Supplementary Online Content

Garcia G-GP, Lavieri MS, Andrews C, et al. Accuracy of Kalman filtering in forecasting visual field and intraocular pressure trajectory in patients with ocular hypertension. *JAMA Ophthalmol*. Published online November 14, 2019. doi:10.1001/jamaophthalmol.2019.4190

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Description of eyes from OHTS which progressed[1] due to changes in VF and did not progress due to changes in VF

	Eyes from OHTS which progressed[1] due to VF		Eyes from OHTS which did not progress[2] due to VF		
	N		*N*		
No of Eyes	108		2698		
	Mean	*SD*	*Mean*	*SD*	*p-value**
Years to First Progression	6.8	3.7	-	-	0.38
Initial MD (dB)	-0.2	1.4	0.0	1.4	0.08
Initial PSD (dB)	2.1	0.4	2.0	0.5	0.01
Initial IOP (mmHg)	26.7	3.4	25.1	3.0	<0.001
MD change[3] (dB)	-0.8	1.6	-0.2	2.0	<0.001
PSD change[3] (dB)	0.7	0.9	0.1	0.9	<0.001
IOP change[3] (mmHg)	-0.5	3.3	-1.1	3.4	0.05

*P-values were computed using a 2-sample Student's t-test

[1]Progressed eyes were identified by the Endpoint Committee based on VF changes

[2]Some eyes in this group may have been identified by the Endpoint Committee as having progressed due to changes in the optic disc

[3]Change computed as: reading at 60 months - initial reading; statistic only computed for those with enough measurements

PSD = pattern standard deviation; IOP = intraocular pressure; MD = mean deviation; dB = decibels; SD = standard deviation; VF = visual field

eTable 2. Proportion of Eyes from OHTS Patients with Forecasts of Pattern Standard Deviation within 0.5, 1.0, and 2.5 dB, and beyond 2.5 dB of the Actual Value at 12, 24, 36, 48, and 60 months into the Future for Each of the Five Forecasting Models

Months Forecasted Ahead	Amount of Error in PSD Forecast (dB)	KF-OHTN		KF-HTG[1,2]		PM[2]		LR1[1,2]		LR2[1,2]	
		# Eyes	*%*	*# Eyes*	*%*	*# Eyes*	*%*	*# Eyes*	*%*	*# Eyes*	*%*
12	0.5	2035	80.2%	2088	82.3%	2137	84.2%	1917	75.6%	1935	76.3%
	1	2372	93.5%	2377	93.7%	2405	94.8%	2316	91.3%	2322	91.5%
	2.5	2502	98.6%	2504	98.7%	2503	98.7%	2490	98.1%	2484	97.9%
	>2.5	35	1.4%	33	1.3%	34	1.3%	47	1.9%	53	2.1%
24	0.5	1881	77.8%	1585	65.6%	2004	82.9%	1528	63.2%	1524	63.0%
	1	2227	92.1%	2237	92.5%	2260	93.5%	2062	85.3%	2063	85.3%
	2.5	2391	98.9%	2392	98.9%	2390	98.8%	2349	97.1%	2347	97.1%
	>2.5	27	1.1%	26	1.1%	28	1.2%	69	2.9%	71	2.9%
36	0.5	1767	76.3%	814	35.1%	1868	80.6%	1259	54.3%	1277	55.1%
	1	2131	92.0%	1961	84.6%	2170	93.7%	1850	79.8%	1874	80.9%
	2.5	2280	98.4%	2279	98.4%	2281	98.4%	2217	95.7%	2218	95.7%
	>2.5	37	1.6%	38	1.6%	36	1.6%	100	4.3%	99	4.3%
48	0.5	1676	74.5%	350	15.6%	1823	81.1%	1085	48.2%	1073	47.7%
	1	2049	91.1%	1408	62.6%	2085	92.7%	1673	74.4%	1681	74.7%
	2.5	2194	97.6%	2202	97.9%	2203	98.0%	2115	94.0%	2107	93.7%
	>2.5	55	2.4%	47	2.1%	46	2.0%	134	6.0%	142	6.3%
60	0.5	1402	66.0%	150	7.1%	1635	77.0%	877	41.3%	875	41.2%
	1	1914	90.1%	671	31.6%	1962	92.4%	1464	68.9%	1487	70.0%
	2.5	2082	98.0%	2075	97.7%	2085	98.2%	1955	92.0%	1955	92.0%
	>2.5	42	2.0%	49	2.3%	39	1.8%	169	8.0%	169	8.0%

[1]This model had a significantly different distribution of prediction errors compared to the KF-OHTN model when predicting PSD 12 months into the future at a significance level of 0.01 based on the Bhapkar test for equality of marginal distributions.
[2]This model had a significantly different distribution of prediction errors compared to the KF-OHTN model when predicting PSD 60 months into the future at a significance level of 0.01 based on the Bhapkar test for equality of marginal distributions.

