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Complete Statistical Methods

Cohorts and Missing Data. Our analyses relating the US parameters to primary unassisted clinical maturation and overall AVF clinical maturation were performed in sub-cohorts of the 602 subjects of the Hemodialysis AVF Maturation Cohort who remained alive without experiencing AVF thrombosis prior to the respective US assessments. Accordingly, the 1 day, 2-week and 6-week cohorts included 587, 570, and 556 subjects, respectively, who remained alive without AVF thrombosis prior to the 1 day, 2-week and 6-week US assessments, respectively. In this way, our prognostic models evaluated the probabilities of the clinical maturation outcomes based on US measurements at the designated assessment times, conditional on survival without thrombosis prior to the assessment times. We used sequential multiple imputation to impute additional missing values for the US measurements, maturation outcomes and baseline case-mix variables prior to subsequent statistical analyses[S1]. A total of 10 imputed data sets were generated using fully sequential multiple imputation as described in the Appendix to Allon et al[35]. Unless indicated otherwise, all results presented in this report are averaged across the 10 imputed data sets, with statistical inferences performed using Rubin's formulae[S2] to account for uncertainty in the imputations.

Descriptive Analyses. Box plots and descriptive statistics including means, standard deviations and designated percentiles were used to summarize the distributions of AVF blood flow, vein diameter, and vein depth within the subgroups of the 1 day, 2-week and 6-week US cohorts who a) achieved unassisted AVF clinical maturation, b) achieved AVF clinical maturation with the assistance of angioplasty or other corrective procedure (assisted maturation), or c) did not achieve AVF clinical maturation.

Models Describing the Association of Clinical Maturation with Ultrasound Parameters. We used separate logistic regression analyses to relate the probabilities of unassisted AVF clinical maturation and of overall AVF clinical maturation to individual US parameters at 1 day, 2-weeks and 6-weeks after AVF creation, while controlling for clinical center and seven case-mix variables (age, sex, race, AVF location (forearm vs. upper arm), dialysis status, diabetic status, and body mass index) as covariates. The US parameters evaluated in these analyses were 1) upper arm blood flow (defined as

brachial artery flow, or summed radial and ulnar artery blood flow in patients with a high brachial artery bifurcation, an anatomic variation), 2) AVF blood flow, 3) vein diameter, 4) vein depth, 5) arterial diameter, 6) an indicator variable for presence of stenosis, and 7) an indicator variable for presence of accessory veins. We used natural cubic splines with knots placed at the quintiles, i.e. 20th, 40th, 60th, and 80th percentiles for each continuous ultrasound parameter to allow for the possibility of nonlinear relationships between the US parameters and the probabilities of AVF clinical maturation on the log odds scale[S3]. In order to provide comparability of results between US parameters measured in different units, associations with AVF maturation were expressed as odds ratios comparing the odds of maturation between the 85th and 15th percentiles for each continuous US parameter. We chose the comparison of the 85th and 15th percentiles because this represents slightly greater than a 2-standard deviation difference in a normally distributed variable, which is roughly comparable to the difference in standard deviation units corresponding to the presence vs. absence of a dichotomous variable with prevalence falling between 1/3 and 2/3.

We applied separate backward elimination procedures to the primary unassisted AVF maturation and overall AVF maturation outcomes to identify joint and independent US predictors of these outcomes among the US parameters listed above, after adjusting for clinical center and the seven case-mix factors. Because AVF blood flow and upper arm blood flow were moderately collinear, we dropped the upper arm blood flow prior to implementing the backward elimination as the 6-week AVF blood flow was more strongly associated with the AVF maturation outcomes than was upper arm blood flow. In the initial steps of the backward elimination procedures we retained cubic splines in each of the continuous US parameters, and successively dropped the US parameter for which the minimum p-value for the odds ratio comparing the 85th to the 15th percentiles, across the three US assessments, was maximized. This process was continued until the minimum p-value across the three US assessments was smaller than 0.10 for each ultrasound parameter than remained in the model. We next dropped nonlinear spline terms for the US parameters which were retained from the preceding step if the minimum p-values for the nonlinear spline terms considered as a block exceeded 0.10 across the three US assessments. A final backward elimination step considered the possible removal of the seven case-mix variables (considered jointly), and clinical center (considered as a single categorical factor), if the minimum p-value for these terms exceeded 0.10 across the three US assessments.

For each of the three US assessments, the relationship between the AVF clinical maturation outcomes and the US parameters in the final models selected by the backward elimination procedures were depicted by displaying curves relating the estimated probability of maturation to AVF blood flow

(which was one of the US parameters retained by the backward elimination procedure) at the 5th, 50th, and 95th percentiles of each of the other US parameters which were retained by the backward elimination model. We used marginal mean adjustment[S4] to adjust the predicted maturation probabilities for clinical center. The relationships between the marginal mean adjusted probabilities of clinical maturation and the US parameters were also depicted using contour plots[27].

We next dropped clinical center from our final models since it would not be practical to include clinical center in a prognostic model intended for general use in clinical practice. The accuracies of our final prognostic models based on AVF blood flow, vein diameter, and vein depth, obtained without clinical center adjustment, were evaluated using cross-validated Receiver Operating Characteristics (ROC) curves and estimates of the Area Under the ROC curves (AUC). We also depicted the sensitivities and specificities provided by the K-DOQI[1] and the University of Alabama criteria for prediction of clinical maturation based on US measurements[10]. We carried out a further set of regression analyses to assess if exclusion of clinical center led to substantial differences in the joint relationships of AVF blood flow, vein diameter and vein depth with unassisted and overall clinical maturation.

Finally, we performed additional exploratory analyses using expansions of the logistic regression models from the backward elimination procedures to test for the presence of pairwise interactions between clinical center and the US parameters in the model. We also evaluated if addition of changes in US parameters from 1 day to 6-week improved the prognostic accuracy of the logistic regression which included only the 6-week US parameters.

Equations Appendix: Prognostic Models for Clinical Maturation

This appendix presents the prognostic models that were used to predict primary unassisted clinical maturation and overall clinical maturation based on the ultrasound measurements. Separate models are presented for the two clinical maturation outcomes and for the three ultrasound assessments at Day 1, Week 2 and Week 6. Following a backward elimination procedure, the prognostic models included terms for vein depth and vein diameter as well as a natural cubic spline using a truncated power basis matrix in AVF blood flow, with internal knot points placed at the 20th, 40th, 60th, and 80th percentiles in AVF blood flow. The models presented here represent aggregated models across the seven HFM clinical centers. Due to clinical center effects, performance may differ when these models are applied at other sites.

The prognostic equations for clinical maturation have the form:

Logit(Pr(Maturation)) =

$$\beta_0 + \beta_1 \times \text{Depth} + \beta_2 \times \text{Diameter} + \alpha_1 \times (\text{flow}/1000) + \alpha_2 \times \max((\text{flow}^* - P_{20})/1000,0)^3 1[\text{flow} \geq P_{20}]$$
$$+ \alpha_3 \times \max((\text{flow}^* - P_{40})/1000,0)^3\, 1[\text{flow} \geq P_{40}] + \alpha_4 \times \max((\text{flow}^* - P_{60})/1000,0)^3 1[\text{flow} \geq P_{60}]$$
$$+ \alpha_5 \times \max((\text{flow}^* - P_{80})/1000,0),$$

where flow* = min(flow,P_{80}), $1[\text{flow} \geq P_{20}]$ is defined as 1 if flow $\geq P_{20}$ and 0 otherwise, with $1[\text{flow} \geq P_{40}]$ and $1[\text{flow} \geq P_{60}]$ defined similarly. This abbreviates the minimum of the flow and the 80th percentile of flows across the respective sets of HFM Study 1 day (587 patients), 2-week (570 patients), and 6-week (556 patients) ultrasound examinations. In the above expression, the functions min(x,y) and max(x,y) respectively designate the minimum and maximum of the two arguments x and y. The terms in the respective models are given below.

Parameters Used in Equations for Estimating Probabilities of Clinical Maturation

Term	Primary Unassisted Maturation			Overall Maturation		
	Day 1	Week 2	Week 6	Day 1	Week 2	Week 6
P_{20}	318	477	483	318	477	483
P_{40}	511	684	765	511	684	765
P_{60}	705	936	1060	705	936	1060
P_{80}	1001	1309	1475	1001	1309	1475
β_0	-1.37965	-1.59621	-1.34226	0.00121	-0.59648	-0.19453
β_1	-2.32157	-2.77121	-4.06638	-1.86337	-2.07121	-2.76060
β_2	0.37206	0.35763	0.14777	0.25987	0.40111	0.09555
α_1	1.25315	1.04482	2.52764	1.06287	0.33822	2.72913
α_2	1.38922	2.18724	1.66265	6.06226	7.30279	-1.93005
α_3	-7.90704	-6.98015	-8.48414	-18.52511	-18.77776	1.54621
α_4	9.88383	6.81718	10.5407	16.67833	15.17475	1.96820
α_5	0.09982	0.25255	0.05165	0.58702	-0.16773	0.38650

Catheter Use After AVF Maturation

Among 127 HFM Study patients who had a catheter in place at time of maturation, the catheter was removed from 107 (84.3%). We tracked catheter use on a monthly basis until study termination. Among patients whose AVFs matured, 51.8% never used a catheter from maturation to end of follow-up. Of the remaining 48.2% who did use a catheter at least once during at least one month, 64% used it during only one month, and 92.7% used it during four months or fewer. Of post-maturation person-months tracked in patients with matured AVFs, including the month in which maturation occurred, 95.5% included no catheter use at any time during the month.

