3. RESULTS

The gestational age at delivery is summarised in Figure 7. The median duration of the pregnancies was 40 weeks with a range between 24 and 43.
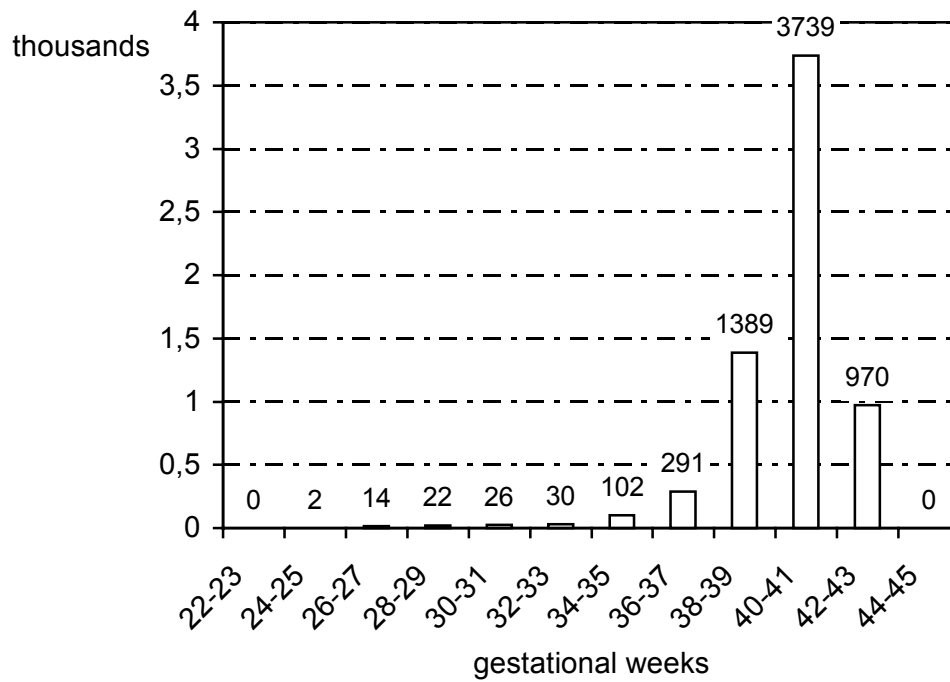

Figure 7: **Gestational Age** Distribution **at Delivery** of the Examined Low Risk Population (n=7,502)

The incidence of various forms of adverse pregnancy outcome of our study group is listed in Table 1.

	N	%
Intrauterine growth retardation	292	3.89 %
Pre-eclampsia	51	0.68 %
Placental abruption	26	0.35 %
IUD / NND	20	0.27 %
Preterm delivery <37 weeks	338	4.51 %
Preterm delivery <33 weeks	94	1.25 %
Preterm delivery <29 weeks	31	0.41 %
Any complication (one or several) (incl. preterm delivery <37 weeks)	625	8.33 %
Any complication (one or several) (incl. preterm delivery <33 weeks)	418	5.57 %
Any complication (one or several) (incl. preterm delivery <29 weeks)	382	5.09 %

Table 1:   Incidence of **Pregnancy Complications**. Percentages are of Total Population (n=7,502).

Table 2 shows the normal values of minimum, maximum and mean PI of both uterine arteries of the total population (n=7,502) in relation to the gestational age.

	Mean PI		
SSW	P50	P90	P95
20	0.920	1.435	1.645
21	0.875	1.355	1.595
22	0.870	1.310	1.510
23	0.835	1.270	1.515

	Min PI		
SSW	P50	P90	P95
20	0.79	1.14	1.32
21	0.74	1.08	1.23
22	0.74	1.06	1.19
23	0.72	1.03	1.16

	Max PI		
SSW	P50	P90	P95
20	1.03	1.69	2.17
21	1.00	1.67	2.06
22	0.99	1.62	1.93
23	0.94	1.53	1.82

Table 2: **Normal Values** of Minimum, Maximum and Mean PI of Uterine Arteries at 20 – 23 Gestational Weeks. Percentiles are Obtained from the Total Study Population (n=7,502).

Table 3 shows the number of screening positive patients for each of the methods.

Method	Positive	%
Notch only		
Uni- or bilateral notch	515	6.9%
Bilateral notch	185	2.5%

PI only	Positive	%
Mean PI > P90	742	9.9%
Min PI > P90	735	9.8%
Max PI > P90	746	9.9%

„Combination 1"	Positive	%
Using Mean PI	522	7.0%
Using Min PI	451	6.0%
Using Max PI	547	7.3%

„Combination 2"	Positive	%
Using Mean PI	896	11.9%
Using Min PI	921	12:3%
Using Max PI	919	12.3%

Table 3:   **Number of Screening Positive Patients**. Percentages are of Total Population (n=7,502).

The sensitivity, specificity, and positive and negative predictive values for all forms of adverse pregnancy outcome using different definitions of pathological waveform of uterine arteries are listed in Tables 4 to 11.

Method	Sensitivity	Specificity	PPV	NPV
Notch only				
Uni- or bilateral notch	51.0%	93.4%	5.0%	99.6%
Bilateral notch	29.4%	97.7%	8.1%	99.5%

PI only	Sensitivity	Specificity	PPV	NPV
Mean PI > P90	52.9%	90.4%	3.6%	99.6%
Min PI > P90	49.0%	90.5%	3.4%	99.6%
Max PI > P90	51.0%	90.3%	3.5%	99.6%

„Combination 1"	Sensitivity	Specificity	PPV	NPV
Using Mean PI	54.9%	93.4%	5.4%	99.7%
Using Min PI	47.1%	94.3%	5.3%	99.6%
Using Max PI	51.0%	93.0%	4.8%	99.6%

„Combination 2"	Sensitivity	Specificity	PPV	NPV
Using Mean PI	58.8%	88.4%	3.3%	99.7%
Using Min PI	52.9%	88.0%	2.9%	99.6%
Using Max PI	58.8%	88.1%	3.3%	99.7%

Table 4:   Sensitivity, Specificity, Positive and Negative Predictive Value in the Prediction of **Pre-Eclampsia** Using Various Definitions of Pathological Waveform.

Method	Sensitivity	Specificity	PPV	NPV
Notch only				
Uni- or bilateral notch	38.5%	93.2%	1.9%	99.8%
Bilateral notch	34.6%	97.6%	4.9%	99.8%

PI only	Sensitivity	Specificity	PPV	NPV
Mean PI > P90	38.5%	90.2%	1.3%	99.8%
Min PI > P90	46.2%	90.3%	1.6%	99.8%
Max PI > P90	42.3%	90.2%	1.5%	99.8%

„Combination 1"	Sensitivity	Specificity	PPV	NPV
Using Mean PI	42.3%	93.2%	2.1%	99.8%
Using Min PI	46.2%	94.1%	2.7%	99.8%
Using Max PI	46.2%	92.8%	2.2%	99.8%

„Combination 2"	Sensitivity	Specificity	PPV	NPV
Using Mean PI	46.2%	88.2%	1.3%	99.8%
Using Min PI	46.2%	87.8%	1.3%	99.8%
Using Max PI	50.0%	87.9%	1.4%	99.8%

Table 5:   Sensitivity, Specificity, Positive and Negative Predictive Value in the Prediction of **Placental Abruption** Using Various Definitions of Pathological Waveform.

Method	Sensitivity	Specificity	PPV	NPV
Notch only				
Uni- or bilateral notch	26.0%	93.9%	14.8%	96.9%
Bilateral notch	17.8%	98.2%	28.1%	96.7%

PI only	Sensitivity	Specificity	PPV	NPV
Mean PI > P90	37.0%	91.2%	14.6%	97.3%
Min PI > P90	30.8%	91.1%	12.2%	97.0%
Max PI > P90	34.6%	91.1%	13.5%	97.2%

„Combination 1"	Sensitivity	Specificity	PPV	NPV
Using Mean PI	31.2%	94.0%	17.4%	97.1%
Using Min PI	28.1%	94.9%	18.2%	97.0%
Using Max PI	30.8%	93.7%	16.5%	97.1%

„Combination 2"	Sensitivity	Specificity	PPV	NPV
Using Mean PI	39.0%	89.2%	12.7%	97.3%
Using Min PI	35.6%	88.7%	11.3%	97.1%
Using Max PI	38.4%	88.8%	12.2%	97.3%

Table 6:   Sensitivity, Specificity, Positive and Negative Predictive Value in the Prediction of **IUGR** Using Various Definitions of Pathological Waveform.

Method	Sensitivity	Specificity	PPV	NPV
Notch only				
Uni- or bilateral notch	20.0%	93.2%	0.8%	99.8%
Bilateral notch	10.0%	97.6%	1.1%	99.8%

PI only	Sensitivity	Specificity	PPV	NPV
Mean　　PI > P90	20.0%	90.1%	0.5%	99.8%
Min　　PI > P90	20.0%	90.2%	0.5%	99.8%
Max　　PI > P90	20.0%	90.1%	0.5%	99.8%

„Combination 1"	Sensitivity	Specificity	PPV	NPV
Using　　Mean PI	20.0%	93.1%	0.8%	99.8%
Using　　Min　PI	15.0%	94.0%	0.7%	99.8%
Using　　Max　PI	20.0%	92.7%	0.7%	99.8%

„Combination 2"	Sensitivity	Specificity	PPV	NPV
Using　　Mean PI	25.0%	88.1%	0.6%	99.8%
Using　　Min　PI	25.0%	87.8%	0.5%	99.8%
Using　　Max　PI	25.0%	87.8%	0.5%	99.8%

Table 7:　　Sensitivity, Specificity, Positive and Negative Predictive Value in the Prediction of **IUD / NND** Using Various Definitions of Pathological Waveform.