*2537/2806 (90.4 %) of eyes from OHTS patients had enough measurements for this analysis
**2124/2806 (75.7%) of eyes from OHTS patients had enough measurements for this analysis
dB = decibels; KF-OHTN = Kalman filter built using a sample of patients with ocular hypertension from OHTS; KF-HTG = Kalman filter built using a sample of patients with high-tension glaucoma; LR = linear regression; PSD = pattern standard deviation; PM = Personalized Mean model.

eTable 3. Proportion of Eyes from OHTS Patients with Forecasts of Intraocular Pressure within 1.0, 2.5, and 5.0 mmHg, and beyond 5.0 mmHg of the Actual Value at 12, 24, 36, 48, and 60 months into the Future for Each of the Five Forecasting Models

Months Forecasted Ahead	Amount of Error in IOP Forecast (mmHg)	KF-OHTN		KF-HTG[1,2]		PM[1,2]		LR1[1,2]		LR2[1,2]	
		# Eyes	*%*	*# Eyes*	*%*	*# Eyes*	*%*	*# Eyes*	*%*	*# Eyes*	*%*
12	1	989	39.0%	854	33.7%	916	36.1%	729	28.7%	792	31.2%
	2.5	1955	77.1%	1773	69.9%	1866	73.6%	1619	63.8%	1602	63.1%
	5	2431	95.8%	2378	93.7%	2409	95.0%	2271	89.5%	2257	89.0%
	>5	106	4.2%	159	6.3%	128	5.0%	266	10.5%	280	11.0%
24	1	797	33.0%	781	32.3%	789	32.6%	510	21.1%	510	21.1%
	2.5	1682	69.6%	1646	68.1%	1711	70.8%	1180	48.8%	1183	48.9%
	5	2258	93.4%	2246	92.9%	2250	93.1%	1850	76.5%	1862	77.0%
	>5	160	6.6%	172	7.1%	168	6.9%	568	23.5%	556	23.0%
36	1	668	28.8%	749	32.3%	701	30.3%	395	17.0%	401	17.3%
	2.5	1477	63.7%	1576	68.0%	1536	66.3%	950	41.0%	946	40.8%
	5	2121	91.5%	2090	90.2%	2091	90.2%	1594	68.8%	1579	68.1%
	>5	196	8.5%	227	9.8%	226	9.8%	723	31.2%	738	31.9%
48	1	574	25.5%	665	29.6%	583	25.9%	300	13.3%	334	14.9%
	2.5	1371	61.0%	1392	61.9%	1321	58.7%	742	33.0%	739	32.9%
	5	2002	89.0%	1974	87.8%	1941	86.3%	1328	59.0%	1333	59.3%
	>5	247	11.0%	275	12.2%	308	13.7%	921	41.0%	916	40.7%
60	1	560	26.4%	517	24.3%	405	19.1%	264	12.4%	251	11.8%
	2.5	1255	59.1%	1118	52.6%	940	44.3%	608	28.6%	599	28.2%
	5	1854	87.3%	1703	80.2%	1594	75.0%	1115	52.5%	1108	52.2%
	>5	270	12.7%	421	19.8%	530	25.0%	1009	47.5%	1016	47.8%

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[2]This model had a significantly different distribution of prediction errors compared to the KF-OHTN model when predicting IOP 60 months into the future at a significance level of 0.01 based on the Bhapkar test for equality of marginal distributions.
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dB = decibels; KF-OHTN = Kalman filter built using a sample of patients with ocular hypertension from OHTS; KF-HTG = Kalman filter built using a sample of patients with high-tension glaucoma; LR = linear regression; IOP = intraocular pressure; PM = Personalized Mean model.

eTable 4. Proportion of Progressed[3] Eyes from OHTS Patients with Forecasts of Mean Deviation within 0.5, 1.0, and 2.5 dB, and beyond 2.5 dB of the Actual Value at 12, 24, 36, 48, and 60 months into the Future for Each of the Five Forecasting Models