Supplement Statistical Methods References

S1. Van Buuren SB, Brand JPL, Groothuis-Oudshoorn CGM, Rubin DB: Fully conditional specification in multivariate imputation. J Stat Comput Simul 76: 1049–1064, 2006

S2. Rubin DB: Multiple Imputation for Nonresponse in Surveys, New York, Wiley, 1987

S3. Harrell F: Relaxing the linearity assumption for continuous predictors. In: Regression Modeling Strategies: With Applications to Linear Models, Logistic and Ordinal Regression, and Survival Analysis, New York, Springer-Verlag, 2001

S4. Williams R: Using the margins command to estimate and interpret adjusted predictions and marginal effects. Stata J 12: 308, 2012

Appendix Table 1

Summary of Ultrasound Parameters and Clinical Maturation Outcomes Among Patients with Ultrasound Assessments

Parameter or Outcome	Day 1 Ultrasound Assessment Cohort (N = 587) (Upper arm: 450, Forearm: 137)		Week 2 Ultrasound Assessment Cohort (N = 570) (Upper arm: 441, Forearm: 129)		Week 6 Ultrasound Assessment Cohort (N = 556) (Upper arm: 430, Forearm: 126)	
	Median (IQR) or Percent	Number non-missing observations	Median (IQR) or Percent	Number non-missing observations	Median (IQR) or Percent	Number non-missing observations
Ultrasound Parameter						
Upper Arm Arterial Flow (ml/min), Full Cohort	742 (488 – 1084)	489	910 (649 – 1277)	491	1004 (699 – 1436)	475
Upper Arm Fistulas	852 (549 – 1177)	379	1016 (708 – 1354)	385	1073 (748 – 1509)	376
Forearm Fistulas	487 (358 – 685)	110	670 (566 – 902)	106	782 (533 – 993)	99
AVF Blood Flow (ml/min), Full Cohort	604 (380 – 936)	539	801 (518 – 1190)	527	916 (568 – 1359)	504
Upper Arm Fistulas	730 (498 – 1033)	412	898 (628 – 1317)	403	1030 (685 – 1483)	393
Forearm Fistulas	327 (211 – 465)	127	510 (306 – 711)	124	603 (403 – 867)	111
Vein Diameter (cm), Full Cohort	0.47 (0.40 – 0.55)	544	0.57 (0.49 – 0.65)	526	0.62 (0.53 – 0.74)	505
Upper Arm Fistulas	0.50 (0.44 – 0.57)	415	0.60 (0.52 – 0.69)	401	0.65 (0.57 – 0.77)	391
Forearm Fistulas	0.39 (0.33 – 0.43)	129	0.47 (0.42 – 0.52)	125	0.52 (0.46 – 0.59)	114
Vein Depth (cm), Full cohort	0.49 (0.34 – 0.68)	544	0.45 (0.32 – 0.65)	526	0.39 (0.29 – 0.55)	505
Upper Arm Fistulas	0.53 (0.37 – 0.76)	415	0.51 (0.36 – 0.69)	401	0.43 (0.31 – 0.59)	391

Parameter or Outcome	Day 1 Ultrasound Assessment Cohort (N = 587) (Upper arm: 450, Forearm: 137)		Week 2 Ultrasound Assessment Cohort (N = 570) (Upper arm: 441, Forearm: 129)		Week 6 Ultrasound Assessment Cohort (N = 556) (Upper arm: 430, Forearm: 126)	
	Median (IQR) or Percent	Number non-missing observations	Median (IQR) or Percent	Number non-missing observations	Median (IQR) or Percent	Number non-missing observations
Forearm Fistulas	0.35 (0.29 – 0.48)	129	0.34 (0.26 – 0.43)	125	0.31 (0.26 – 0.40)	114
Arterial Diameter (cm), Full Cohort	0.43 (0.34 – 0.51)	526	0.46 (0.37 – 0.53)	530	0.48 (0.39 – 0.55)	507
Upper Arm Fistulas	0.46 (0.40 – 0.52)	409	0.49 (0.43 – 0.55)	405	0.51 (0.44 – 0.57)	393
Forearm Fistulas	0.28 (0.25 – 0.33)	117	0.33 (0.28 – 0.38)	125	0.34 (0.28 – 0.39)	114
Presence of Stenosis (%), Full Cohort	14.7	551	28.0	521	30.1	488
Upper Arm Fistulas	14.4	422	29..5	397	30.5	380
Forearm Fistulas	15.5	129	23.4	124	28.7	108
Presence of Accessory Veins (%), Full Cohort	70.9	554	74.3	533	72.8	512
Upper Arm Fistulas	65.4	425	67.8	407	66.7	396
Forearm Fistulas	89.2	129	95.2	126	94.0	116
Clinical Maturation Outcomes						
Primary Unassisted Maturation (%), Full Cohort	46.9	561	48.2	544	49.4	530
Upper Arm Fistulas	47.5	434	48.2	425	49.5	414
Forearm Fistulas	44.9	127	47.9	119	49.1	116

Parameter or Outcome	Day 1 Ultrasound Assessment Cohort (N = 587) (Upper arm: 450, Forearm: 137)		Week 2 Ultrasound Assessment Cohort (N = 570) (Upper arm: 441, Forearm: 129)		Week 6 Ultrasound Assessment Cohort (N = 556) (Upper arm: 430, Forearm: 126)	
	Median (IQR) or Percent	Number non-missing observations	Median (IQR) or Percent	Number non-missing observations	Median (IQR) or Percent	Number non-missing observations
Overall Maturation (%), Full Cohort	71.9	548	73.2	532	74.9	518
Upper Arm Fistulas	72.0	425	72.8	416	74.6	405
Forearm Fistulas	71.5	123	74.1	116	76.1	113

Appendix Table 2

Multivariable Relationship of Overall Maturation with US and Other Predictor Variables

Ultrasound Assessment	Predictor Variables	Odds Ratio	95% Confidence Interval	P Value
Day 1	AVF Blood Flow (85th vs. 15th)	3.97	2.00 - 7.85	<0.001
	Vein Diameter (85th vs. 15th)	1.94	1.06 - 3.55	0.03
	Vein Depth (85th vs. 15th)	0.50	0.31 - 0.80	0.004
	Clinical Center	.	.	0.002
Week 2	AVF Blood Flow (85th vs. 15th)	2.18	1.12 - 4.26	0.02
	Vein Diameter (85th vs. 15th)	3.71	1.82 - 7.59	<0.001
	Vein Depth (85th vs. 15th)	0.45	0.28 - 0.73	0.001
	Clinical Center	.	.	0.004
Week 6	AVF Blood Flow (85th vs. 15th)*	6.78	2.86 - 16.08	<0.001
	Vein Diameter (85th vs. 15th)	1.62	0.78 - 3.37	0.20
	Vein Depth (85th vs. 15th)	0.39	0.23 - 0.66	<0.001
	Clinical Center	.	.	0.004

The table summarizes results from multivariable logistic regressions relating overall clinical maturation to AVF blood flow, vein diameter, and vein depth after controlling for the seven case mix variables and clinical center. P-values for the seven case mix variables considered as a group were 0.50, 0.37, and 0.35 at Day 1, Week 2 and Week 6, respectively. P-values for fistula location exceeded 0.10 at each of the three US assessments. Odds ratios comparing the 7 Clinical Centers are intentionally omitted to simplify the presentation.

* The p-value for a nonlinear relationship between overall maturation and the 6-Week AVF blood flow on the log odds ratio scale was 0.01.

Appendix Table 3A

Association of Previous Changes in Ultrasound Parameters with Primary Unassisted Clinical Maturation, Controlling for 6-Week Ultrasound Values

Ultrasound Variable	Effect of Change in US Variables from 1 Day to 6-Week			Effect of Change in US Variables from 2-Week to 6-Week		
	Odds Ratio	95% Confidence Interval	P-Value	Odds Ratio	95% Confidence Interval	P-Value
AVF Blood Flow (per 100 ml/min)	1.05	0.97 - 1.14	0.22	1.04	0.97 - 1.12	0.26
Vein Diameter (per cm)	0.82	0.61 - 1.12	0.21	0.85	0.56 - 1.28	0.44
Vein Depth (per 0.1 cm)	0.92	0.77 - 1.09	0.34	1.07	0.90 - 1.27	0.45

The table summarizes results from multivariable logistic regressions relating primary unassisted clinical maturation to changes from 1 Day to 6-weeks (left) and from 2-weeks to 6-weeks (right) in AVF blood flow, vein diameter, and vein depth after controlling for the 6-week values of the same ultrasound parameters, the seven case mix variables and clinical center.

Appendix Table 3B

Association of Previous Changes in Ultrasound Parameters with Overall Clinical Maturation, Controlling for Week 6 Ultrasound Values

Ultrasound Variable	Effect of Change in US Variables from 1 Day to 6-Week			Effect of Change in US Variables from 2-Week to 6-Week		
	Odds Ratio	95% Confidence Interval	P-Value	Odds Ratio	95% Confidence Interval	P-Value
AVF Blood Flow (per 100 ml/min)	0.96	0.87 - 1.06	0.42	0.96	0.87 - 1.06	0.42
Vein Diameter (per cm)	1.00	0.71 - 1.41	0.99	1.00	0.71 - 1.41	0.99
Vein Depth (per 0.1 cm)	1.01	0.85 - 1.19	0.95	1.01	0.85 - 1.19	0.95

The table summarizes results from multivariable logistic regressions relating overall clinical maturation to changes from 1 Day to 6-weeks (left) and from 2-weeks to 6-weeks (right) in AVF blood flow, vein diameter, and vein depth after controlling for the 6-week values of the same ultrasound parameters, the seven case mix variables and clinical center.

Appendix Table 4A

Association of Primary Unassisted Maturation with AVF Blood Flow, Vein Diameter and Vein Depth, With and Without Clinical Center Adjustment

Ultrasound Assessment	Ultrasound Parameter	With Clinical Center Adjustment		Without Clinical Center Adjustment	
		Odds Ratio	95% Confidence Interval	Odds Ratio	95% Confidence Interval
Day 1	AVF Blood Flow (85th vs. 15th)	2.49	1.36 – 4.58	2.04	1.16 – 3.56
	Vein Diameter (85th vs. 15th)	2.66	1.59 – 4.45	2.39	1.47 – 3.91
	Vein Depth (85th vs. 15th)	0.30	0.20 – 0.47	0.28	0.18 – 0.43
Week 2	AVF Blood Flow (85th vs. 15th)	2.77	1.51 – 5.07	2.39	1.36 – 4.19
	Vein Diameter (85th vs. 15th)	3.37	1.86 – 6.12	2.61	1.52 – 4.47
	Vein Depth (85th vs. 15th)	0.25	0.16 – 0.40	0.24	0.16 – 0.38
Week 6	AVF Blood Flow (85th vs. 15th)	10.35	4.87 – 21.99	7.52	3.83 – 14.75
	Vein Diameter (85th vs. 15th)	1.89	1.01 – 3.54	1.60	0.89 – 2.88
	Vein Depth (85th vs. 15th)	0.16	0.10 – 0.27	0.18	0.11 – 0.28

