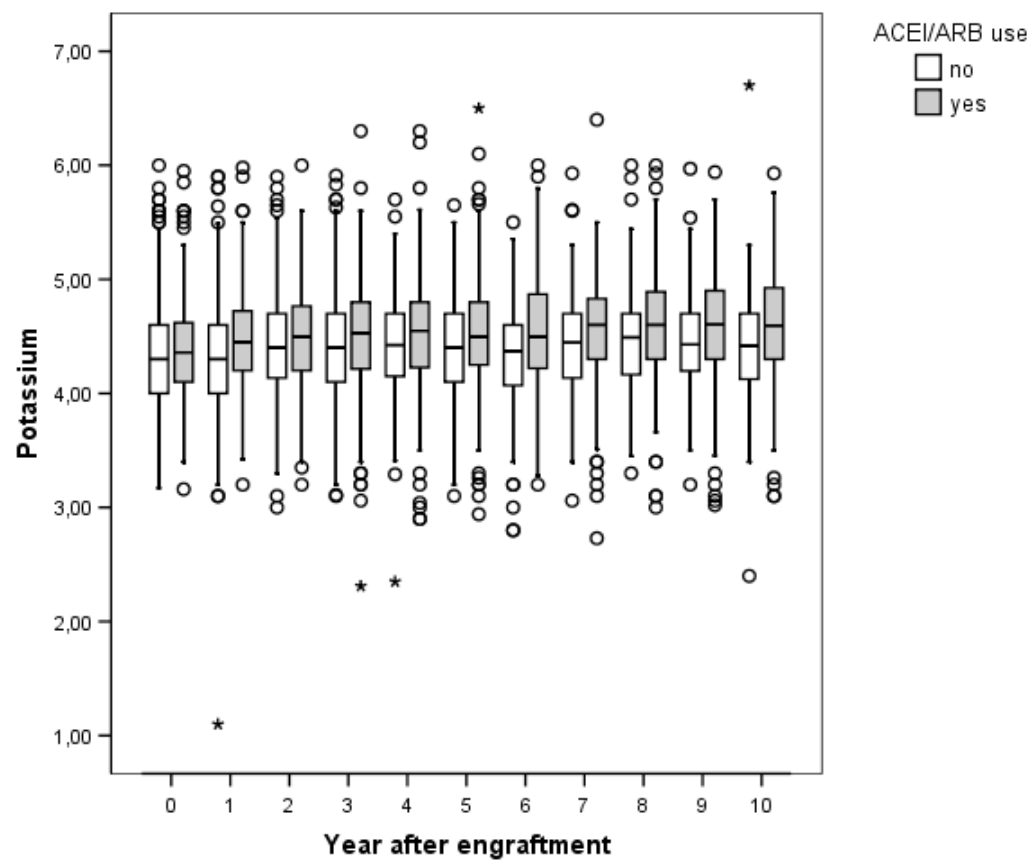
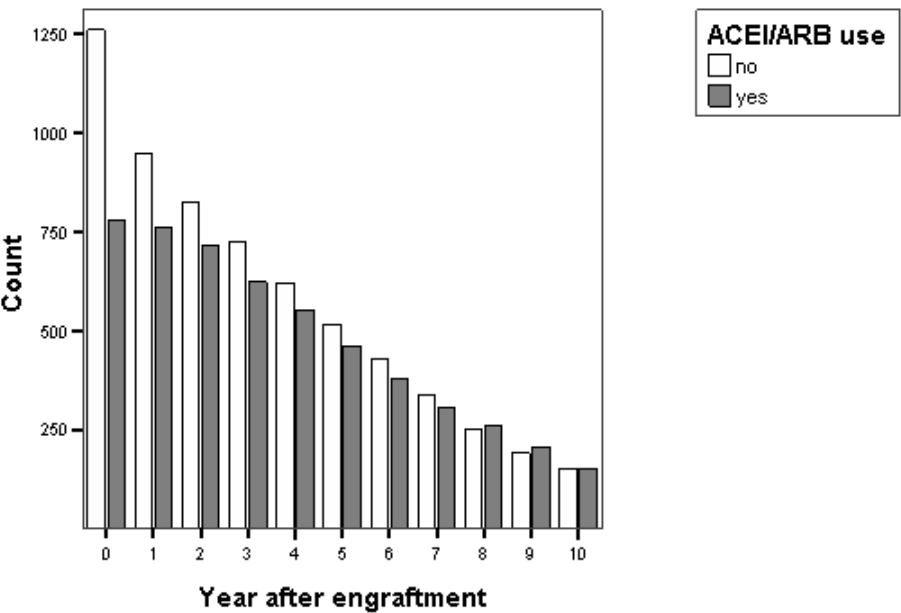