Months Forecasted Ahead	Amount of Error in MD Forecast (dB)	KF-OHTN		KF-HTG		PM[2]		LR1[1,2]		LR2[2]	
		# *Eyes*	*%*	# *Eyes*	*%*	# *Eyes*	*%*	# *Eyes*	*%*	# *Eyes*	*%*
12*	0.5	33	39.8%	30	36.1%	37	44.6%	24	28.9%	36	43.4%
	1	54	65.1%	55	66.3%	58	69.9%	41	49.4%	49	59.0%
	2.5	80	96.4%	78	94.0%	78	94.0%	77	92.8%	79	95.2%
	>2.5	3	3.6%	5	6.0%	5	6.0%	6	7.2%	4	4.8%
24	0.5	21	29.6%	19	26.8%	21	29.6%	14	19.7%	15	21.1%
	1	40	56.3%	37	52.1%	40	56.3%	30	42.3%	30	42.3%
	2.5	66	93.0%	65	91.5%	67	94.4%	54	76.1%	55	77.5%
	>2.5	5	7.0%	6	8.5%	4	5.6%	17	23.9%	16	22.5%
36	0.5	24	40.7%	22	37.3%	20	33.9%	13	22.0%	14	23.7%
	1	37	62.7%	36	61.0%	32	54.2%	23	39.0%	24	40.7%
	2.5	56	94.9%	54	91.5%	53	89.8%	41	69.5%	46	78.0%
	>2.5	3	5.1%	5	8.5%	6	10.2%	18	30.5%	13	22.0%
48	0.5	19	33.9%	19	33.9%	17	30.4%	5	8.9%	3	5.4%
	1	36	64.3%	33	58.9%	30	53.6%	14	25.0%	15	26.8%
	2.5	53	94.6%	52	92.9%	51	91.1%	35	62.5%	35	62.5%
	>2.5	3	5.4%	4	7.1%	5	8.9%	21	37.5%	21	37.5%
60**	0.5	13	29.5%	13	29.5%	7	15.9%	3	6.8%	2	4.5%
	1	30	68.2%	30	68.2%	22	50.0%	8	18.2%	8	18.2%
	2.5	41	93.2%	41	93.2%	41	93.2%	24	54.5%	26	59.1%
	>2.5	3	6.8%	3	6.8%	3	6.8%	20	45.5%	18	40.9%

[1]This model had a significantly different distribution of prediction errors compared to the KF-OHTN model when predicting MD 12 months into the future at a significance level of 0.01 based on the Bhapkar test for equality of marginal distributions.
[2]This model had a significantly different distribution of prediction errors compared to the KF-OHTN model when predicting MD 60 months into the future at a significance level of 0.01 based on the Bhapkar test for equality of marginal distributions.

[3]Progressed eyes were identified by the Endpoint Committee due to changes in VF during the OHTS study
*83/108 (76.9%) of progressed eyes from OHTS patients had enough measurements for this analysis
**44/108 (40.7%) of progressed eyes from OHTS patients had enough measurements for this analysis
dB = decibels; KF-OHTN = Kalman filter built using a sample of patients with ocular hypertension from OHTS; KF-HTG = Kalman filter built using a sample of patients with high-tension glaucoma; LR = linear regression; MD = mean deviation; PM = Personalized Mean model.

eTable 5. Proportion of Progressed[3] Eyes from OHTS Patients with Forecasts of Pattern Standard Deviation within 0.5, 1.0, and 2.5 dB, and beyond 2.5 dB of the Actual Value at 12, 24, 36, 48, and 60 months into the Future for Each of the Five Forecasting Models