Method	Sensitivity	Specificity	PPV	NPV
Notch only				
Uni- or bilateral notch	38.7%	93.3%	2.3%	99.7%
Bilateral notch	25.8%	97.6%	4.3%	99.7%

PI only	Sensitivity	Specificity	PPV	NPV
Mean PI > P90	45.2%	90.3%	1.9%	99.7%
Min PI > P90	35.5%	90.3%	1.5%	99.7%
Max PI > P90	38.7%	90.2%	1.6%	99.7%

„Combination 1"	Sensitivity	Specificity	PPV	NPV
Using Mean PI	45.2%	93.2%	2.1%	99.8%
Using Min PI	35.5%	94.1%	1.7%	99.7%
Using Max PI	41.9%	92.9%	1.9%	99.7%

„Combination 2"	Sensitivity	Specificity	PPV	NPV
Using Mean PI	42.3%	87.1%	1.3%	99.7%
Using Min PI	34.6%	87.0%	1.0%	99.7%
Using Max PI	38.5%	87.0%	1.2%	99.8%

Table 8:   Sensitivity, Specificity, Positive and Negative Predictive Value in the Prediction of **Preterm Delivery (<29 weeks)** Using Various Definitions of Pathological Waveform.

Method	Sensitivity	Specificity	PPV	NPV
Notch only				
Uni- or bilateral notch	34.0%	93.5%	6.2%	99.1%
Bilateral notch	26.6%	97.8%	13.5%	99.1%

PI only	Sensitivity	Specificity	PPV	NPV
Mean PI > P90	44.7%	90.6%	5.7%	99.2%
Min PI > P90	38.3%	90.6%	4.9%	99.1%
Max PI > P90	42.6%	90.5%	5.4%	99.2%

„Combination 1"	Sensitivity	Specificity	PPV	NPV
Using Mean PI	41.5%	93.5%	7.5%	99.2%
Using Min PI	37.2%	94.4%	7.8%	99.2%
Using Max PI	39.4%	93.1%	6.8%	99.2%

„Combination 2"	Sensitivity	Specificity	PPV	NPV
Using Mean PI	45.7%	88.5%	4.8%	99.2%
Using Min PI	41.5%	88.1%	4.2%	99.2%
Using Max PI	44.7%	88.2%	4.6%	99.2%

Table 9:   Sensitivity, Specificity, Positive and Negative Predictive Value in the Prediction of **Preterm Delivery (<33 weeks)** Using Various Definitions of Pathological Waveform.

Method	Sensitivity	Specificity	PPV	NPV
Notch only				
Uni- or bilateral notch	20.1%	93.8%	13.2%	96.1%
Bilateral notch	11.5%	98.0%	21.1%	95.9%

PI only	Sensitivity	Specificity	PPV	NPV
Mean PI > P90	25.7%	90.9%	11.7%	96.3%
Min PI > P90	24.0%	90.9%	11.0%	96.2%
Max PI > P90	26.6%	90.8%	12.1%	96.3%

„Combination 1"	Sensitivity	Specificity	PPV	NPV
Using Mean PI	22.5%	93.8%	14.6%	96.2%
Using Min PI	19.8%	94.6%	14.9%	96.2%
Using Max PI	21.6%	93.4%	13.3%	96.2%

„Combination 2"	Sensitivity	Specificity	PPV	NPV
Using Mean PI	28.7%	88.8%	10.8%	96.4%
Using Min PI	27.2%	88.4%	10.0%	96.3%
Using Max PI	29.6%	88.6%	10.9%	96.4%

Table 10: Sensitivity, Specificity, Positive and Negative Predictive Value in the Prediction of **Preterm Delivery (<37 weeks)** Using Various Definitions of Pathological Waveform.

Method	Sensitivity	Specificity	PPV	NPV
Notch only				
Uni- or bilateral notch	27.5%	94.2%	20.4%	96.0%
Bilateral notch	17.8%	98.4%	36.8%	95.7%

PI only	Sensitivity	Specificity	PPV	NPV
Mean PI > P90	36.4%	91.5%	18.7%	96.4%
Min PI > P90	30.6%	91.3%	15.9%	96.1%
Max PI > P90	34.6%	91.4%	17.7%	96.3%

„Combination 1"	Sensitivity	Specificity	PPV	NPV
Using Mean PI	32.2%	94.4%	23.6%	96.3%
Using Min PI	28.0%	95.2%	23.7%	96.1%
Using Max PI	31.9%	94.0%	22.3%	96.3%

„Combination 2"	Sensitivity	Specificity	PPV	NPV
Using Mean PI	38.3%	89.6%	17.9%	96.1%
Using Min PI	34.2%	89.0%	15.5%	95.8%
Using Max PI	37.8%	89.3%	17.2%	96.1%

Table 11: Sensitivity, Specificity, Positive and Negative Predictive Value in the Prediction of **Any Problem, Including Preterm Delivery < 29 Weeks**, Using Various Definitions of Pathological Waveform.

Method	Sensitivity	Specificity	PPV	NPV
Notch only				
Uni-- or bilateral notch	26.3%	94.3%	21.4%	95.6%
Bilateral notch	17.0%	98.4%	38.4%	95.3%

PI only	Sensitivity	Specificity	PPV	NPV
Mean PI > P90	35.6%	91.6%	20.1%	96.0%
Min PI > P90	29.9%	91.4%	17.0%	95.7%
Max PI > P90	34.0%	91.5%	19.0%	95.9%

„Combination 1"	Sensitivity	Specificity	PPV	NPV
Using Mean PI	31.1%	94.5%	24.9%	95.9%
Using Min PI	27.0%	95.2%	25.1%	95.7%
Using Max PI	30.9%	94.1%	23.6%	95.8%

„Combination 2"	Sensitivity	Specificity	PPV	NPV
Using Mean PI	38.3%	89.6%	17.9%	96.1%
Using Min PI	34.2%	89.0%	15.5%	95.8%
Using Max PI	37.8%	89.3%	17.2%	96.1%

Table 12: Sensitivity, Specificity, Positive and Negative Predictive Value in the Prediction of **Any Problem, Including Preterm Delivery < 33 Weeks**, Using Various Definitions of Pathological Waveform.

Method	Sensitivity	Specificity	PPV	NPV
Notch only				
Uni-- or bilateral notch	21.1%	94.4%	25.6%	92.9%
Bilateral notch	12.2%	98.4%	41.1%	92.5%

PI only	Sensitivity	Specificity	PPV	NPV
Mean PI > P90	28.6%	91.8%	24.1%	93.4%
Min PI > P90	25.0%	91.6%	21.2%	93.1%
Max PI > P90	28.2%	91.7%	23.6%	93.4%

„Combination 1"	Sensitivity	Specificity	PPV	NPV
Using Mean PI	24.3%	94.6%	29.1%	93.2%
Using Min PI	21.1%	95.4%	29.3%	93.0%
Using Max PI	24.0%	94.2%	27.4%	93.2%

"Combination 2"	Sensitivity	Specificity	PPV	NPV
Using Mean PI	31.4%	89.8%	21.9%	93.5%
Using Min PI	29.0%	89.2%	19.7%	93.3%
Using Max PI	31.7%	89.5%	21.5%	93.5%

Table 13:   Sensitivity, Specificity, Positive and Negative Predictive Value in the Prediction of **Any Problem, Including Preterm Delivery < 37 Weeks**, Using Various Definitions of Pathological Waveform.