Supplemental diagrams

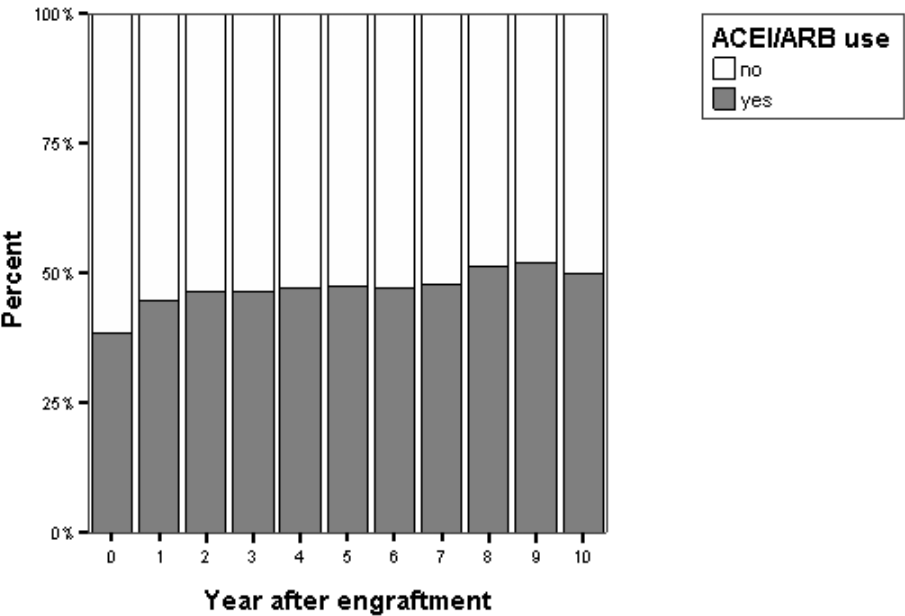
Boxplot of potassium levels vs. year after engraftment, stratified for ACEI/ARB use:



Number of ACEI/ARB user/nonusers vs. year after engraftment:

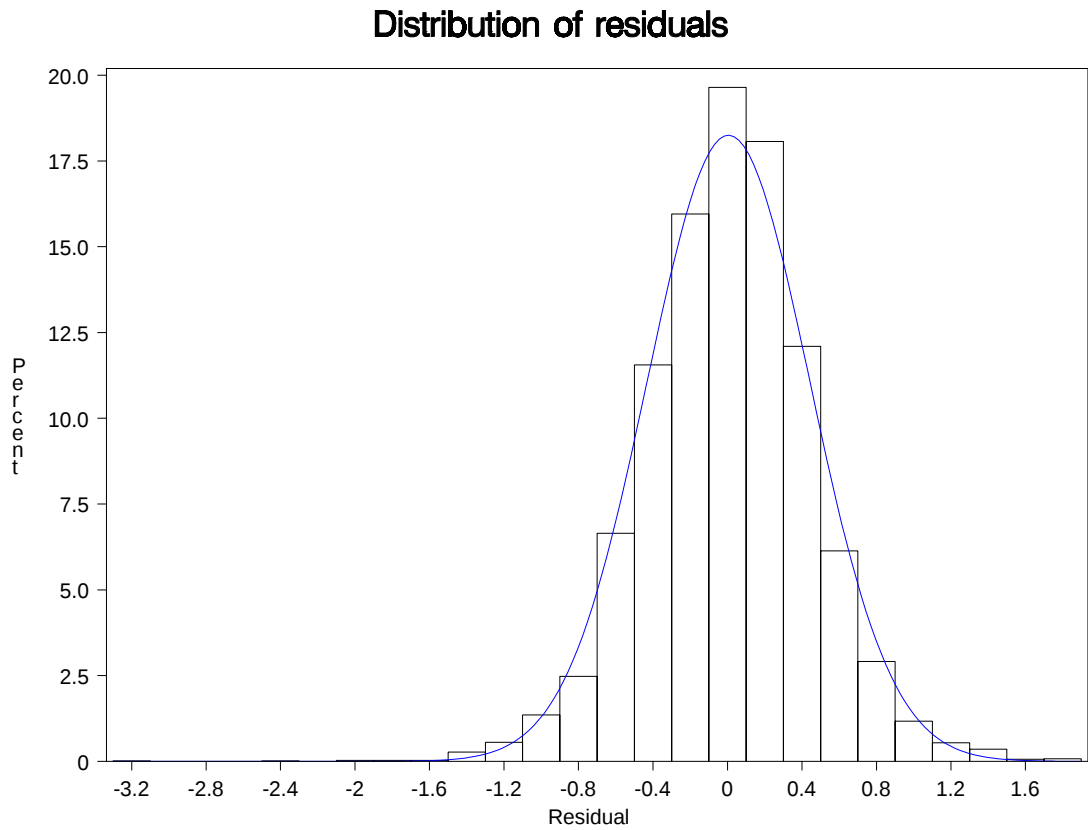


Percentage of ACEI/ARB user/nonuser vs. year after engraftment:



Residual diagnostics

Histogram of residuals

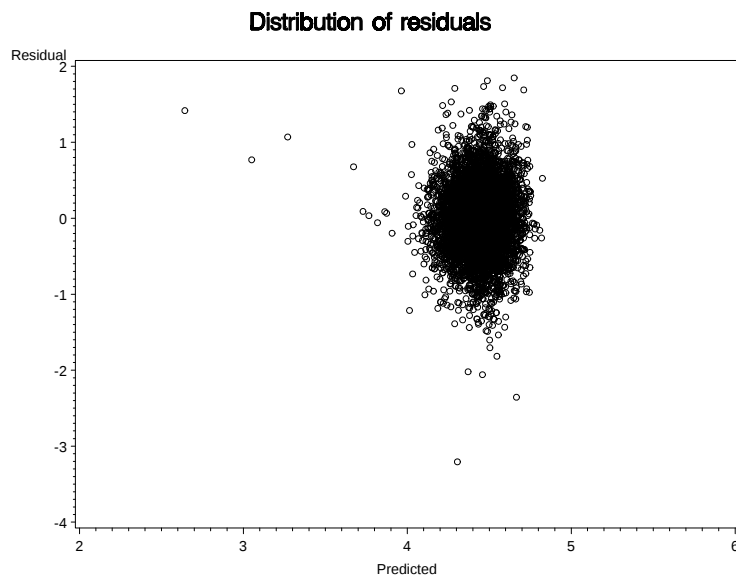


Quantiles for Normal Distribution

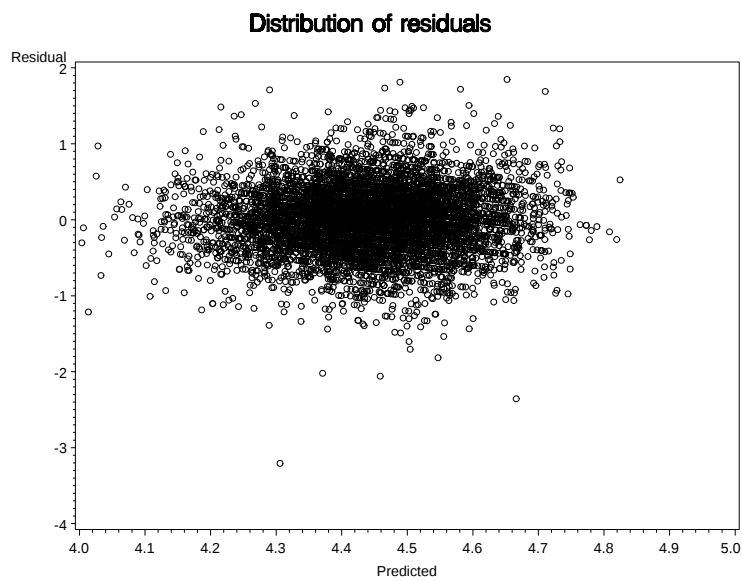
Percent	-----Quantile-----	
	Observed	Estimated
1.0	-1.06248	-1.01153
5.0	-0.69091	-0.71359
10.0	-0.53376	-0.55477
25.0	-0.27404	-0.28937
50.0	0.00970	0.00550
75.0	0.28006	0.30038
90.0	0.52527	0.56577
95.0	0.70576	0.72460
99.0	1.10267	1.02254

The residuals show perfect agreement with a normal distribution.