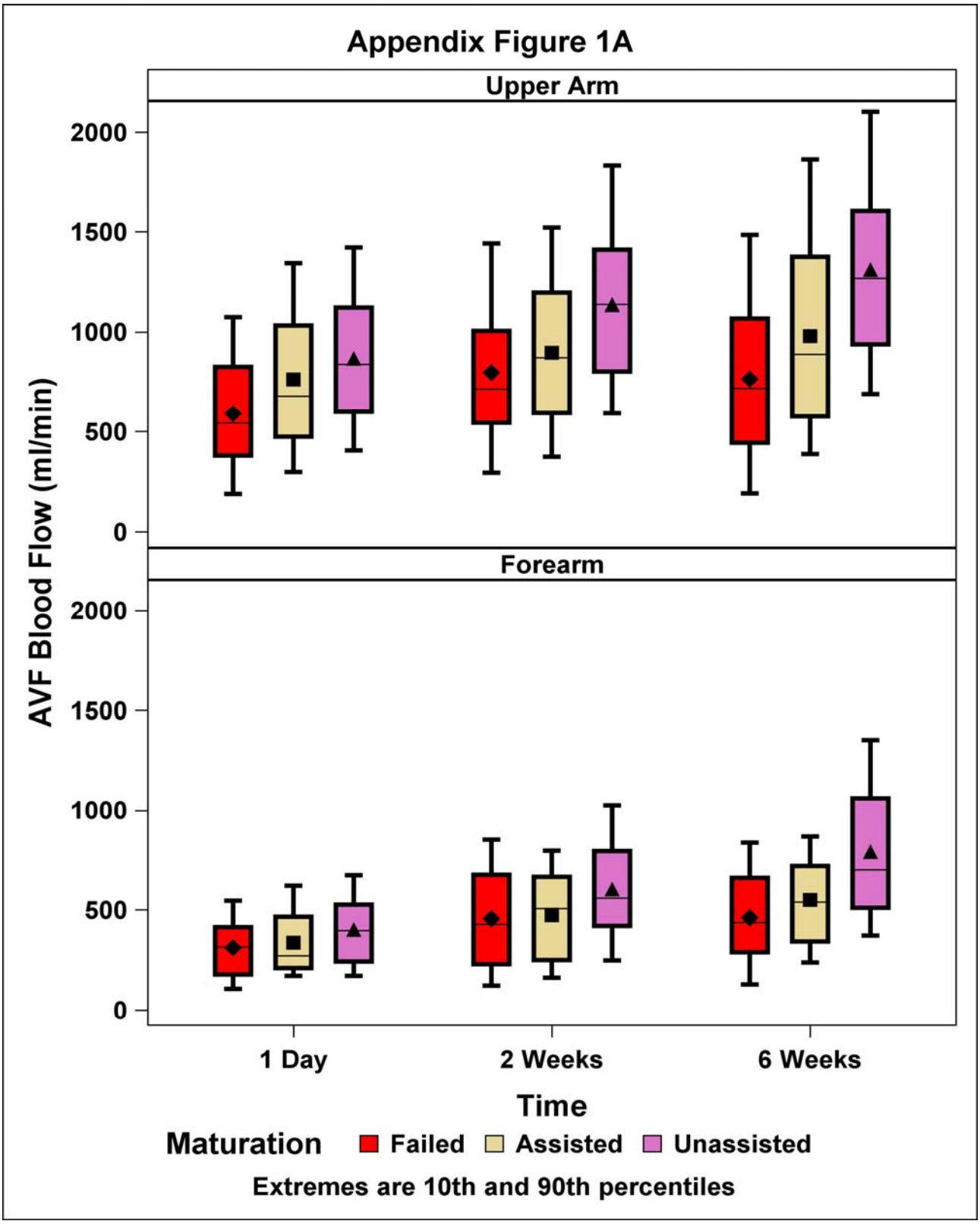
Shown are odds ratios relating unassisted clinical maturation to each of the indicated ultrasound parameters with and without statistical adjustment for clinical center. All odds ratios compare odds of unassisted clinical maturation between the 85th and 15th percentile of the ultrasound parameters. The model assumed linear effects of AVF blood flow and vein diameter, and used a cubic spline to account for a nonlinear effect of AVF blood flow.

Appendix Table 4B

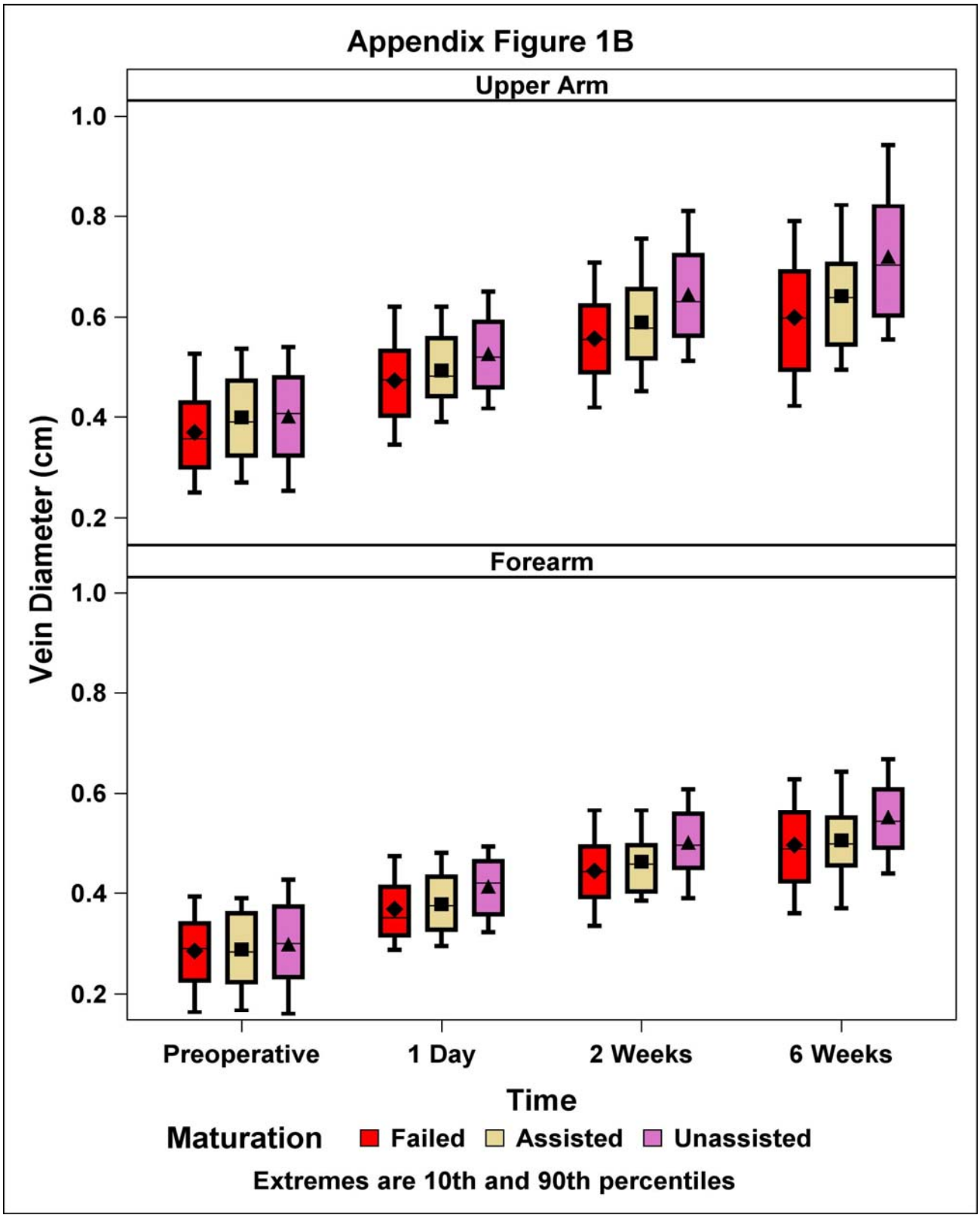
Association of Overall Maturation with AVF Blood Flow, Vein Diameter and Vein Depth, With and Without Clinical Center Adjustment

Ultrasound Assessment	Ultrasound Parameter	With Clinical Center Adjustment		Without Clinical Center Adjustment	
		Odds Ratio	95% Confidence Interval	Odds Ratio	95% Confidence Interval
Day 1	AVF Blood Flow (85th vs. 15th)	3.52	1.85 – 6.71	2.83	1.56 – 5.12
	Fistula Vein Diameter (85th vs. 15th)	1.95	1.11 – 3.44	1.84	1.06 – 3.17
	Fistula Depth (85th vs. 15th)	0.42	0.28 – 0.62	0.36	0.24 - 0.54
Week 2	AVF Blood Flow (85th vs. 15th)	2.27	1.20 – 4.30	2.01	1.09 – 3.69
	Fistula Vein Diameter (85th vs. 15th)	3.55	1.83 – 6.91	2.93	1.56 – 5.50
	Fistula Depth (85th vs. 15th)	0.37	0.25 – 0.56	0.35	0.23 - 0.52
Week 6	AVF Blood Flow (85th vs. 15th)	6.75	3.05 – 14.94	5.75	2.77 – 11.94
	Fistula Vein Diameter (85th vs. 15th)	1.54	0.80 – 2.97	1.35	0.72 – 2.52
	Fistula Depth (85th vs. 15th)	0.33	0.22 – 0.52	0.31	0.20 – 0.47

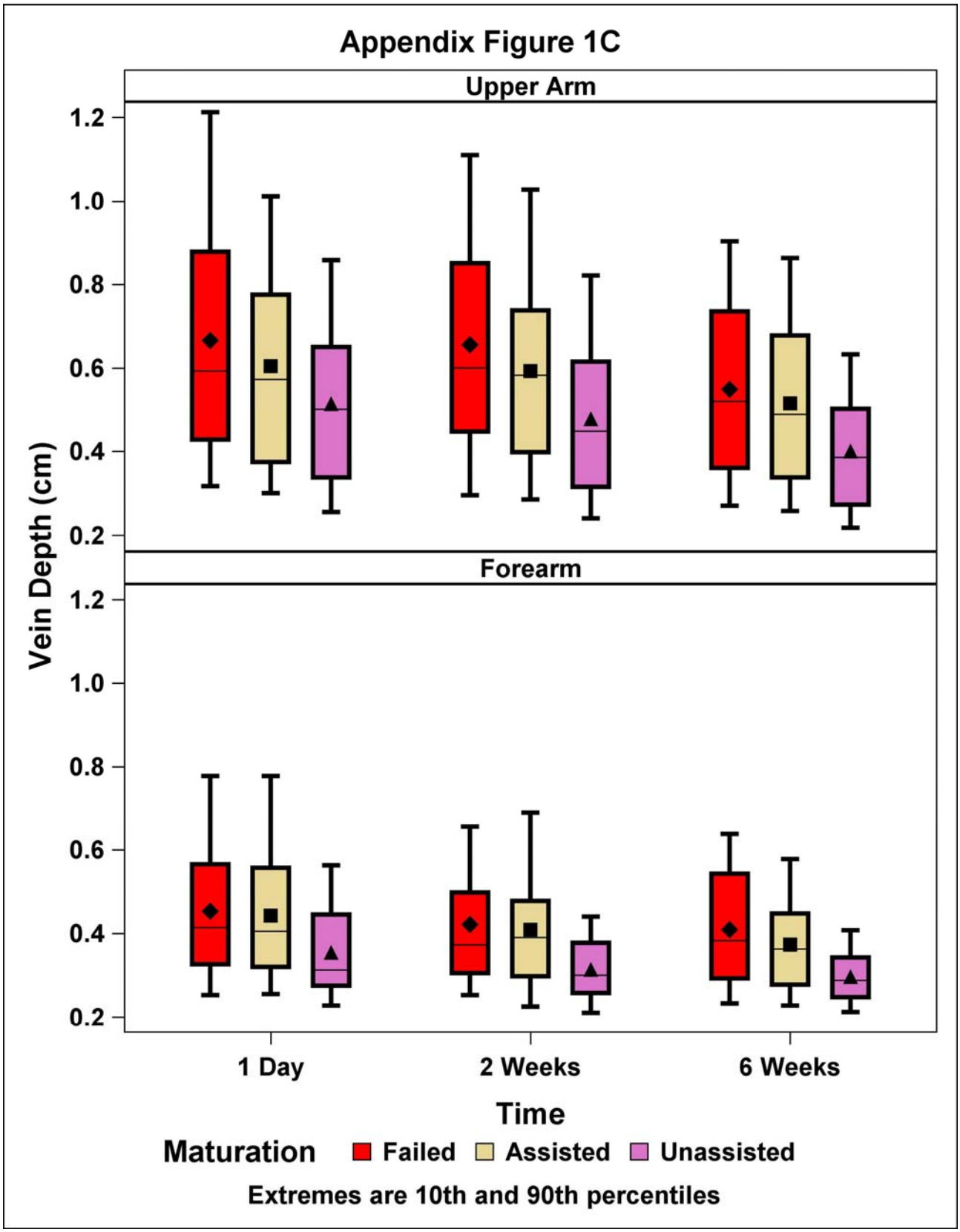
Shown are odds ratios relating overall clinical maturation to each of the indicated ultrasound parameters with and without statistical adjustment for clinical center. All odds ratios compare odds of unassisted clinical maturation between the 85th and 15th percentile of the ultrasound parameters. The model assumed linear effects of AVF blood flow and vein diameter, and used a cubic spline to account for a nonlinear effect of AVF blood flow.