Figures 8 to 51 show the diagnostic efficacy of PI in combination with missing, uni- or bilateral notching as well as for all patients for the different forms of pathological pregnancy outcome. Figures 12 to 23 use Min PI, Max PI and Mean PI. All other figures use Mean PI only.
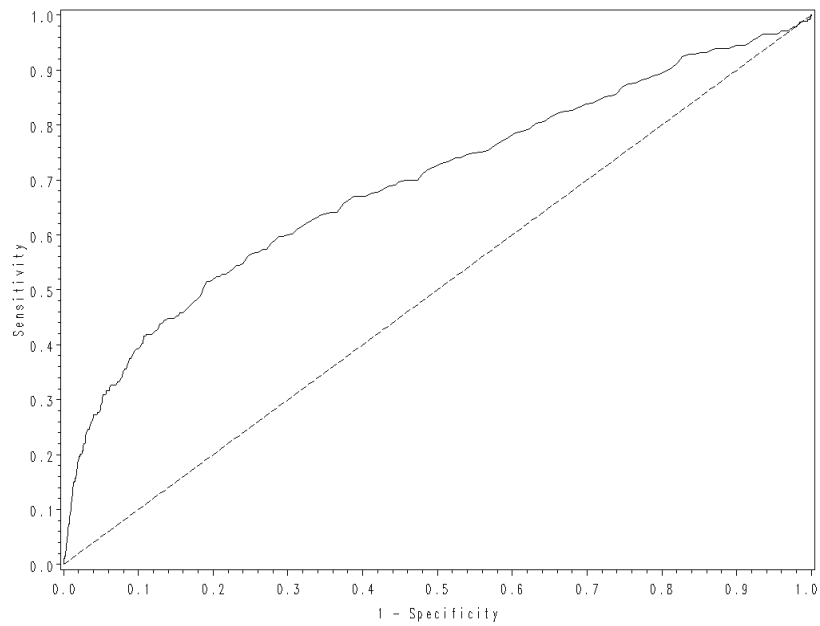
Figure 8:   ROC Curve for Prediction of:
             "Any Problem" (including preterm delivery <29 weeks)
             All Patients (n=7,502)
             MEAN PI
             AUC 0.694, SE 0.016
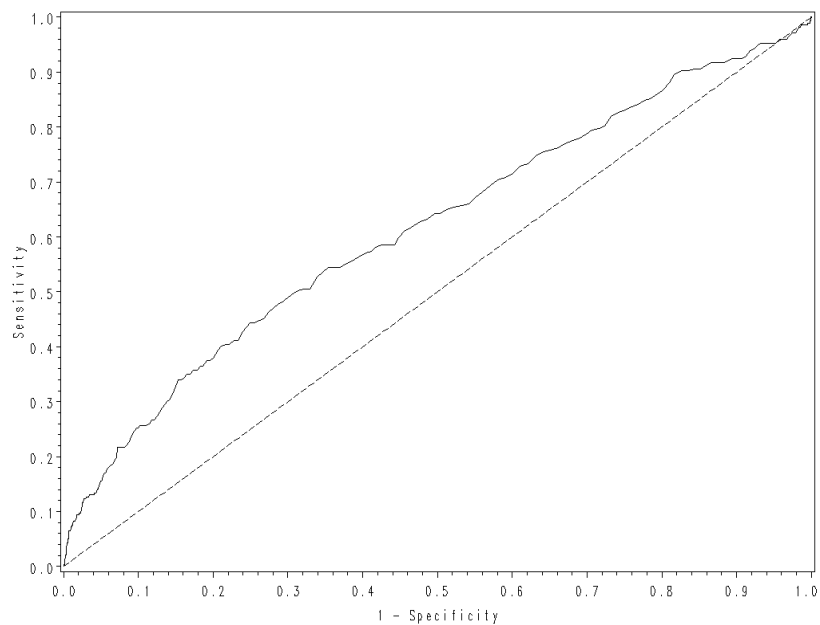
Figure 9:   ROC Curve for Prediction of:
             "Any Problem" (including preterm delivery <29 weeks)
             No Notch
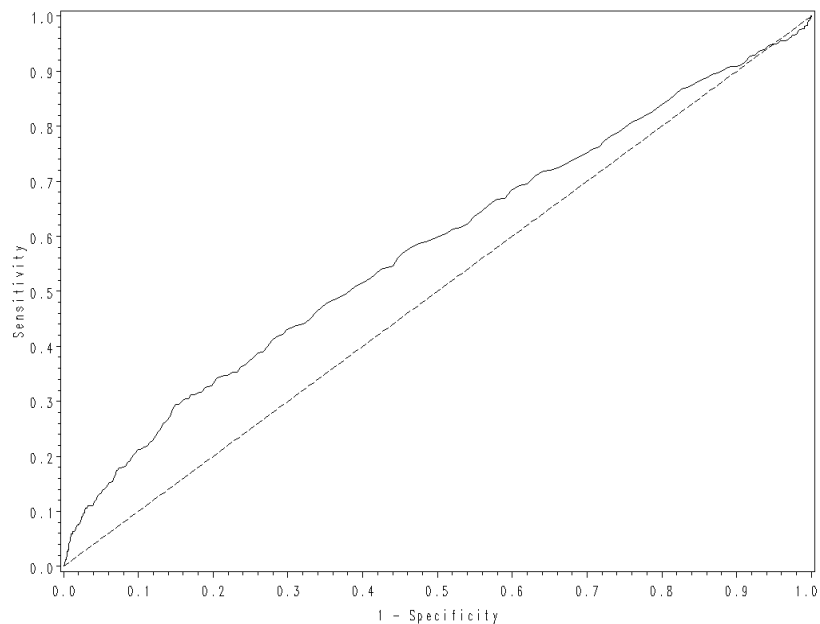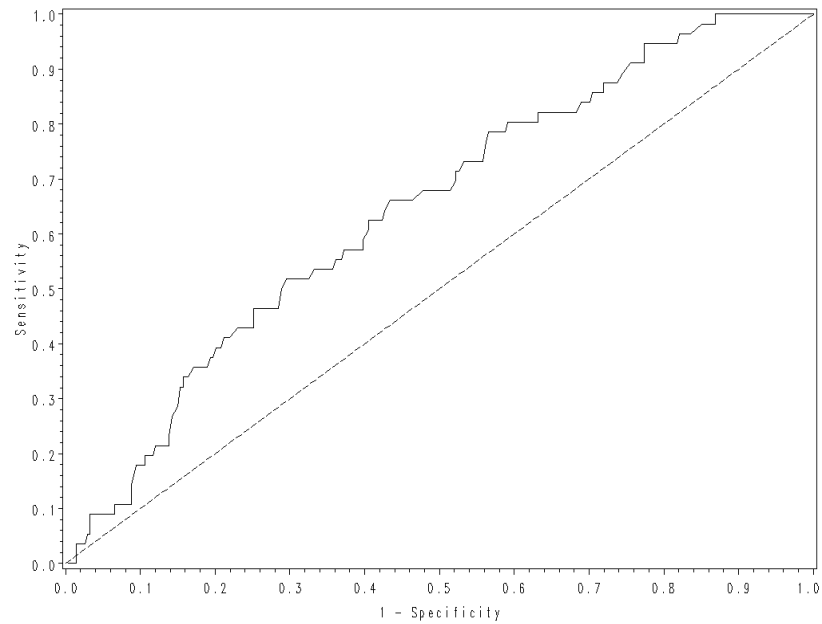   MEAN PI
             AUC 0.616, SE 0.019
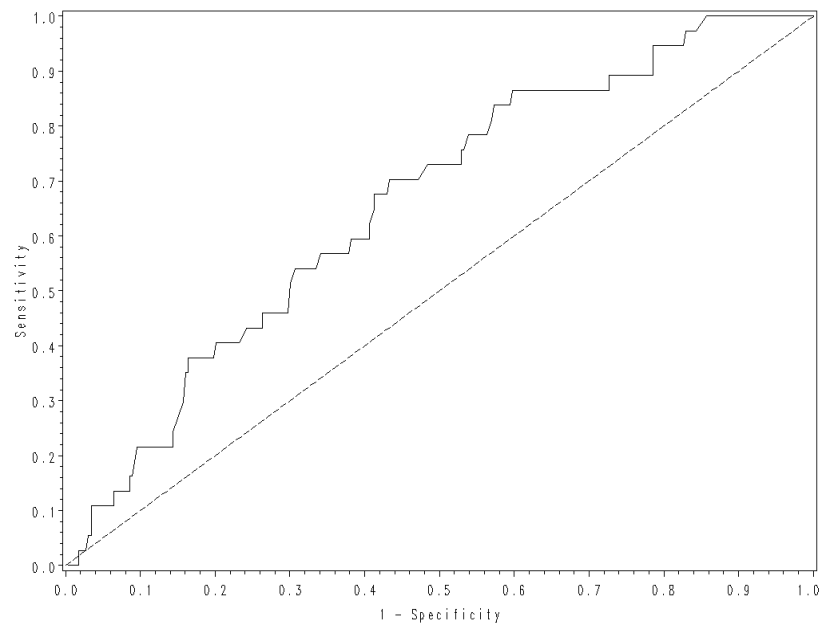
Figure 10: ROC Curve for Prediction of:
"Any Problem" (including preterm delivery <29 weeks)
Unilateral Notch
MEAN PI
AUC 0.659, SE 0.044
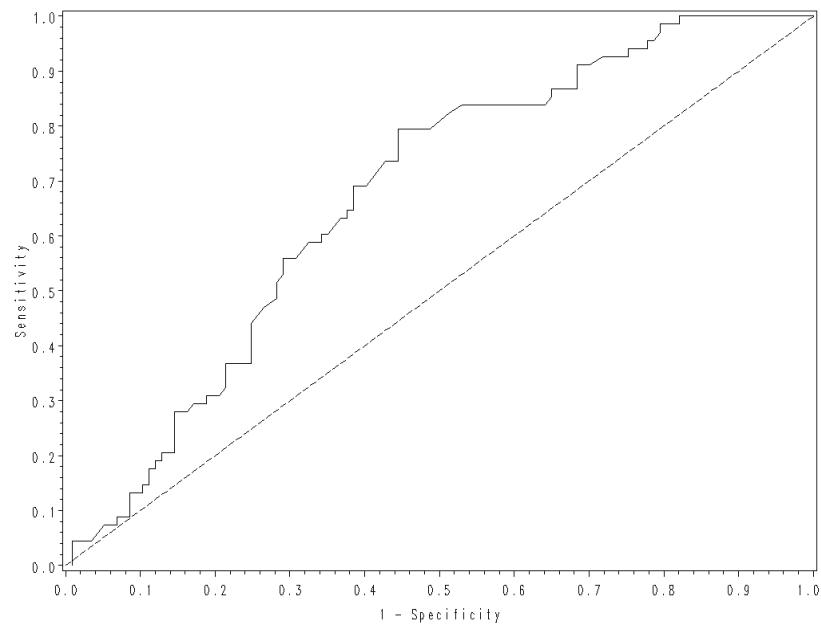
Figure 11: ROC Curve for Prediction of:
"Any Problem" (including preterm delivery <29 weeks)
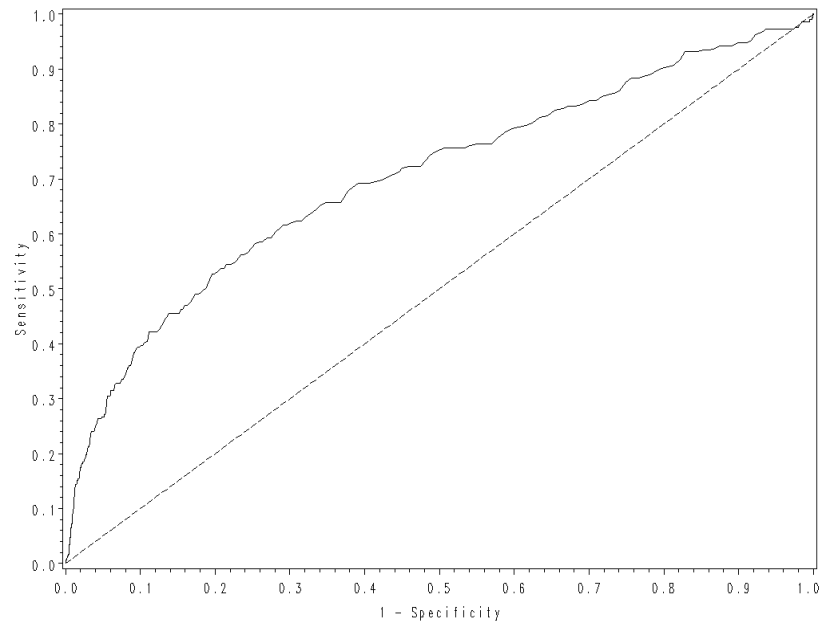**Bilateral Notch**