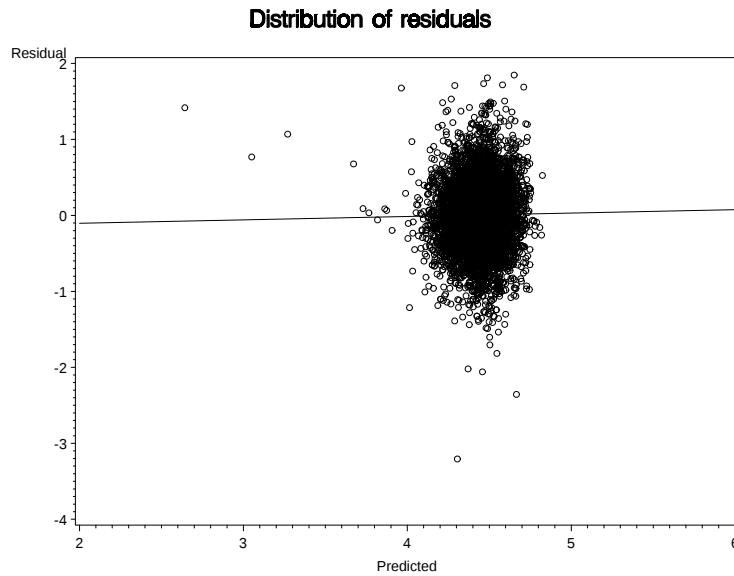
Residuals against predicted values



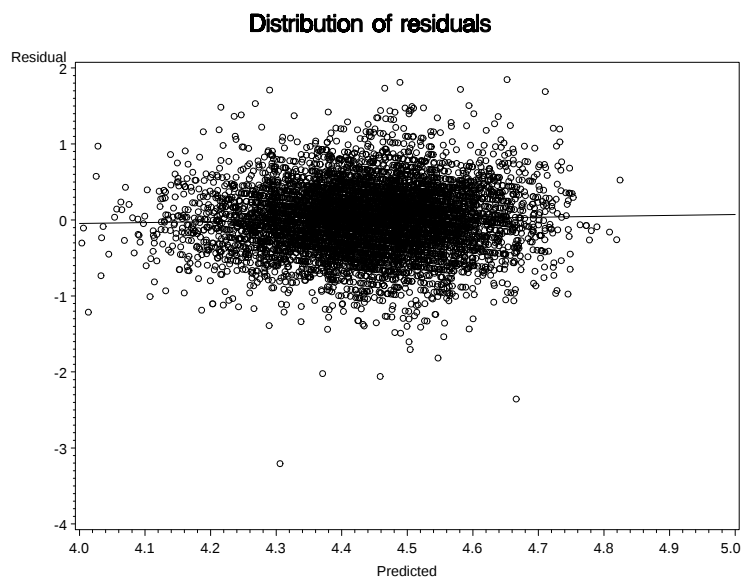
Residuals against predicted values, zoomed into range of [4, 5]



Absolute residuals against predicted values (to detect heteroscedasticity)



Absolute residuals against predicted values (to detect heteroscedasticity), zoomed into range [4, 5]



The absolute residuals show a significant ($p=0.02$) yet irrelevant positive correlation ($r=0.028$) with predicted values, such that the magnitude of the observed heteroscedasticity can be regarded as negligible.

Assessment of working correlation structure

The following working correlation structures offered by SAS/PROC MIXED were used to assess the validity of the original choice (AR(1)).

Structure	Description	Parms	(i,j)th element
AR(1)	Autoregressive(1)	2	$\sigma^2 \rho^{ i-j }$
CS	Compound Symmetry	2	$\sigma_1 + \sigma^2 1(i=j)$
CSH	Heterogeneous CS	$t+1$	$\sigma_i \sigma_j [\rho 1(i \neq j) + 1(i=j)]$
TOEP	Toeplitz	t	$\sigma_{ i-j +1}$
TOEPH	Heterogeneous TOEP	$2t-1$	$\sigma_i \sigma_j \rho_{ i-j }$
UN	Unstructured	$t(t+1)/2$	σ_{ij}

Correlation structure	Effect of ACEI/ARB use on potassium level	p-value
AR(1)	0.08283	<.0001
CS	0.08120	<.0001
CSH	0.07889	<.0001
TOEP	0.08009	<.0001
TOEPH	0.07712	<.0001
UN	0.08422	<.0001

Conclusion: the choice of correlation structure does not affect our main results.

Mixed linear model with “sticky” group definition

Subjects stay in the ACEI/ARB group once they used it. The results are virtually identical to the dynamic group model presented in table 3 in the manuscript.