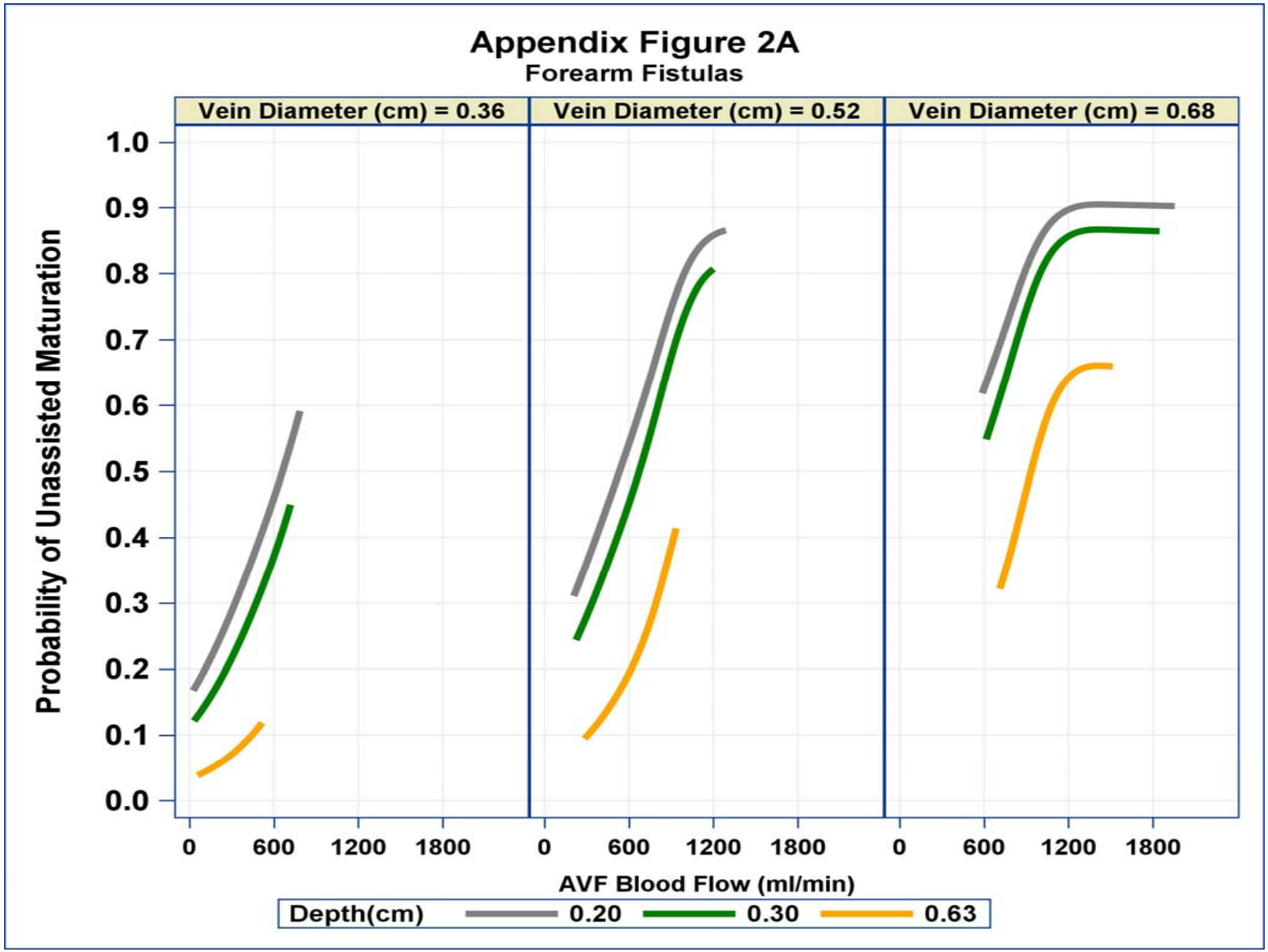
Appendix Figure 1A: Trends in AVF blood flow over time by AVF clinical maturation status. Figure displays the 10th, 25th, 50th, 75th, 90th percentiles and means (solid diamonds, squares or triangles) over time among patient groups whose AVFs later failed to achieve clinical maturation (red), achieved assisted clinical maturation (tan), or achieved unassisted clinical maturation (purple).



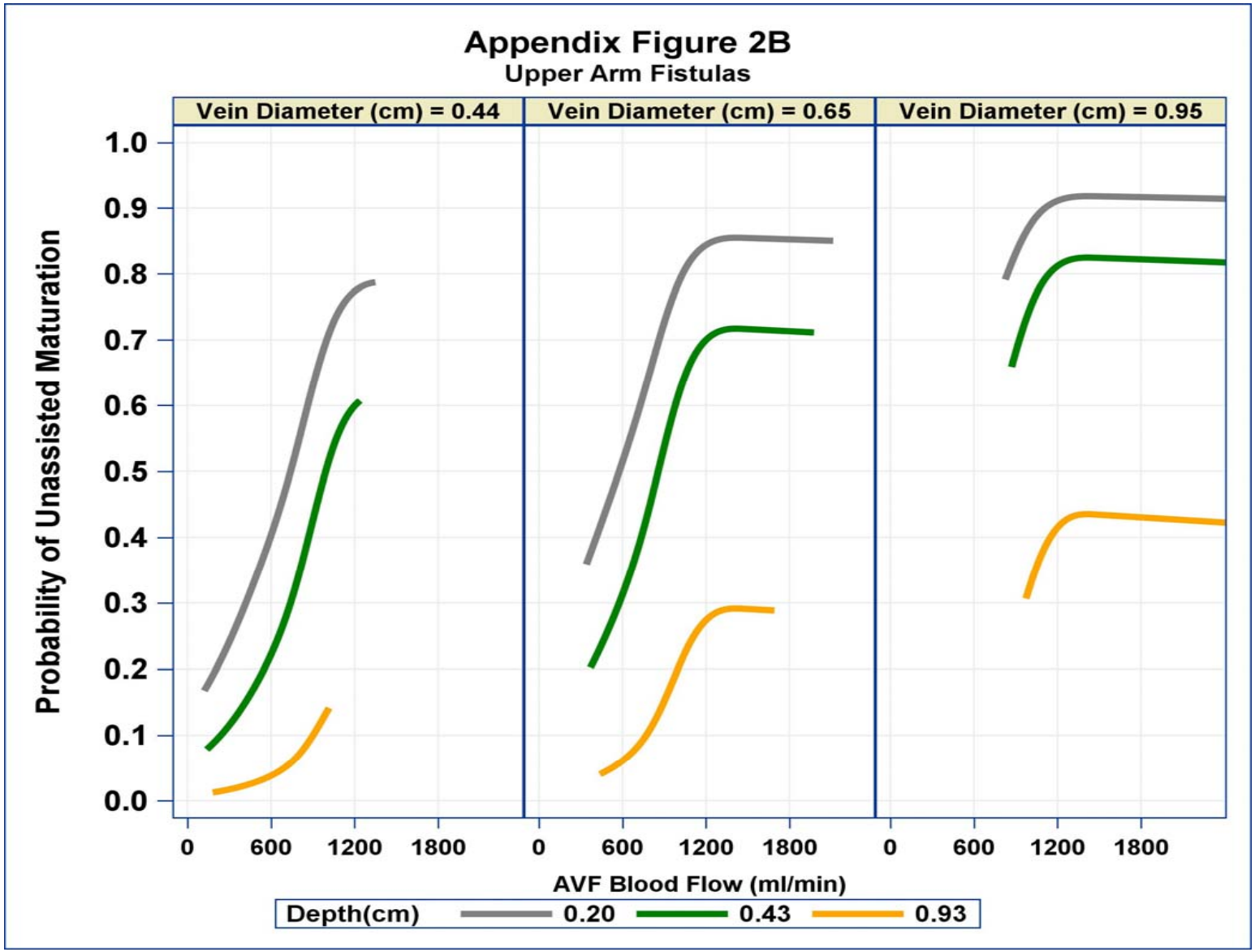
Appendix Figure 1B: Trends in vein diameter over time by AVF clinical maturation status. Figure displays the 10th, 25th, 50th, 75th, 90th percentiles and means (solid diamonds, squares or triangles) over time among patient groups whose AVFs later failed to achieve clinical maturation (red), achieved assisted clinical maturation (tan), or achieved unassisted clinical maturation (purple).