MEAN PI
AUC 0.674, SE 0.039
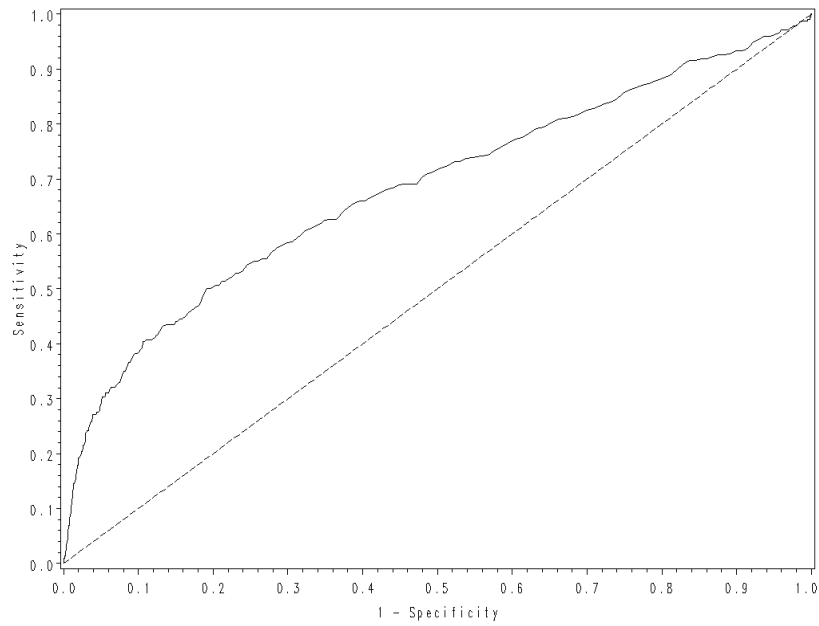
Figure 12: ROC Curve for Prediction of:
"Any Problem" (including preterm delivery <33 weeks)
All Patients (n=7,502)
MEAN PI
AUC 0.683, SE 0.016
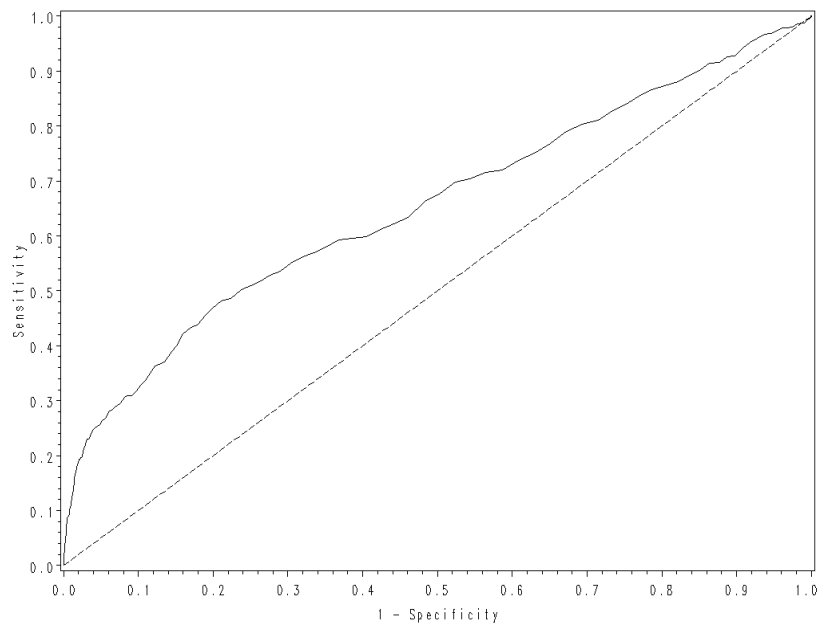
Figure 13: ROC Curve for Prediction of:
"Any Problem" (including preterm delivery <33 weeks)
All Patients (n=7,502)
MIN PI
AUC 0.654, SE 0.016
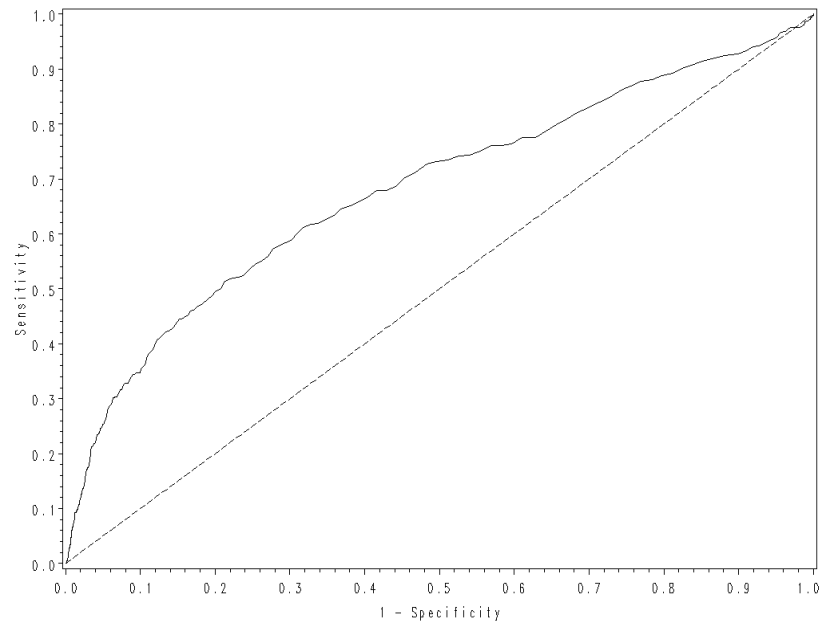
Figure 14:   ROC Curve for Prediction of:
"Any Problem" (including preterm delivery <33 weeks)
All Patients (n=7,502)
MAX PI
AUC 0.681, SE 0.015
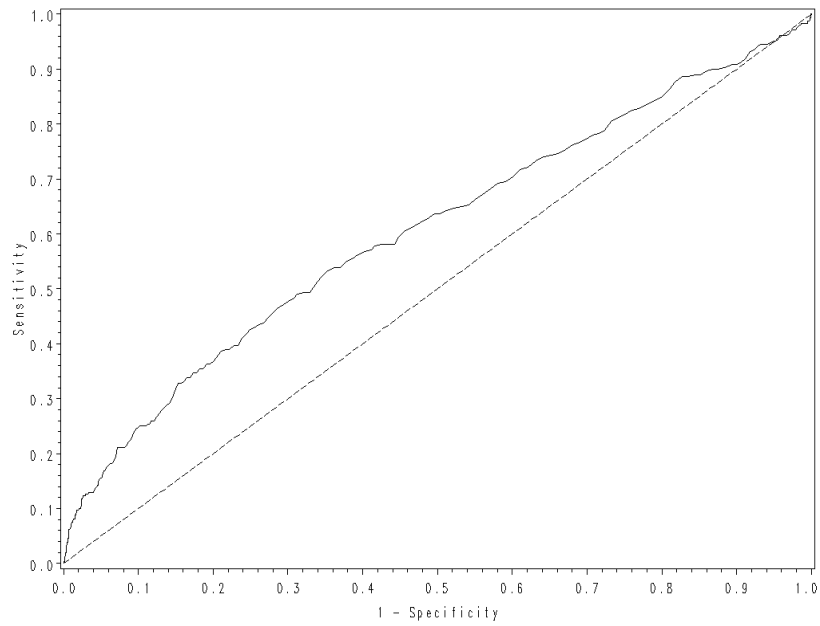
Figure 15:   ROC Curve for Prediction of:
"Any Problem" (including preterm delivery <33 weeks)
No Notch
MEAN PI
AUC 0.607, SE 0.018
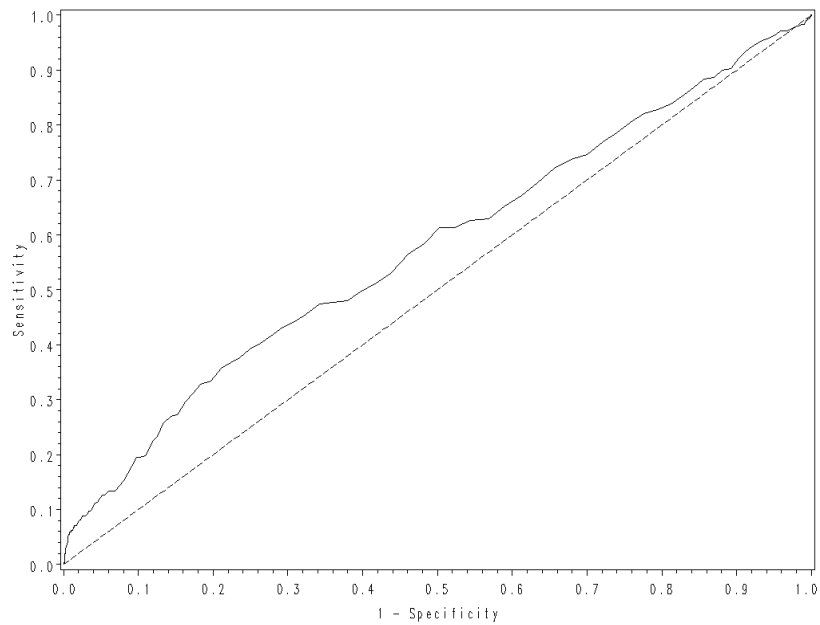
Figure 16:   ROC Curve for Prediction of:
"Any Problem" (including preterm delivery <33 weeks)
No Notch
MIN PI
AUC 0.577, SE 0.018
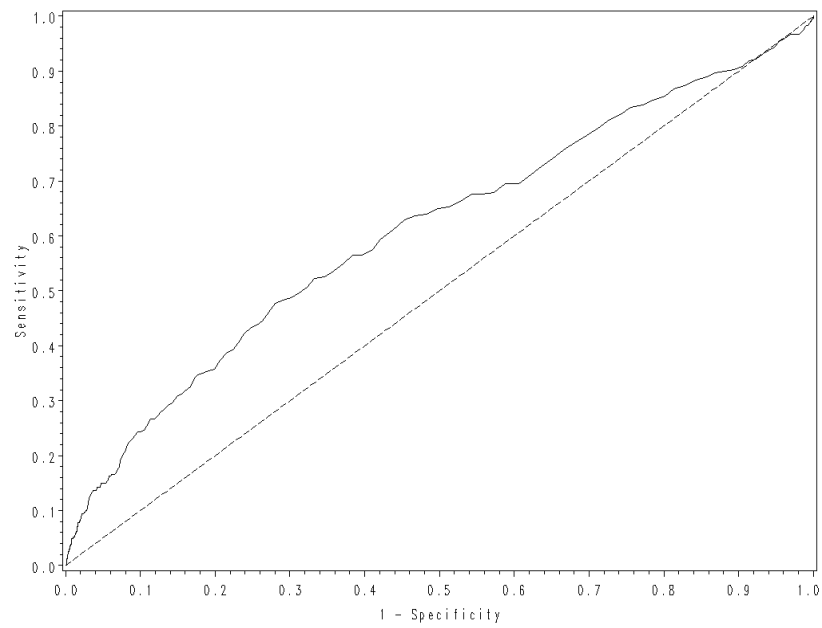
Figure 17: ROC Curve for Prediction of:
"Any Problem" (including preterm delivery <33 weeks)
No Notch
MAX PI
AUC 0.610, SE 0.018
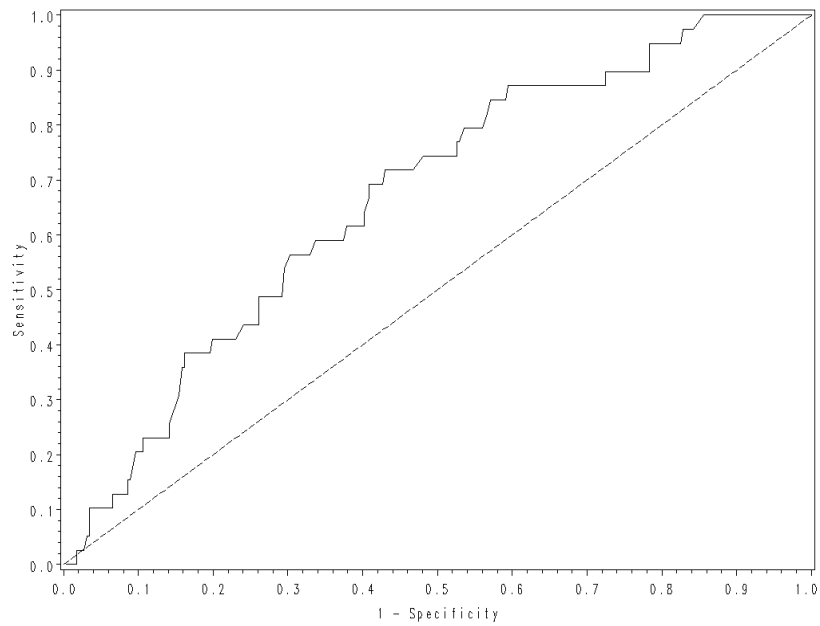
Figure 18:   ROC Curve for Prediction of:
"Any Problem" (including preterm delivery <33 weeks)
Unilateral Notch
MEAN PI
AUC 0.670, SE 0.042
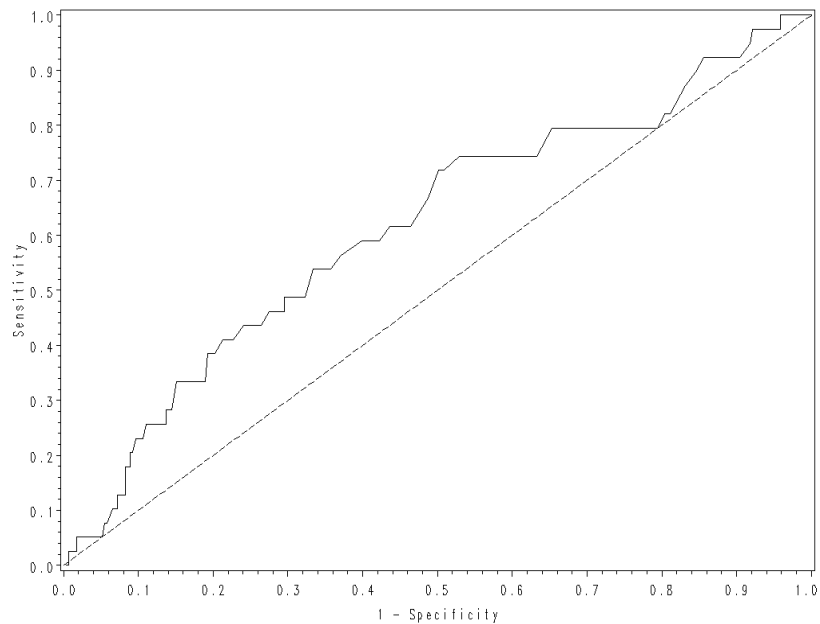
Figure 19:   ROC Curve for Prediction of:
"Any Problem" (including preterm delivery <33 weeks)
Unilateral Notch
MIN PI
AUC 0.616, SE 0.050
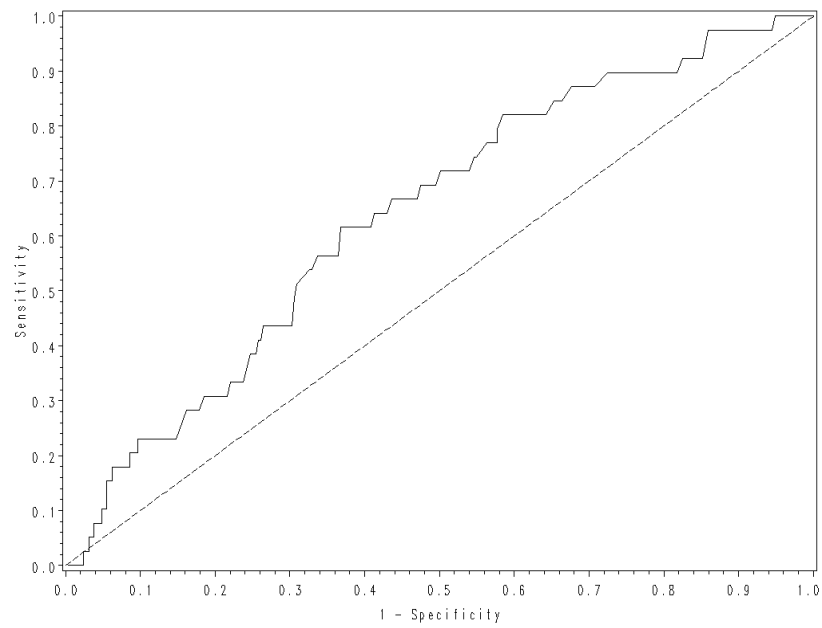
Figure 20:   ROC Curve for Prediction of:
"Any Problem" (including preterm delivery <33 weeks)
Unilateral Notch
MAX PI
AUC 0.639, SE 0.045
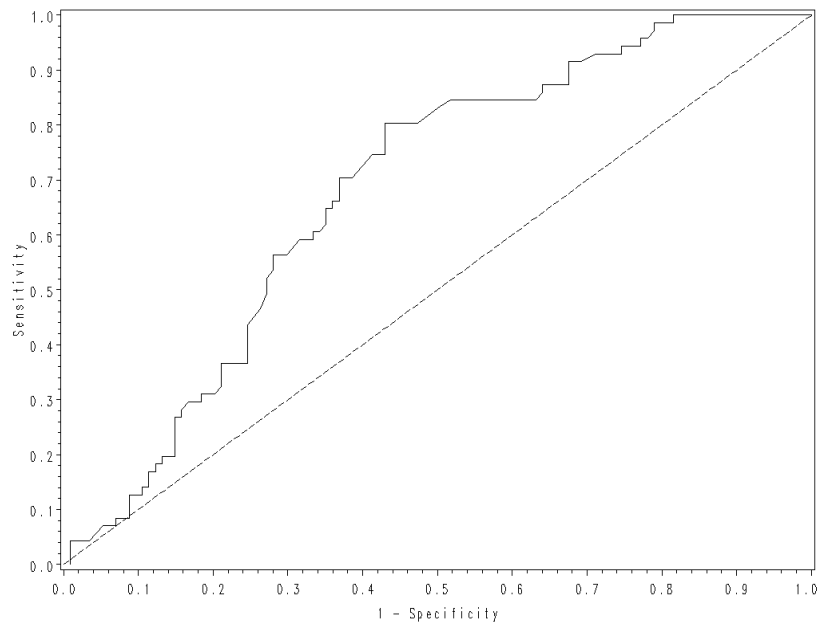
Figure 21: ROC Curve for Prediction of:
"Any Problem" (including preterm delivery <33 weeks)
Bilateral Notch
MEAN PI
AUC 0.682, SE 0.039
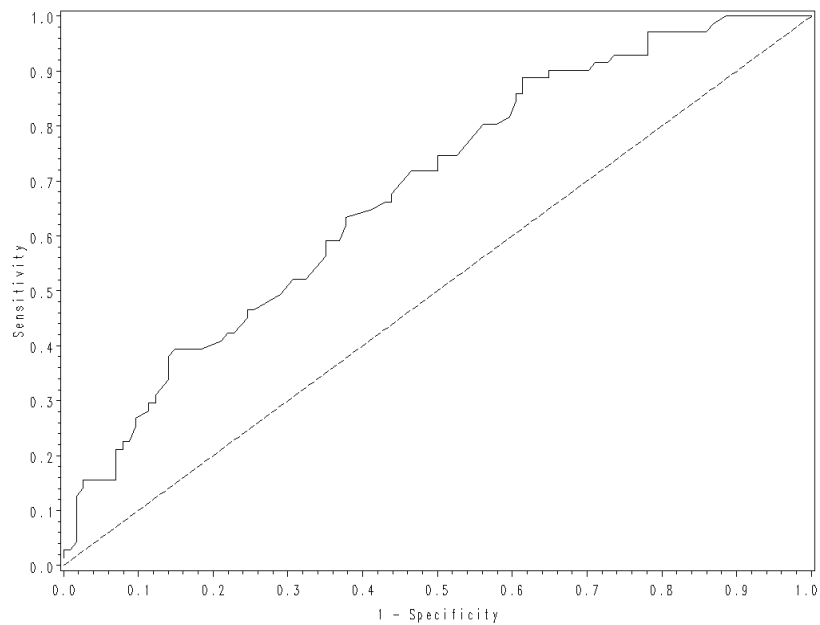
Figure 22: ROC Curve for Prediction of:
"Any Problem" (including preterm delivery <33 weeks)
Bilateral Notch
MIN PI
AUC 0.681, SE 0.039
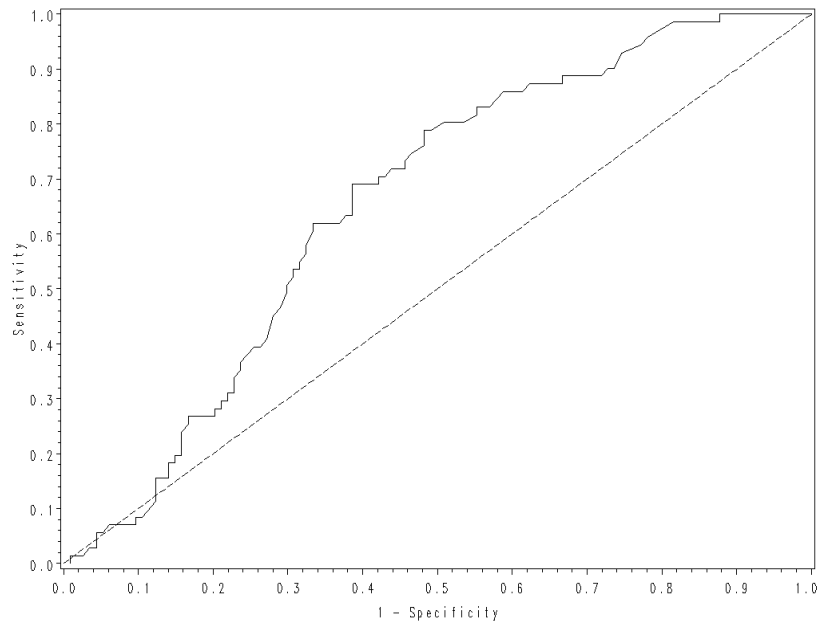
Figure 23:   ROC Curve for Prediction of:
"Any Problem" (including preterm delivery <33 weeks)
Bilateral Notch
MAX PI
AUC 0.657, SE 0.040
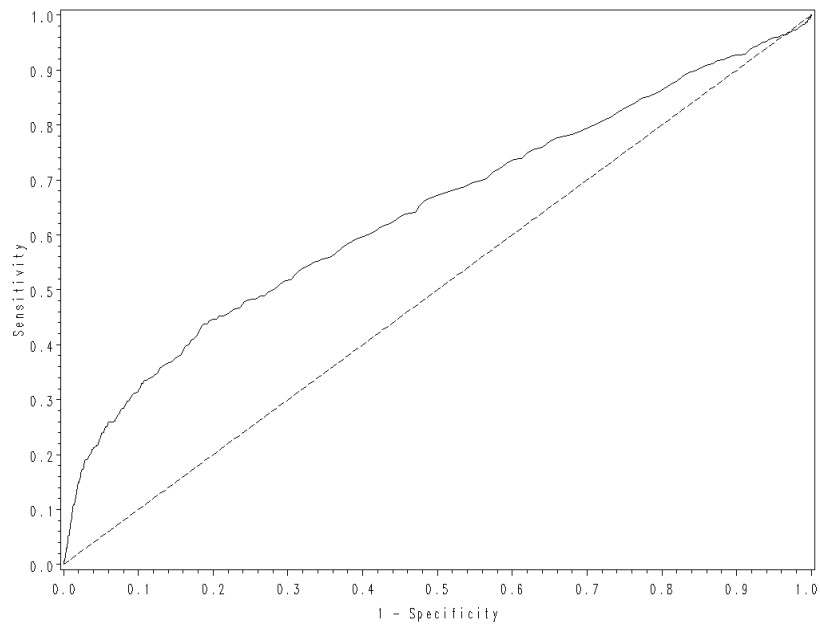
Figure 24: ROC Curve for Prediction of:
"Any Problem" (including preterm delivery <37 weeks)
All Patients
MEAN PI
AUC 0.642, SE 0.013