Months Forecasted Ahead	Amount of Error in PSD Forecast (dB)	KF-OHTN		KF-HTG[2]		PM		LR1		LR2	
		# Eyes	*%*	*# Eyes*	*%*	*# Eyes*	*%*	*# Eyes*	*%*	*# Eyes*	*%*
12	0.5	56	67.5%	60	72.3%	58	69.9%	59	71.1%	59	71.1%
	1	77	92.8%	74	89.2%	75	90.4%	73	88.0%	74	89.2%
	2.5	82	98.8%	82	98.8%	81	97.6%	82	98.8%	82	98.8%
	>2.5	1	1.2%	1	1.2%	2	2.4%	1	1.2%	1	1.2%
24	0.5	50	70.4%	44	62.0%	51	71.8%	35	49.3%	40	56.3%
	1	58	81.7%	62	87.3%	60	84.5%	60	84.5%	60	84.5%
	2.5	71	100.0%	71	100.0%	71	100.0%	70	98.6%	69	97.2%
	>2.5	0	0.0%	0	0.0%	0	0.0%	1	1.4%	2	2.8%
36	0.5	37	62.7%	30	50.8%	39	66.1%	28	47.5%	30	50.8%
	1	50	84.7%	53	89.8%	51	86.4%	44	74.6%	44	74.6%
	2.5	58	98.3%	59	100.0%	58	98.3%	55	93.2%	55	93.2%
	>2.5	1	1.7%	0	0.0%	1	1.7%	4	6.8%	4	6.8%
48	0.5	36	64.3%	23	41.1%	35	62.5%	27	48.2%	32	57.1%
	1	52	92.9%	49	87.5%	51	91.1%	42	75.0%	42	75.0%
	2.5	56	100.0%	56	100.0%	56	100.0%	53	94.6%	54	96.4%
	>2.5	0	0.0%	0	0.0%	0	0.0%	3	5.4%	2	3.6%
60	0.5	31	70.5%	14	31.8%	26	59.1%	18	40.9%	18	40.9%
	1	39	88.6%	29	65.9%	36	81.8%	27	61.4%	29	65.9%
	2.5	44	100.0%	44	100.0%	44	100.0%	41	93.2%	41	93.2%
	>2.5	0	0.0%	0	0.0%	0	0.0%	3	6.8%	3	6.8%

[1]This model had a significantly different distribution of prediction errors compared to the KF-OHTN model when predicting MD 12 months into the future at a significance level of 0.01 based on the Bhapkar test for equality of marginal distributions.
[2]This model had a significantly different distribution of prediction errors compared to the KF-OHTN model when predicting MD 60 months into the future at a significance level of 0.01 based on the Bhapkar test for equality of marginal distributions.

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eTable 6. Proportion of Progressed[3] Eyes from OHTS Patients with Forecasts of Intraocular Pressure within 1.0, 2.5, and 5.0 dB, and beyond 5.0 dB of the Actual Value at 12, 24, 36, 48, and 60 months into the Future for Each of the Five Forecasting Models

Months Forecasted Ahead	Amount of Error in IOP Forecast (mmHg)	KF-OHTN		KF-HTG		PM		LR1[1,2]		LR2[2]	
		# Eyes	*%*	*# Eyes*	*%*	*# Eyes*	*%*	*# Eyes*	*%*	*# Eyes*	*%*
12	1	30	36.1%	24	28.9%	33	39.8%	20	24.1%	21	25.3%
	2.5	56	67.5%	54	65.1%	54	65.1%	48	57.8%	46	55.4%
	5	75	90.4%	73	88.0%	74	89.2%	68	81.9%	67	80.7%
	>5	8	9.6%	10	12.0%	9	10.8%	15	18.1%	16	19.3%
24	1	14	19.7%	21	29.6%	18	25.4%	13	18.3%	9	12.7%
	2.5	41	57.7%	41	57.7%	43	60.6%	28	39.4%	28	39.4%
	5	64	90.1%	61	85.9%	64	90.1%	52	73.2%	50	70.4%
	>5	7	9.9%	10	14.1%	7	9.9%	19	26.8%	21	29.6%
36	1	13	22.0%	21	35.6%	23	39.0%	7	11.9%	3	5.1%
	2.5	32	54.2%	36	61.0%	38	64.4%	20	33.9%	14	23.7%
	5	54	91.5%	51	86.4%	52	88.1%	37	62.7%	34	57.6%
	>5	5	8.5%	8	13.6%	7	11.9%	22	37.3%	25	42.4%
48	1	10	17.9%	12	21.4%	14	25.0%	5	8.9%	4	7.1%
	2.5	25	44.6%	30	53.6%	31	55.4%	13	23.2%	11	19.6%
	5	46	82.1%	45	80.4%	45	80.4%	25	44.6%	22	39.3%
	>5	10	17.9%	11	19.6%	11	19.6%	31	55.4%	34	60.7%
60	1	10	22.7%	7	15.9%	4	9.1%	4	9.1%	3	6.8%
	2.5	21	47.7%	15	34.1%	14	31.8%	11	25.0%	6	13.6%
	5	34	77.3%	29	65.9%	29	65.9%	17	38.6%	16	36.4%
	>5	10	22.7%	15	34.1%	15	34.1%	27	61.4%	28	63.6%

[1]This model had a significantly different distribution of prediction errors compared to the KF-OHTN model when predicting IOP 12 months into the future at a significance level of 0.01 based on the Bhapkar test for equality of marginal distributions.