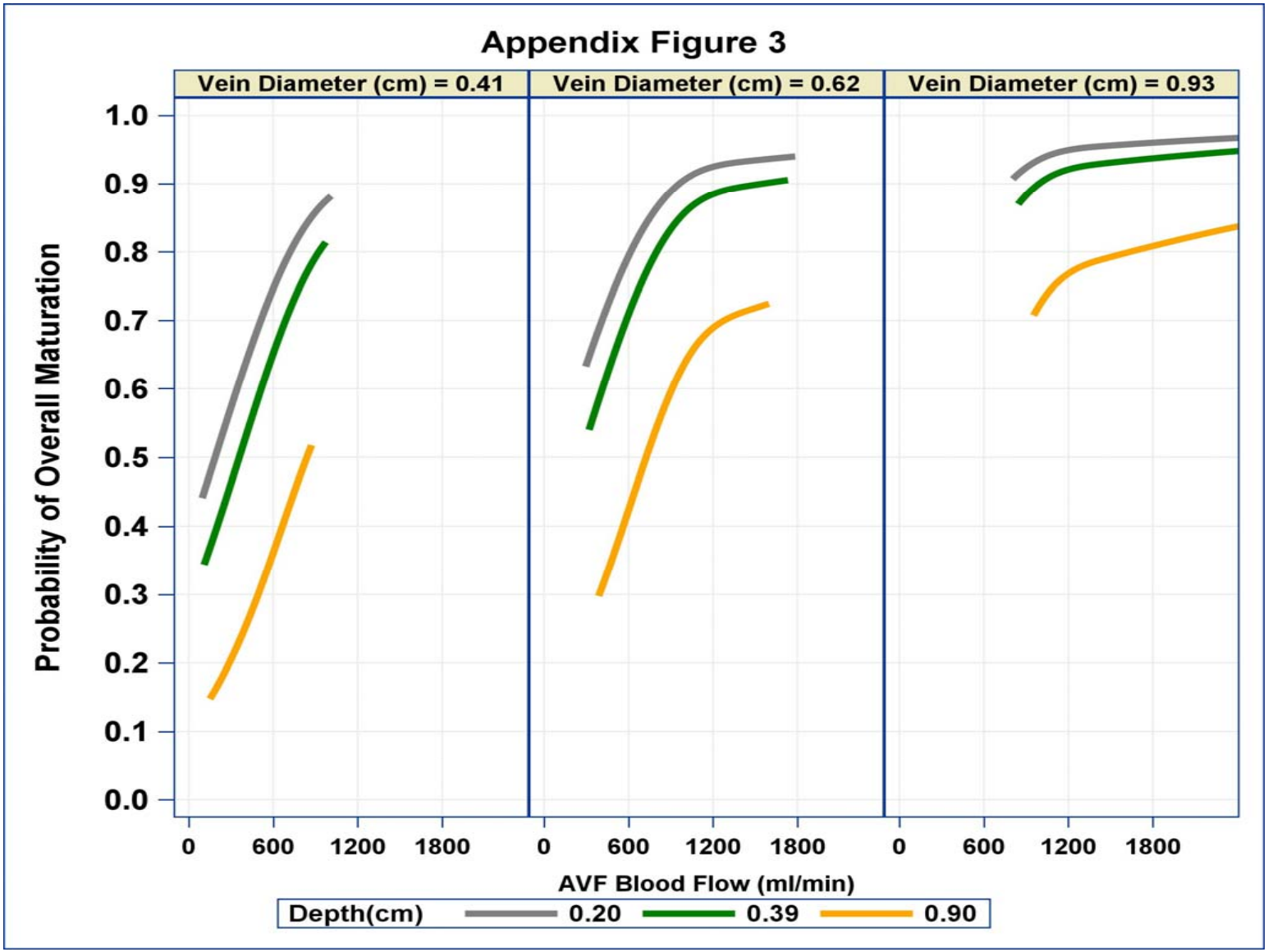
Appendix Figure 1C: Trends in vein depth over time by AVF clinical maturation status. Figure displays the 10th, 25th, 50th, 75th, 90th percentiles and means (solid diamonds, squares or triangles) over time among patient groups whose AVFs later failed to achieve clinical maturation (red), achieved assisted clinical maturation (tan), or achieved unassisted clinical maturation (purple).



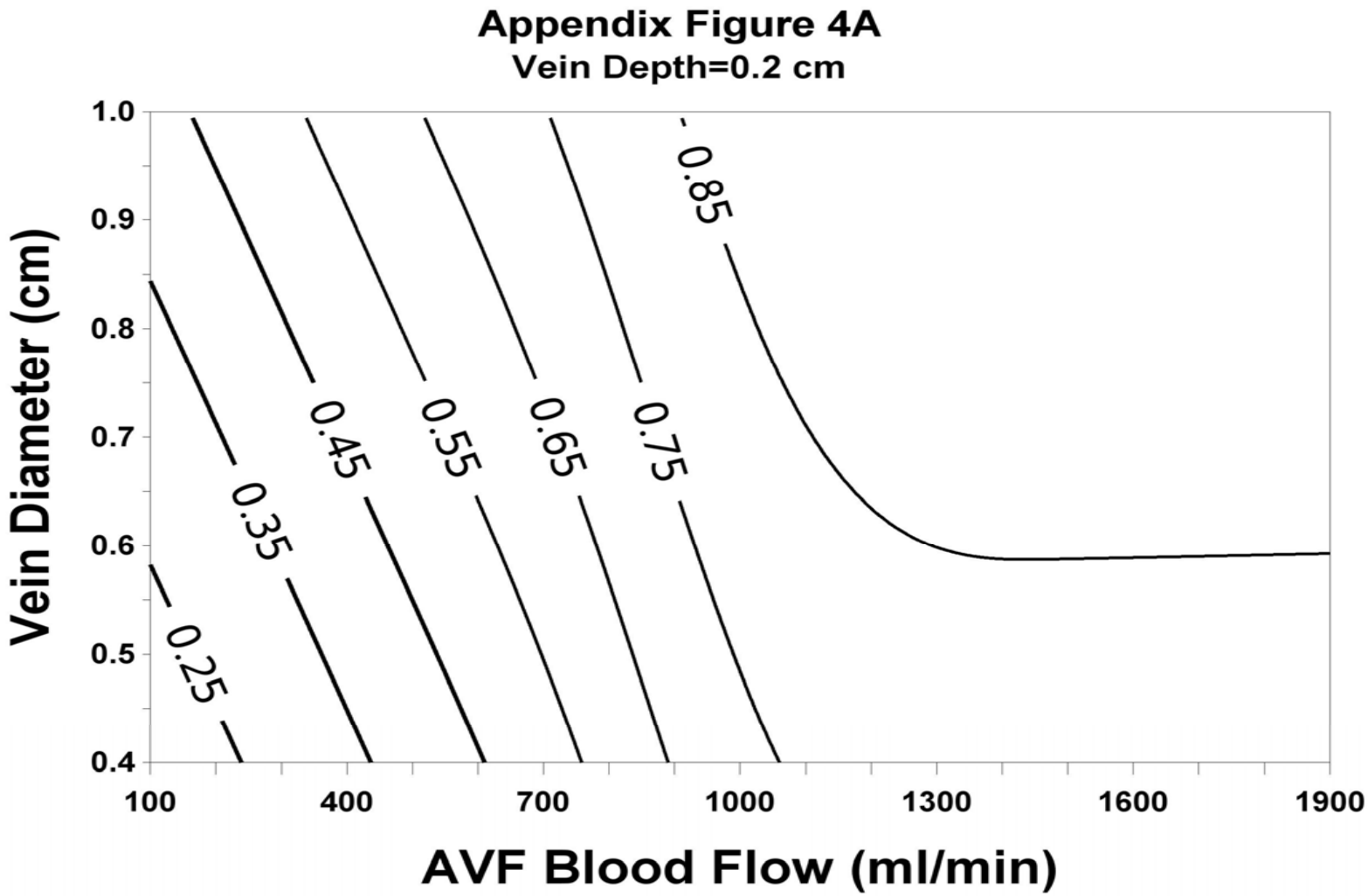
Appendix Figure 2A: Estimated probabilities of clinical unassisted maturation in forearm fistulas (Figure 2A) based on a logistic regression with 6-week AVF blood flow, vein diameter and vein depth as predictors variables. A cubic spline in AVF blood flow accounted for nonlinear association. The depicted levels of vein diameter and vein depth a 5th, 50th, and 95th percentiles.



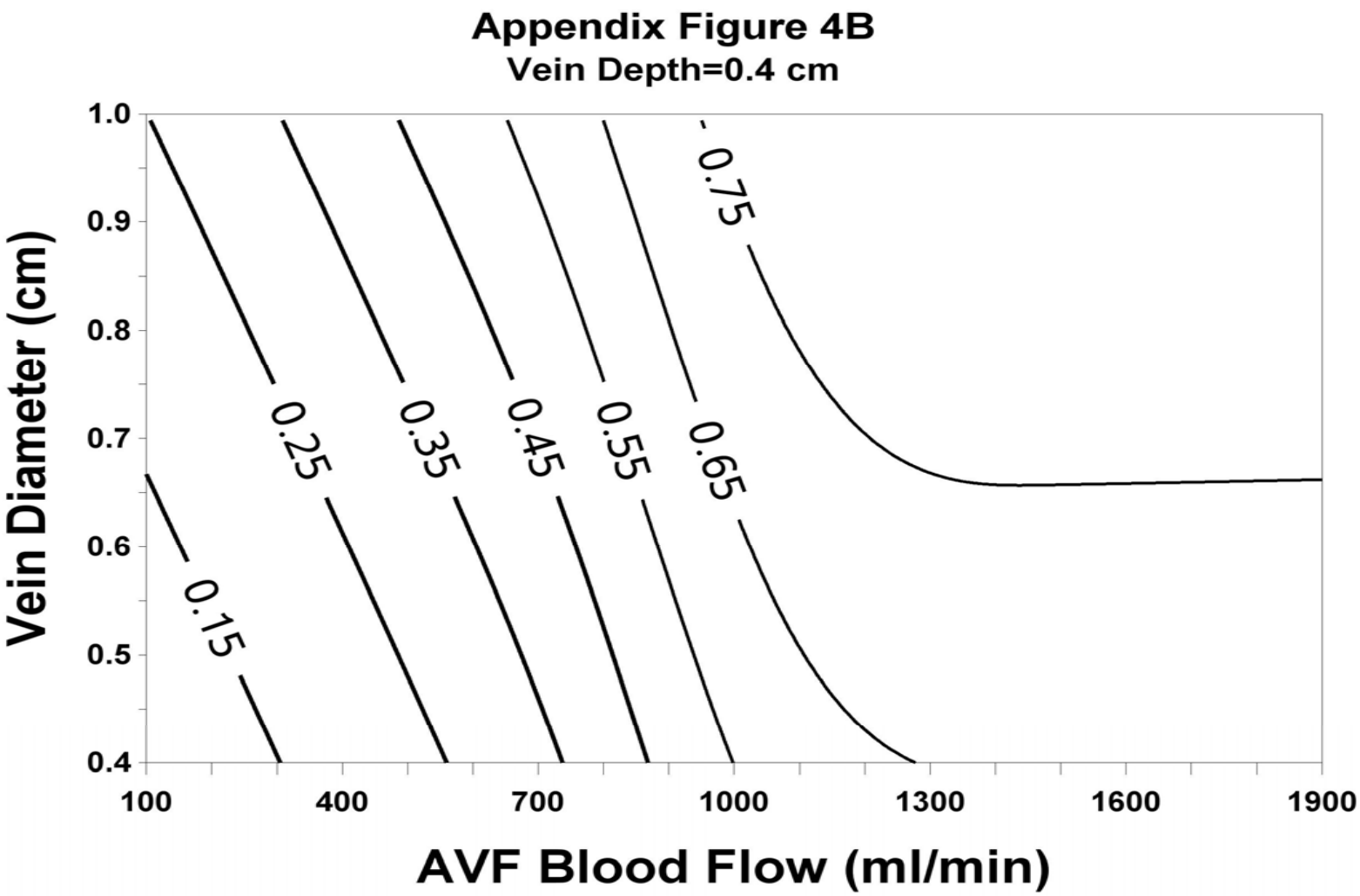
Appendix Figure 2B: Estimated probabilities of clinical unassisted maturation in upper-arm fistulas based on a logistic regression with 6-week AVF blood flow, vein diameter and vein depth as predictors variables. A cubic spline in AVF blood flow accounted for nonlinear association. The depicted levels of vein diameter and vein depth a 5th, 50th, and 95th percentiles