Solution for Fixed Effects							
Effect	acei_arb_g	year	Estimate	Standard Error	DF	t Value	Pr > t
Intercept			4.5891	0.03994	1463	114.91	<.0001
acei_arb	1		0.08028	0.01631	189	4.92	<.0001
acei_arb	0		0	.	.	.	.
CNI			0.05863	0.01892	4468	3.10	0.0019
year		10	0.1659	0.03400	4468	4.88	<.0001
year		9	0.1985	0.03033	4468	6.54	<.0001
year		8	0.1887	0.02798	4468	6.74	<.0001
year		7	0.1599	0.02610	4468	6.13	<.0001
year		6	0.1126	0.02479	4468	4.54	<.0001
year		5	0.1245	0.02335	4468	5.33	<.0001
year		4	0.1452	0.02234	4468	6.50	<.0001
year		3	0.1330	0.02107	4468	6.31	<.0001
year		2	0.1339	0.01947	4468	6.88	<.0001
year		1	0.08613	0.01662	4468	5.18	<.0001
year		0	0	.	.	.	.
age_tpl			-0.00280	0.000610	1463	-4.59	<.0001
dialyseyears			-0.00179	0.004843	1463	-0.37	0.7123
GFR			-0.00421	0.000308	4468	-13.69	<.0001
diuretics			-0.1112	0.01521	4468	-7.31	<.0001
betablock			0.004371	0.01458	4468	0.30	0.7644
diabetes			0.04258	0.02107	4468	2.02	0.0433

Type 3 Tests of Fixed Effects				
Effect	Num DF	Den DF	F Value	Pr > F
acei_arb	1	189	24.23	<.0001
CNI	1	4468	9.61	0.0019
year	10	4468	7.72	<.0001
age_tpl	1	1463	21.06	<.0001
dialyseyears	1	1463	0.14	0.7123
GFR	1	4468	187.33	<.0001
diuretics	1	4468	53.42	<.0001
betablock	1	4468	0.09	0.7644
diabetes	1	4468	4.09	0.0433

Testing for interaction between ACEI/ARB and year of use (sticky group definition)

There was no statistical interaction (effect modification) between these two variables.

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
acei_arb_g	1	238	21.90	<.0001
year	10	5087	14.34	<.0001
acei_arb_g*year	10	5087	1.26	0.2457
age_tpl	1	5087	18.91	<.0001
dialyseyears	1	1549	0.81	0.3678
GFR	1	5087	227.47	<.0001
n0_diur	1	5087	53.93	<.0001
n0_betablock	1	5087	0.35	0.5525

Mixed linear model without ACEI/ARB changers

Subjects who switched groups were eliminated as suggested by the reviewer. The results are materially identical to the other models presented above and in the manuscript in table 3.

Solution for Fixed Effects							
Effect	acei_arb_full	year	Estimate	Standard Error	DF	t Value	Pr > t
Intercept			4.5545	0.04439	1312	102.59	<.0001
acei_arb	1		0.1125	0.01985	1312	5.67	<.0001
acei_arb	0		0	.	.	.	.
CNI			0.04683	0.02219	3079	2.11	0.0349
year		10	0.1955	0.04728	3079	4.13	<.0001
year		9	0.2602	0.03975	3079	6.55	<.0001
year		8	0.2493	0.03533	3079	7.06	<.0001
year		7	0.1711	0.03153	3079	5.42	<.0001
year		6	0.1170	0.02873	3079	4.07	<.0001
year		5	0.1220	0.02665	3079	4.58	<.0001
year		4	0.1464	0.02517	3079	5.82	<.0001
year		3	0.1372	0.02341	3079	5.86	<.0001
year		2	0.1464	0.02136	3079	6.85	<.0001
year		1	0.09693	0.01806	3079	5.37	<.0001
year		0	0	.	.	.	.
age_tpl			-0.00268	0.000668	1312	-4.01	<.0001
dialyseyears			0.004662	0.005389	1312	0.87	0.3871
GFR			-0.00405	0.000339	3079	-11.96	<.0001
diuretics			-0.1183	0.01797	3079	-6.58	<.0001
betablock			0.009296	0.01711	3079	0.54	0.5870
diabetes			0.04306	0.02375	3079	1.81	0.0699

Type 3 Tests of Fixed Effects				
Effect	Num DF	Den DF	F Value	Pr > F
acei_arb	1	1312	32.12	<.0001
CNI	1	3079	4.45	0.0349
year	10	3079	8.38	<.0001
age_tpl	1	1312	16.07	<.0001
dialyseyears	1	1312	0.75	0.3871
GFR	1	3079	143.06	<.0001
diuretics	1	3079	43.35	<.0001
betablock	1	3079	0.30	0.5870
diabetes	1	3079	3.29	0.0699

Test for interaction of ACEI/ARB and CNI use:

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
acei_arb_full*immg	1	3079	0.57	0.4522