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eTable 7. Comparison of the Root Mean Square Error of the 5 Models at Forecasting Key Glaucoma Metrics for Progressed[1] Eyes from OHTS patients at 12, 24, 36, 48, and 60 Months into the Future

Months Ahead	Metric	I F-OHTS*		KF-HTG		PM		LR1	LR2	
		RMSE	*% Improvement*	*RMSE*	*% Improvement*	*RMSE*	*% Improvement*	*RMSE*	*RMSE*	*% Improvement*
12	MD	1.21	11.1%	1.29	4.8%	1.39	-2.1%	1.36	1.29	4.8%
24		1.46	31.4%	1.43	32.9%	1.41	33.8%	2.13	2.09	1.8%
36		1.39	40.6%	1.31	44.1%	1.51	35.4%	2.34	2.25	3.7%
48		1.60	46.5%	1.48	50.5%	1.82	39.0%	2.99	2.89	3.5%
60		1.20	64.9%	1.19	64.9%	1.40	58.7%	3.40	3.28	3.6%
12	PSD	0.63	2.9%	0.64	0.3%	0.74	-15.4%	0.65	0.65	-0.2%
24		0.67	25.5%	0.61	32.5%	0.64	28.6%	0.90	0.90	-0.4%
36		0.71	33.1%	0.70	34.4%	0.73	31.7%	1.07	1.07	-0.5%
48		0.56	49.1%	0.75	31.8%	0.62	43.8%	1.10	1.10	0.0%
60		0.58	51.8%	0.95	20.5%	0.67	43.8%	1.20	1.16	3.0%
12	IOP	2.94	22.0%	3.29	12.8%	3.01	20.1%	3.77	3.95	-4.7%
24		3.13	39.7%	3.36	35.3%	2.97	42.8%	5.19	5.44	-4.8%
36		3.17	47.2%	3.19	46.8%	3.10	48.3%	6.00	5.93	1.1%
48		3.97	48.0%	4.04	47.1%	3.99	47.8%	7.64	7.57	1.0%
60		4.46	46.8%	5.33	36.5%	6.06	27.7%	8.38	8.12	3.1%

RMSE values closer to 0 indicate predictions closer to the actual values obtained in the trial / clinic. % Improvement measured with respect to the LR1 model and computed as $(RMSE_{LR1}\text{-}RMSE_{M})/(RMSE_{LR1})$ where $RMSE_{M}$ is the RMSE belonging to the KF-OHTN, KF-HTG, PM, or LR2 model. Positive values of % Improvement indicates improved performance compared to the LR1 model.

[1]Progressed eyes were identified by the Endpoint Committee due to changes in VF during the OHTS study

*RMSE estimated using leave-one-out cross validation.