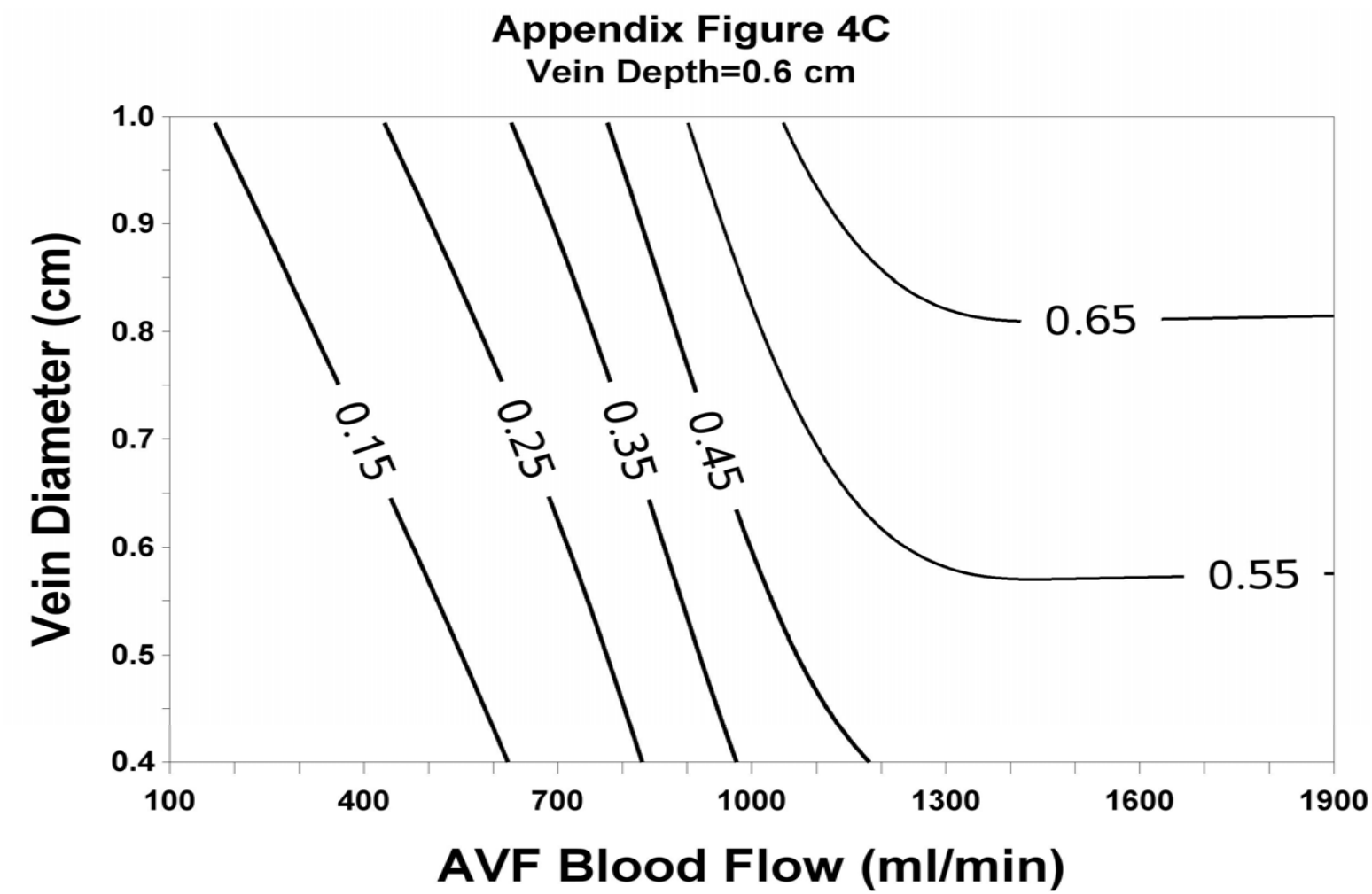
Appendix Figure 3: Estimated probabilities of overall clinical maturation in all fistulas, based on a logistic regression model with 6-week AVF blood flow, vein diameter and vein depth as predictor variables. A cubic spline in AVF blood flow was used to account for nonlinear association. The depicted levels of vein diameter and vein depth represent the 5th, 50th, and 95th percentiles.



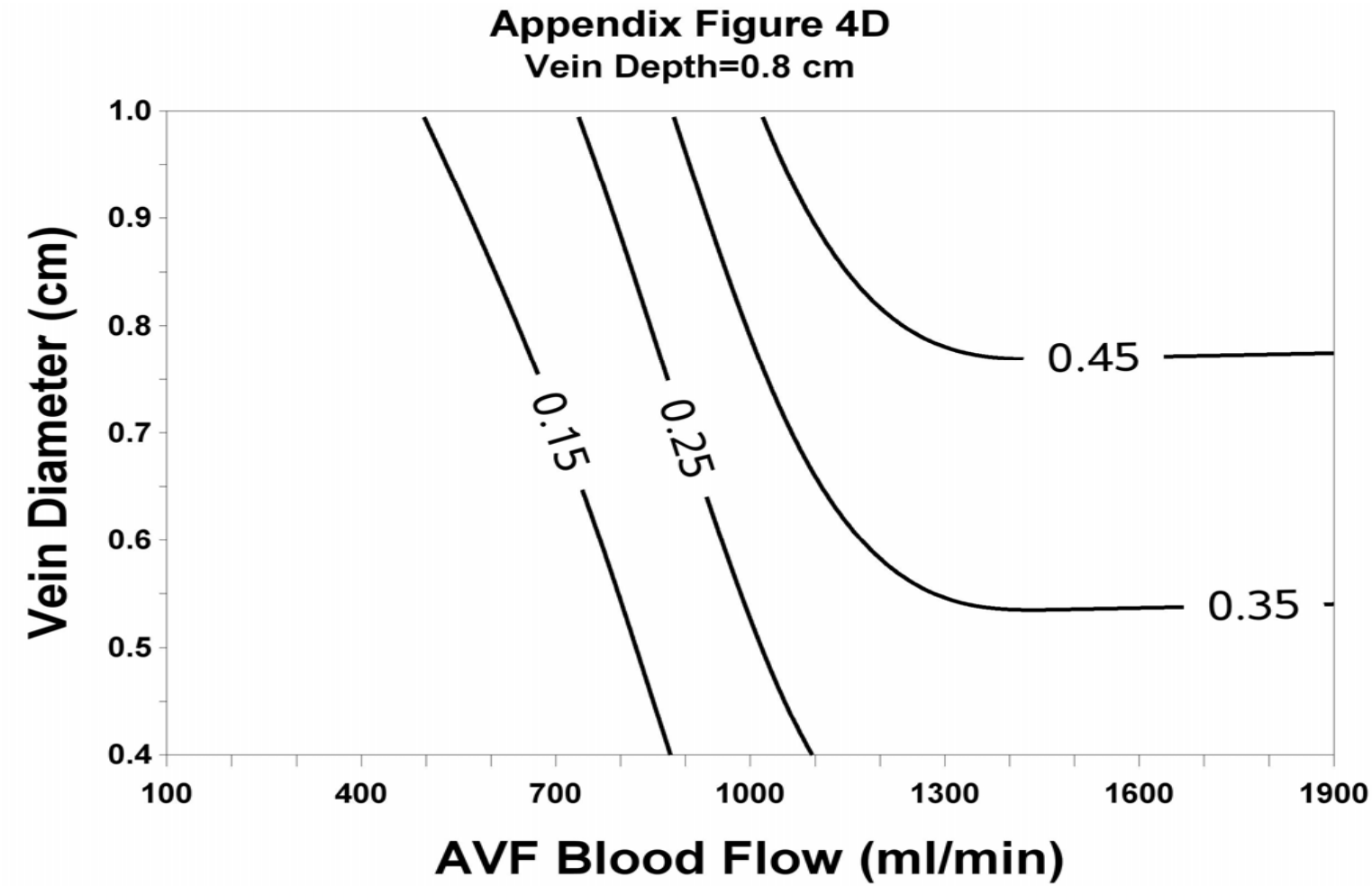
Appendix Figure 4A: Contour plots displaying the estimated probabilities of unassisted clinical maturation for different combinations of AVF blood flow, vein diameter, and vein depth. The clinically relevant depicted vein depths of **0.2 (this panel)**, 0.4, 0.6 and 0.8 cm represents the 5th, 52nd, 80th and 91st percentiles in the parameter. The contour plots can be used to look up combinations of AVF blood flow, vein diameter, and vein depth that lead to designated probabilities of unassisted clinical maturation. The US-prognostic models classified 6%, 11%, and 19% of subjects as having a ≤ 0.20 probability of unassisted clinical maturation at 1 day, 2-weeks and 6-weeks, respectively, and classified 2%, 7% and 16% as having a > 0.80 probability of unassisted clinical maturation at the same assessment times



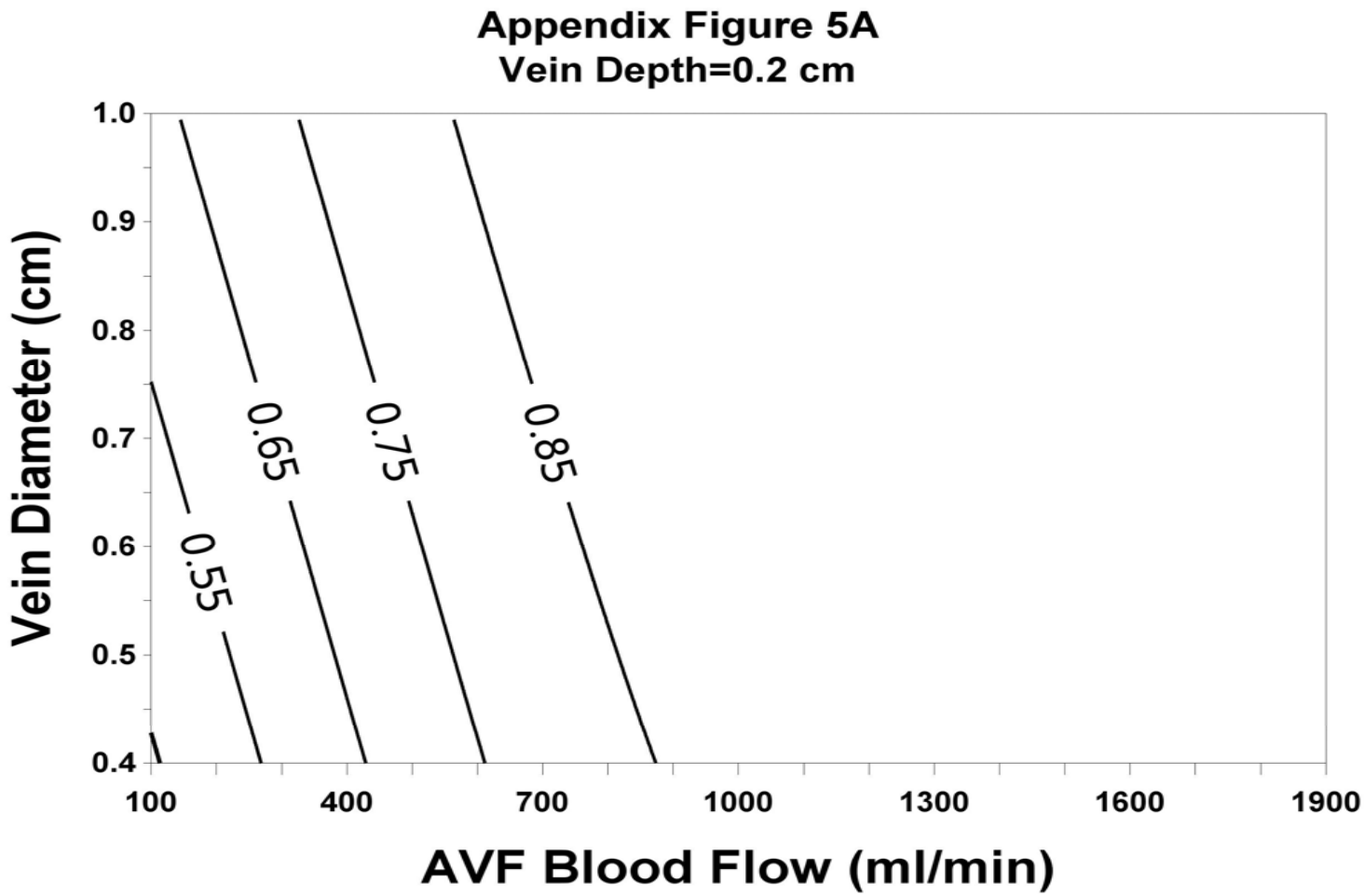
Appendix Figure 4B: Contour plots displaying the estimated probabilities of unassisted clinical maturation for different combinations of AVF blood flow, vein diameter, and vein depth. The clinically relevant depicted vein depths of 0.2, **0.4 (this panel)**, 0.6 and 0.8 cm represents the 5th, 52nd, 80th and 91st percentiles in the parameter. The contour plots can be used to look up combinations of AVF blood flow, vein diameter, and vein depth that lead to designated probabilities of unassisted clinical maturation. The US-prognostic models classified 6%, 11%, and 19% of subjects as having a ≤ 0.20 probability of unassisted clinical maturation at 1 day, 2-weeks and 6-weeks, respectively, and classified 2%, 7% and 16% as having a > 0.80 probability of unassisted clinical maturation at the same assessment times.