Figure 25: ROC Curve for Prediction of:
"Any Problem" (including preterm delivery <37 weeks)
No Notch
MEAN PI
AUC 0.580, SE 0.014

Figure 26:   ROC Curve for Prediction of:
"Any Problem" (including preterm delivery <37 weeks)
Unilateral Notch
MEAN PI
AUC 0.645, SE 0.038
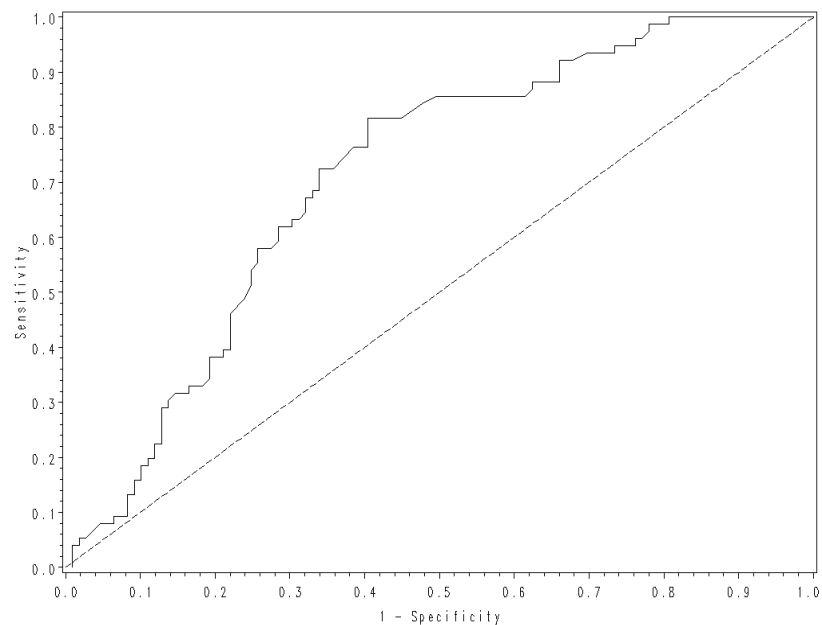
Figure 27:   ROC Curve for Prediction of:
"Any problem" (including preterm delivery <37 weeks)
Bilateral Notch
MEAN PI
AUC 0.711, SE 0.038