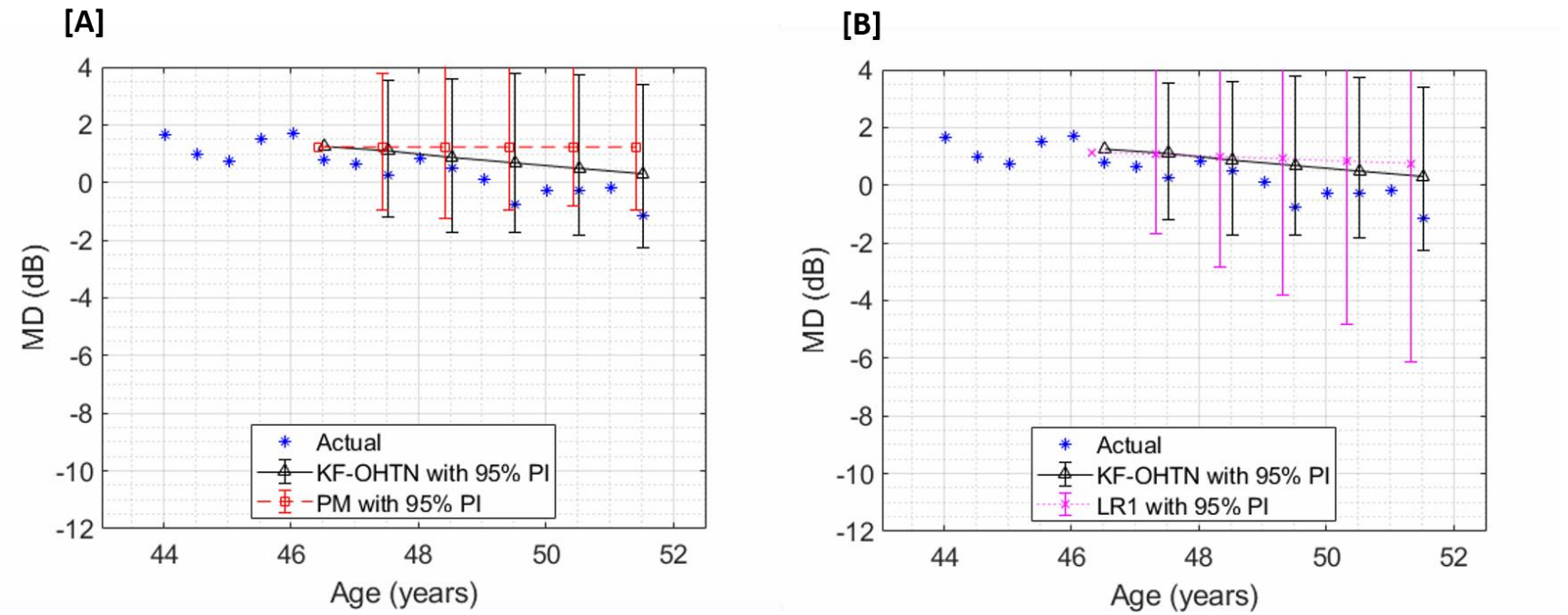
IOP = intraocular pressure; KF-OHTN = Kalman filter built using a sample of patients with ocular hypertension from OHTS; KF-HTG = Kalman filter built using a sample of patients with high-tension glaucoma; LR = linear regression; MD = mean deviation; PM = Personalized Mean model; PSD = pattern standard deviation; RMSE = root mean square error.

eTable 8. Characteristics of Patients with Ocular Hypertension stratified by whether the KF-OHTN Model Accurately Forecasted Mean Deviation 60 Months Into the Future

	Characteristics of Eyes Whose Mean Deviation Was Accurately Forecasted		**Characteristics of Eyes Whose Mean Deviation Was Forecasted >2.5 dB Higher Than Actual Value**		**Characteristics of Eyes Whose Mean Deviation Was Forecasted >2.5 dB Lower Than Actual Value**				
	N		*N*		*N*				
No of Eyes	1980		88		56				
	Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*	*3 Group Comparison P-value*[2]	*High vs. Accurate Forecast P-value*[3]	*Low vs. Accurate Forecast P-value*[4]
Initial MD (dB)	0.1	1.4	0.0	1.4	-0.4	1.4	0.06	0.81	0.06
Initial PSD (dB)	2.0	0.5	2.1	0.5	2.0	0.4	0.18	0.17	0.92
Initial IOP (mmHg)	25.1	2.9	25.4	3.3	24.5	2.7	0.15	0.60	0.22
MD change[1] (dB)	0.0	1.5	-1.7	5.1	0.6	3.9	<0.001	<0.001	0.06
PSD change[1] (dB)	0.1	0.7	0.8	1.8	-0.4	1.8	<0.001	<0.001	<0.001
IOP change[1] (mmHg)	-1.3	3.2	-1.6	3.8	0.7	3.8	<0.001	0.63	<0.001