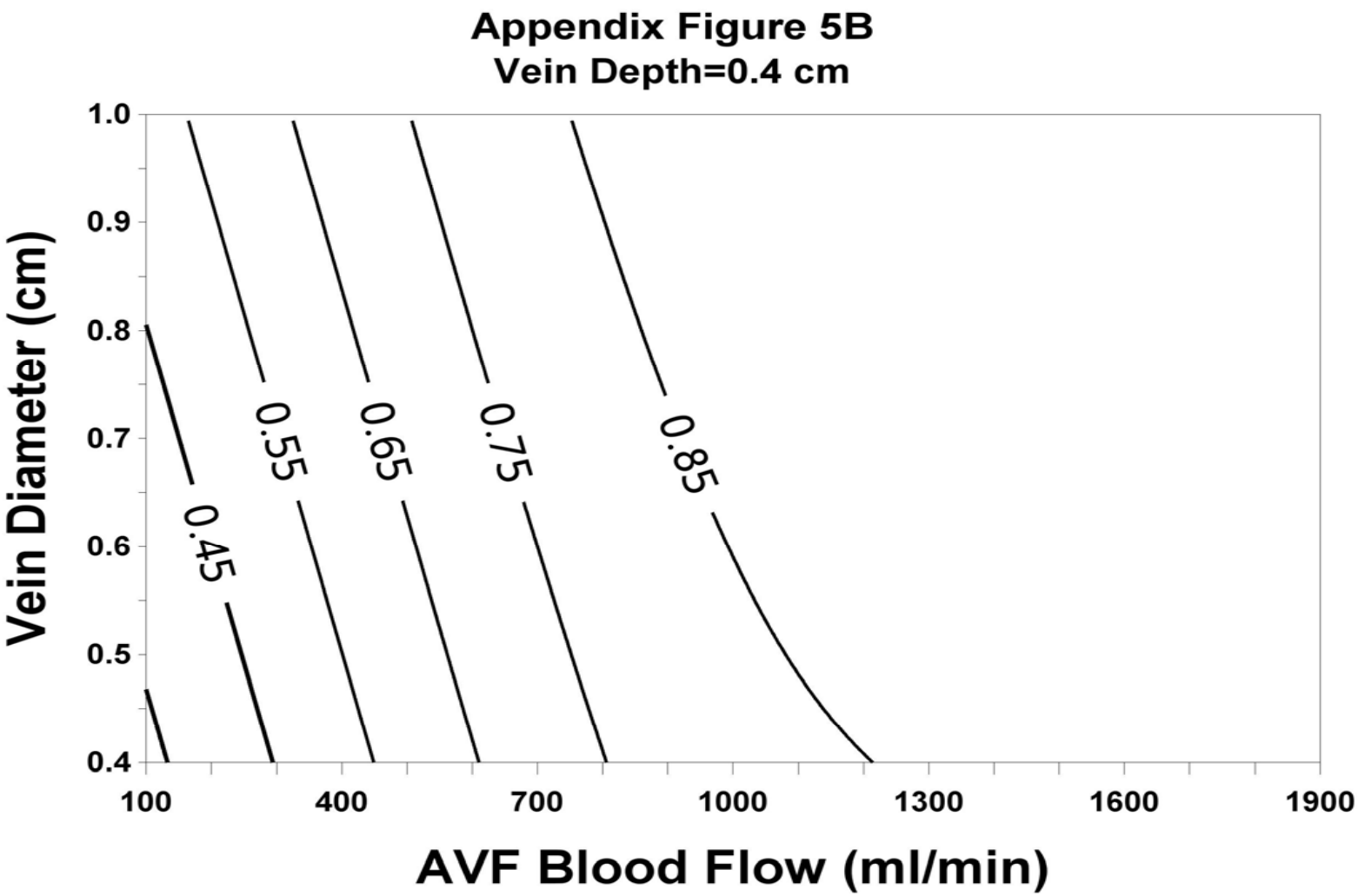
Appendix Figure 4C: Contour plots displaying the estimated probabilities of unassisted clinical maturation for different combinations of AVF blood flow, vein diameter, and vein depth. The clinically relevant depicted vein depths of 0.2, 0.4, **0.6 (this panel)** and 0.8 cm represents the 5th, 52nd, 80th and 91st percentiles in the parameter. The contour plots can be used to look up combinations of AVF blood flow, vein diameter, and vein depth that lead to designated probabilities of unassisted clinical maturation. The US-prognostic models classified 6%, 11%, and 19% of subjects as having a ≤ 0.20 probability of unassisted clinical maturation at 1 day, 2-weeks and 6-weeks, respectively, and classified 2%, 7% and 16% as having a > 0.80 probability of unassisted clinical maturation at the same assessment times.



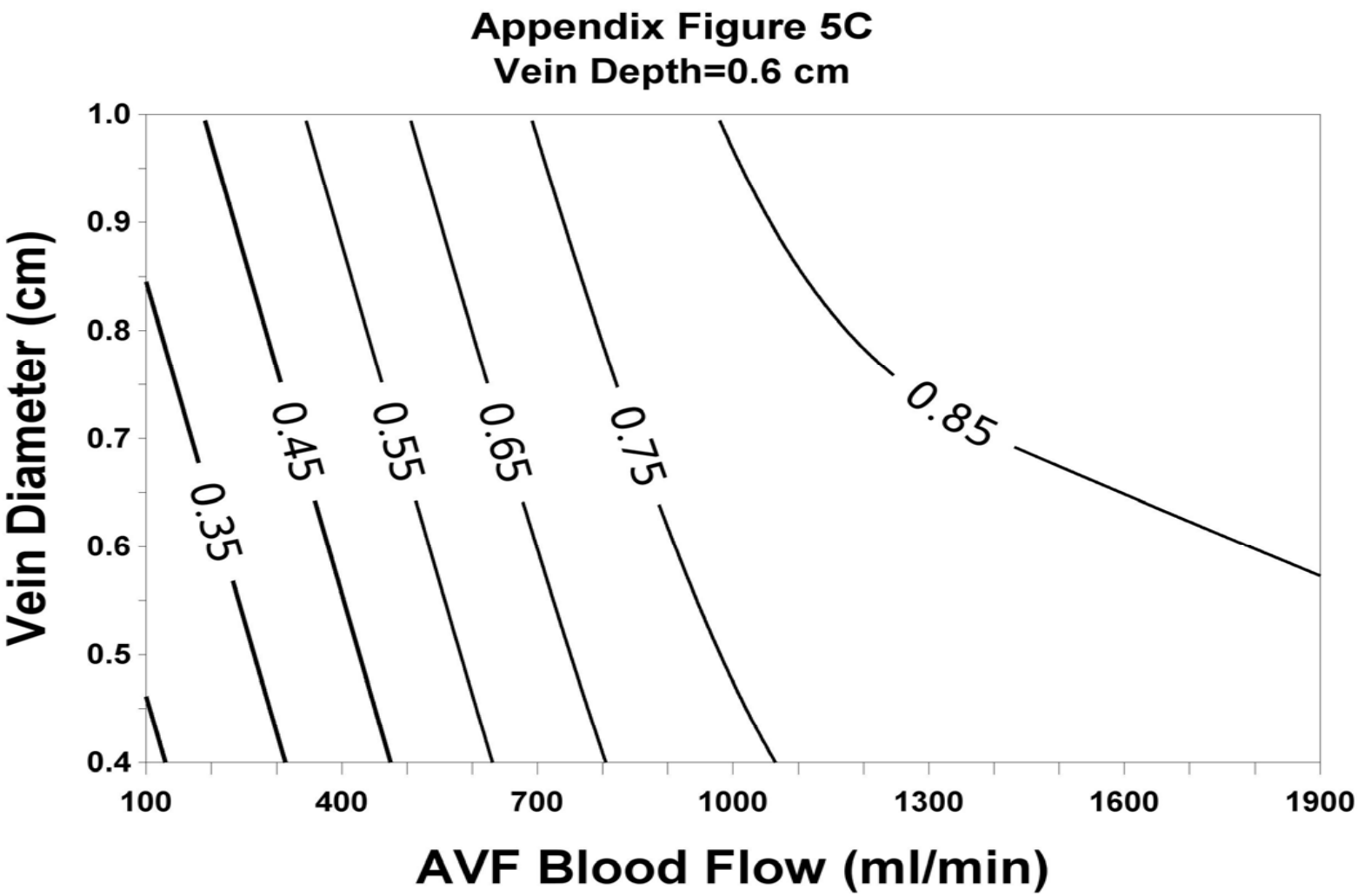
Appendix Figure 4D: Contour plots displaying the estimated probabilities of unassisted clinical maturation for different combinations of AVF blood flow, vein diameter, and vein depth. The clinically relevant depicted vein depths of 0.2 (this panel), 0.4, 0.6 and **0.8 (this panel)** cm represents the 5th, 52nd, 80th and 91st percentiles in the parameter. The contour plots can be used to look up combinations of AVF blood flow, vein diameter, and vein depth that lead to designated probabilities of unassisted clinical maturation. The US-prognostic models classified 6%, 11%, and 19% of subjects as having a ≤ 0.20 probability of unassisted clinical maturation at 1 day, 2-weeks and 6-weeks, respectively, and classified 2%, 7% and 16% as having a > 0.80 probability of unassisted clinical maturation at the same assessment times.