Figure 28:   ROC Curve for Prediction of:
IUGR
All Patients
MEAN PI
AUC 0.702, SE 0.018
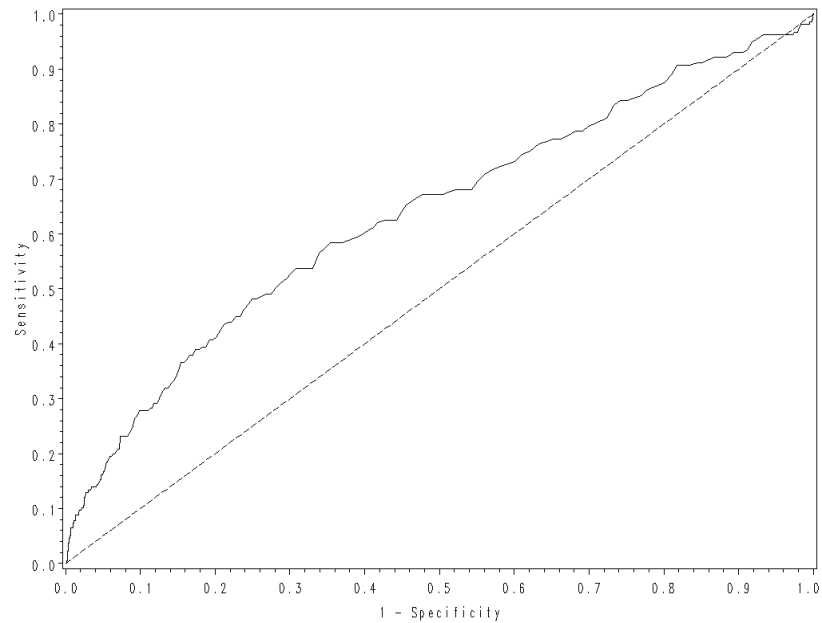
Figure 29:   ROC Curve for Prediction of:
IUGR
No Notch
MEAN PI
AUC 0.637, SE 0.021
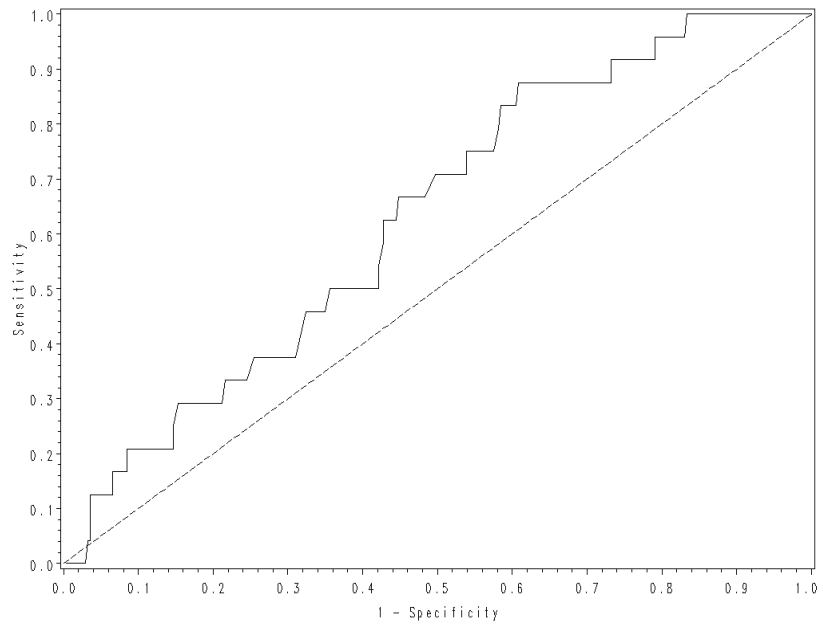
Figure 30:   ROC Curve for Prediction of:
IUGR
Unilateral Notch
MEAN PI
AUC 0.631, SE 0.053
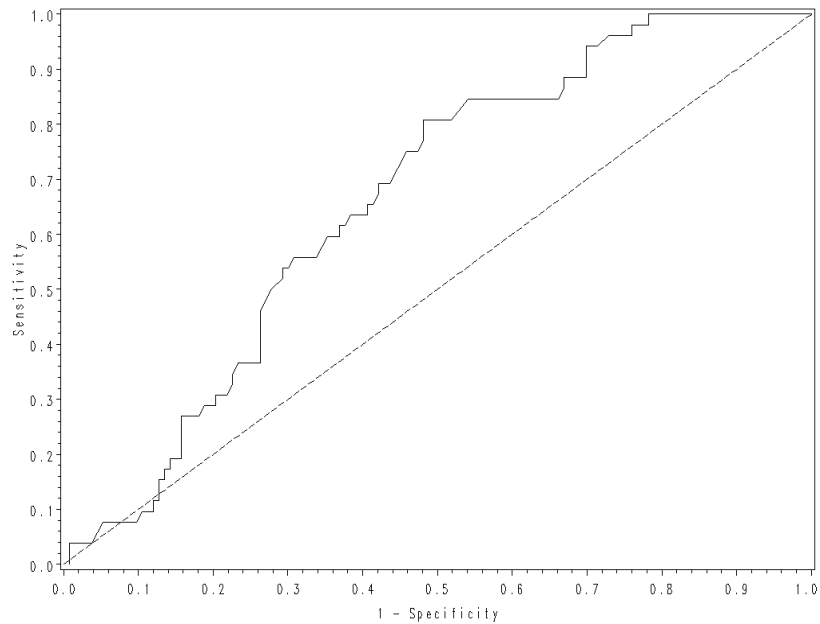
Figure 31:   ROC Curve for Prediction of:
IUGR
Bilateral Notch
MEAN PI
AUC 0.663, SE 0.041
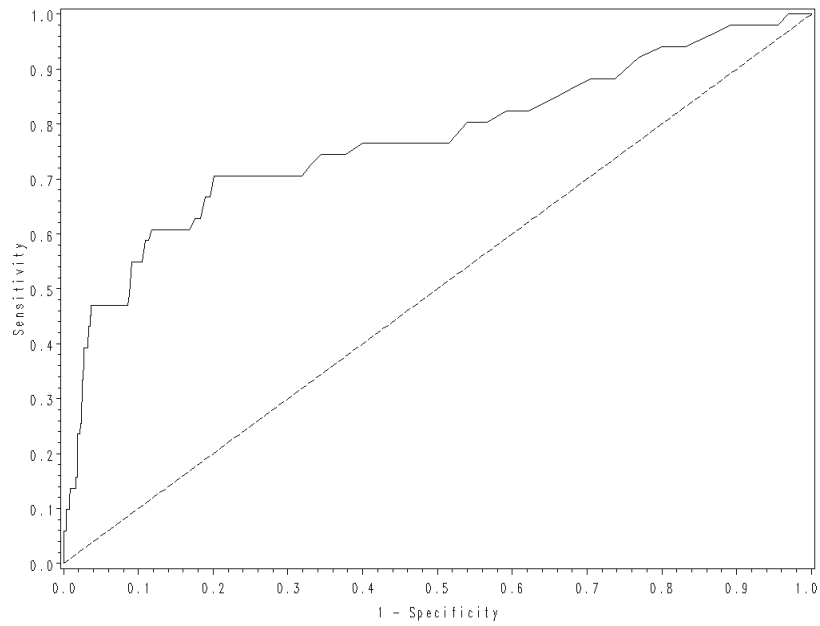
Figure 32: ROC Curve for Prediction of:
Pre-Eclampsia
All Patients
MEAN PI
AUC 0.771, SE 0.041
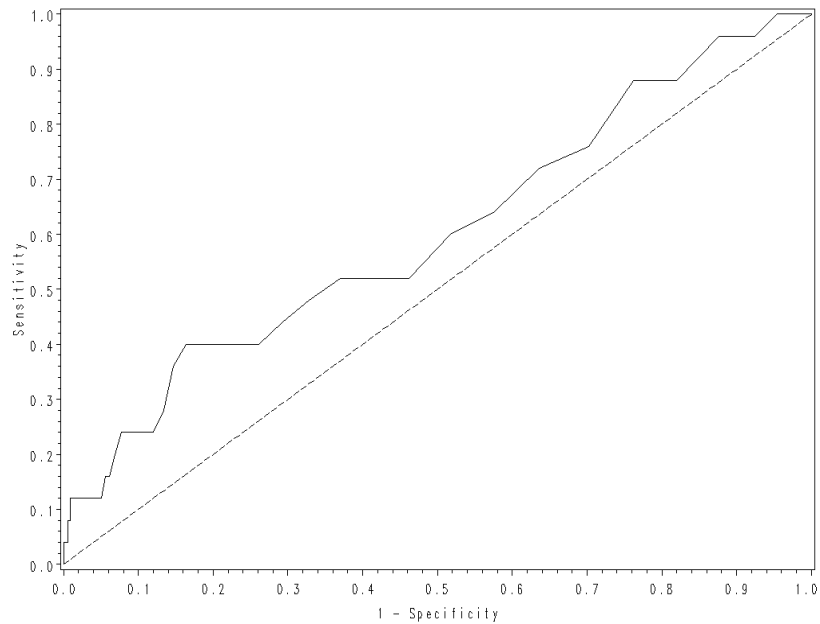
Figure 33: ROC Curve for Prediction of:
Pre-Eclampsia
No Notch
MEAN PI
AUC 0.600, SE 0.063
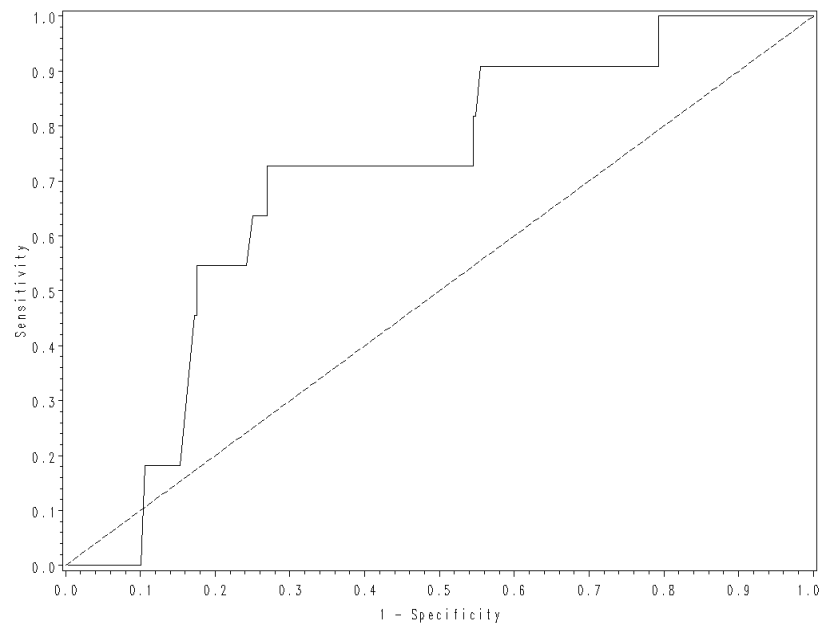