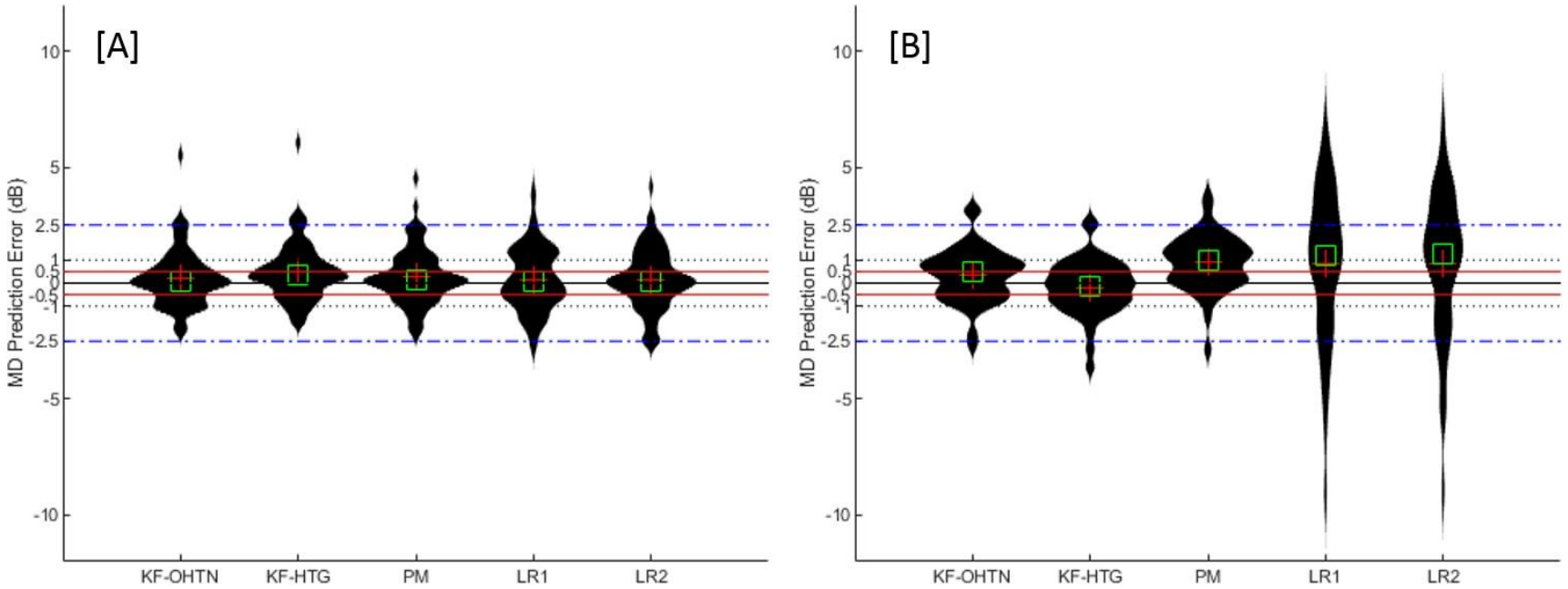
Prediction error is defined as forecasted value – actual value. “Accurately Forecasted” means the forecasted value is within 2.5dB of the actual value observed in the trial or clinic visit. [1]Change computed as: reading at 60 months - initial reading [2]p-value simultaneously compares non-outliers, prediction error >2.5, and prediction error<-2.5 dB using 1-way ANOVA unless otherwise specified [3]p-value compares Non-outliers with Prediction error > 2.5 dB using Tukey’s post-hoc method [4]p-value compares Non-outliers with Prediction error <-2.5 dB using Tukey’s post-hoc method *p-value computed using Pearson’s Chi-square test for independent samples **2124/2806 (90.4%) patients with OHTN had enough measurements for this analysis
MD = mean deviation; PSD = pattern standard deviation; SD = standard deviation; IOP = intraocular pressure; dB = decibels; OHTN = ocular hypertension; KF-OHTN = Kalman filter built using a sample of patients with OHTN

eFigure 1: Forecast of sample patient with ocular hypertension from the OHTS trial comparing [A] KF-OHTN with PM and [B] KF-OHTN with LR1



OHTS = Ocular Hypertension Treatment Study; KF-OHTN = Kalman filter model parameterized using patients with ocular hypertension; PM = personalized mean; LR1 = linear regression 1; Observed = actual measurements; Filtered = self-corrected past forecasts; Predicted = forecasted measurements; MD = Mean deviation; dB = decibels; IOP = intraocular pressure

eFigure 2: Violin plots showing the proportion of MD forecasting errors between 0.5, 1.0, and 2.5 dB of the actual value for patients with ocular hypertension who progressed to open-angle glaucoma.



Progression from ocular hypertension to open-angle glaucoma was determined by the Endpoint Committee; [A] forecasting 12 months into the future; [B] forecasting 60 months into the future; KF-OHTN = Kalman filter model parameterized using patients with ocular hypertension; KF-HTG = Kalman filter model parameterized using patients with high tension glaucoma; PM = personalized mean model; LR1 = linear regression 1 model; LR2 = linear regression 2 model; MD = mean deviation; dB = decibels