS	1,495 (11)
	MPN	552 (4)
	AML	4,801 (34)
	ALL	1,795 (13)
	CML	428 (3)
	CLL	316 (2)
	CMML	244 (1.5)
	Other malignant	296 (2)
	Bone Marrow Aplasia	806 (6)
	Primary Immune Deficiencies	442 (3)
	Other inherited disorders	169 (1)
	Histiocytic disorders	77 (<1)
	Haemoglobinopathies	225 (1.5)
	Autoimmune	36 (<1)
	Other non-malignant	65 (<1)

Variable		Allogeneic, n (%)
Sex at birth	Recipient Female	5,441 (39)
	Donor Female	4,671 (33)
	Missing	R: 18 (<1); D: 225 (2)
Donor age	Cord	683 (5)
	0-18	525 (4)
	19-59	8,886 (64)
	≥ 60	443 (3)
	Missing	3,441 (24)
Type of donor	Related	4,268 (30)
	Unrelated	8,540 (61)
	Cord	683 (5)
	MMRD/Haploidentical	487 (4)
T cell depletion	None	3,620 (26)
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