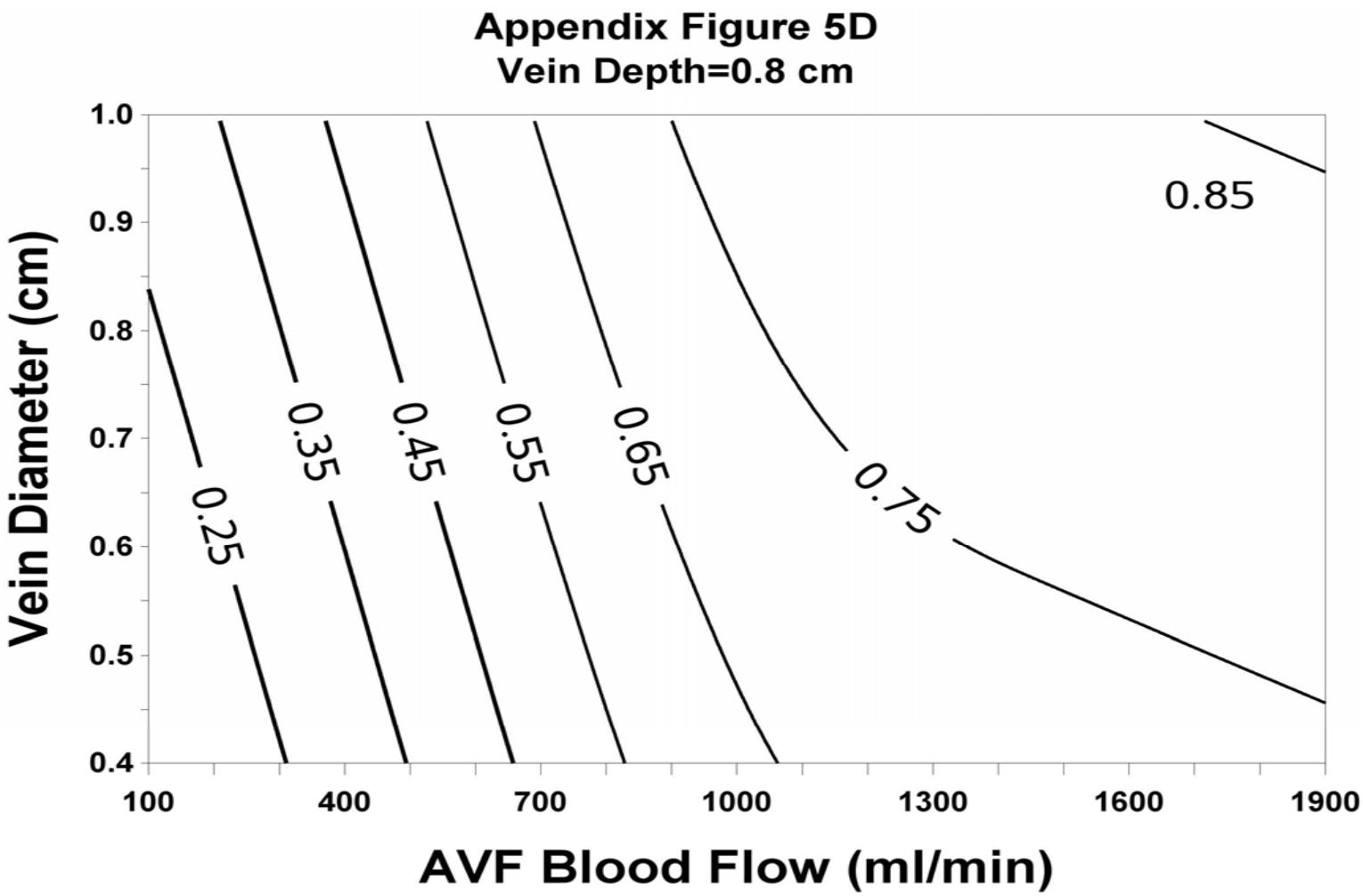
Appendix Figure 5A: Contour plots displaying the estimated probabilities of overall clinical maturation for different combinations of AVF blood flow, vein diameter, and vein depth. The clinically relevant depicted vein depths of **0.2 (this panel)**, 0.4, 0.6 and 0.8 cm represents the 5th, 52nd, 80th and 91st percentiles in the parameter. The contour plots can be used to look up combinations of AVF blood flow, vein diameter, and vein depth that lead to designated probabilities of overall clinical maturation. The US-prognostic models classified 1% of subjects as having a ≤ 0.20 probability of overall clinical maturation at each of the 1 day, 2-week and 6-week assessments, and classified 33%, 39% and 50% as having a > 0.80 probability of overall clinical maturation at the same assessment times.



Appendix Figure 5B: Contour plots displaying the estimated probabilities of overall clinical maturation for different combinations of AVF blood flow, vein diameter, and vein depth. The clinically relevant depicted vein depths of 0.2, **0.4 (this panel)**, 0.6 and 0.8 cm represents the 5th, 52nd, 80th and 91st percentiles in the parameter. The contour plots can be used to look up combinations of AVF blood flow, vein diameter, and vein depth that lead to designated probabilities of overall clinical maturation. The US-prognostic models classified 1% of subjects as having a ≤ 0.20 probability of overall clinical maturation at each of the 1 day, 2-week and 6-week assessments, and classified 33%, 39% and 50% as having a > 0.80 probability of overall clinical maturation at the same assessment times.

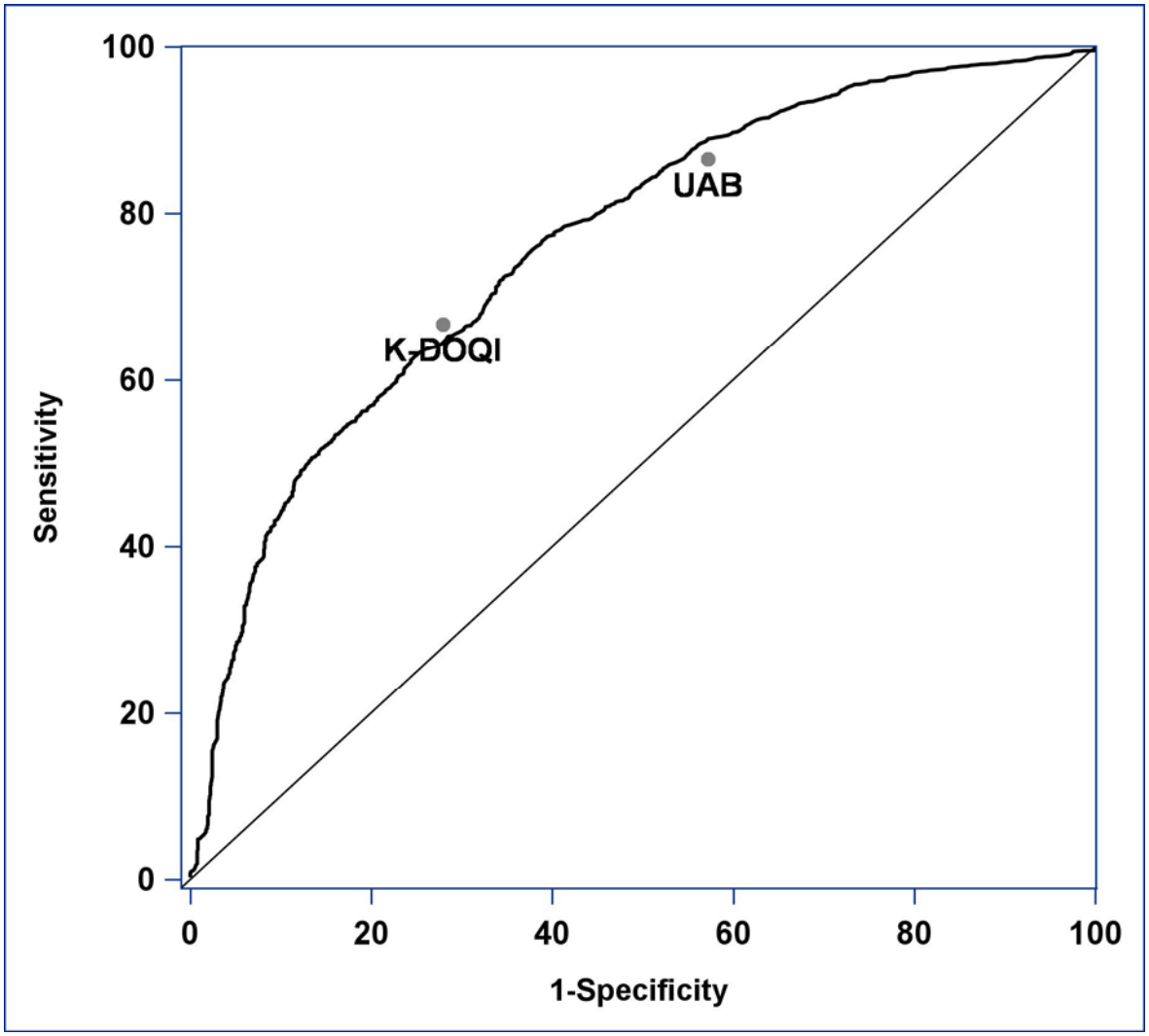


Appendix Figure 5C: Contour plots displaying the estimated probabilities of overall clinical maturation for different combinations of AVF blood flow, vein diameter, and vein depth. The clinically relevant depicted vein depths of 0.2, 0.4, **0.6 (this panel)** and 0.8 cm represents the 5th, 52nd, 80th and 91st percentiles in the parameter. The contour plots can be used to look up combinations of AVF blood flow, vein diameter, and vein depth that lead to designated probabilities of overall clinical maturation. The US-prognostic models classified 1% of subjects as having a ≤ 0.20 probability of overall clinical maturation at each of the 1 day, 2-week and 6-week assessments, and classified 33%, 39% and 50% as having a > 0.80 probability of overall clinical maturation at the same assessment times.



Appendix Figure 5D: Contour plots displaying the estimated probabilities of overall clinical maturation for different combinations of AVF blood flow, vein diameter, and vein depth. The clinically relevant depicted vein depths of 0.2, 0.4, 0.6 and **0.8 (this panel)** cm represents the 5th, 52nd, 80th and 91st percentiles in the parameter. The contour plots can be used to look up combinations of AVF blood flow, vein diameter, and vein depth that lead to designated probabilities of overall clinical maturation. The US-prognostic models classified 1% of subjects as having a ≤ 0.20 probability of overall clinical maturation at each of the 1 day, 2-week and 6-week assessments, and classified 33%, 39% and 50% as having a > 0.80 probability of overall clinical maturation at the same assessment times.

Appendix Figure 6



Appendix Figure 6: Cross-validated ROC Curve for prediction of overall clinical maturation from AVF blood flow, vein diameter and vein depth. The sensitivities and specificities of prediction of clinical maturation using the K-DOQI* and UAB** criteria are also displayed. Cross-validated areas under ROC curves for prognostic models based on only the three US parameters increased from 0.69, 0.71, and 0.76 respectively. *KDOQI Criteria: AVF Blood Flow ≥ 600 ml/min & AVF Vein Diameter ≥ 0.6 cm & AVF Vein Depth ≤ 0.6 cm; **UAB Criteria: AVF Blood Flow ≥ 500 ml/min & AVF Vein Diameter ≥ 0.4 cm.