Figure 34: ROC Curve for Prediction of:
Pre-Eclampsia
UnilateralNotch
MEAN PI
AUC 0.701, SE 0.071
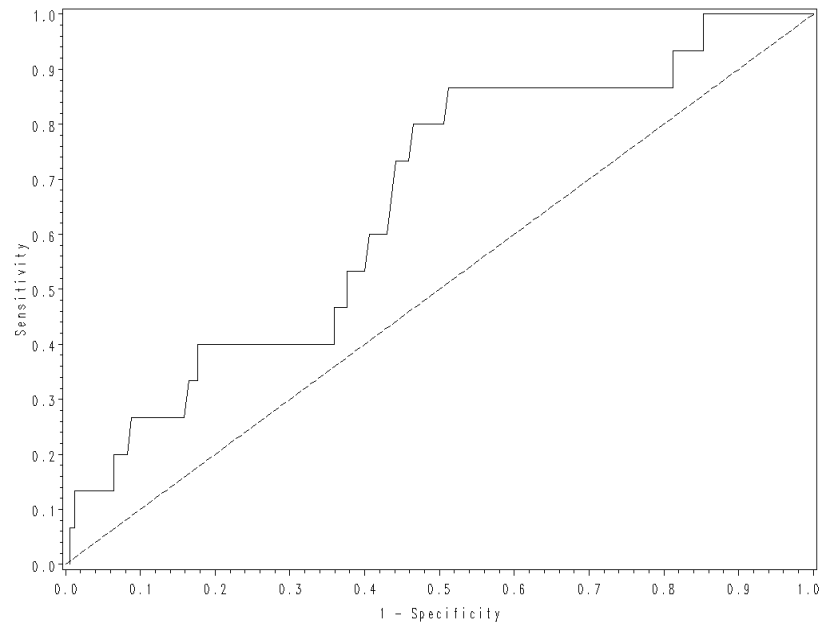
Figure 35: ROC Curve for Prediction of:
Pre-Eclampsia
Bilateral Notch
MEAN PI
AUC 0.656, SE 0.072
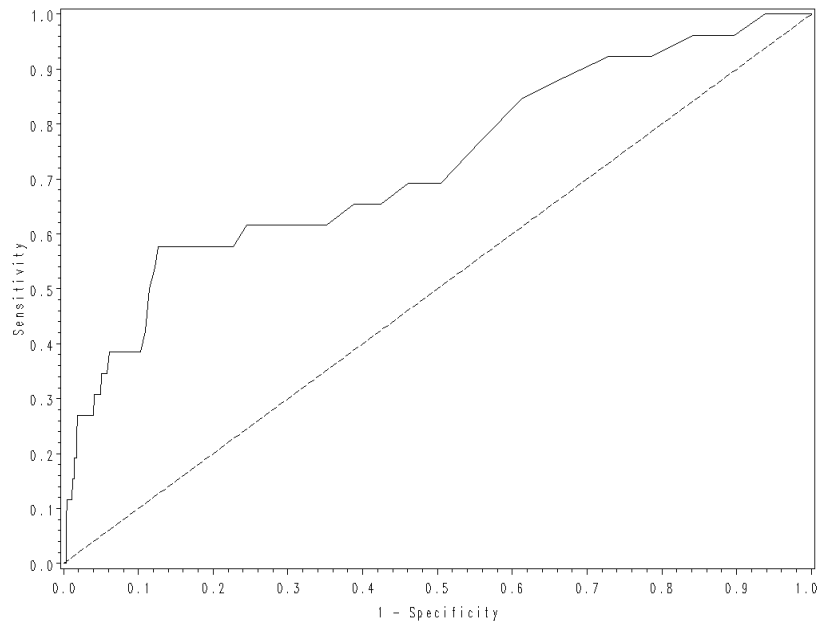
Figure 36:   ROC Curve for Prediction of:
Placental abruption
All Patients
MEAN PI
AUC 0.726, SE 0.057
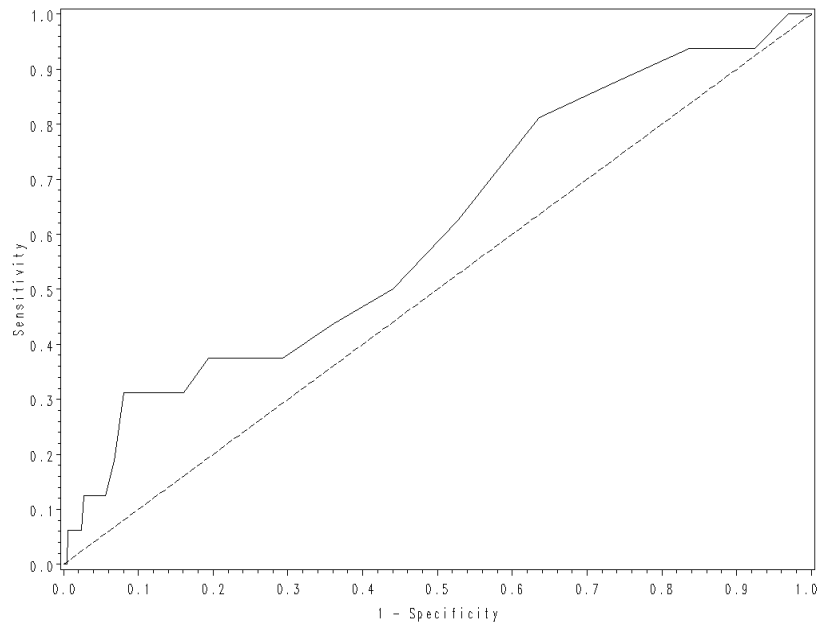
Figure 37:   ROC Curve for Prediction of:
Placental abruption
No Notch
MEAN PI
AUC 0.610, SE 0.073
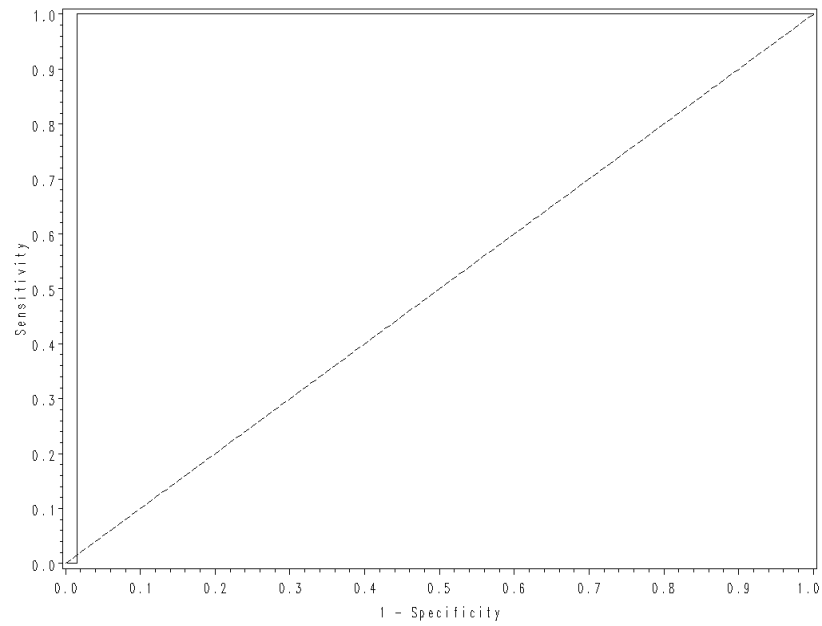
Figure 38:   ROC Curve for Prediction of:
Placental abruption
Unilateral Notch
MEAN PI
AUC 0.985
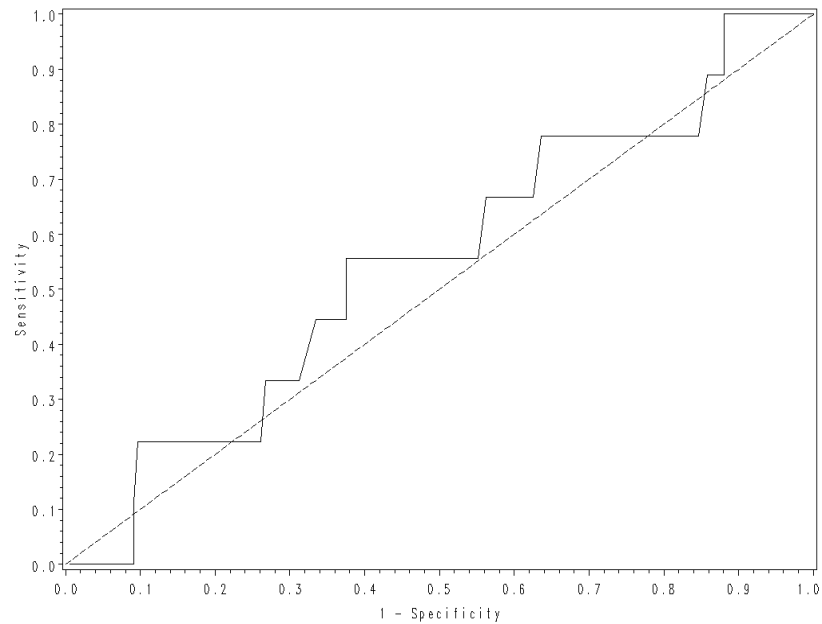
Figure 39:   ROC Curve for Prediction of:
Placental abruption
Bilateral Notch
MEAN PI
AUC 0.549, SE 0.102
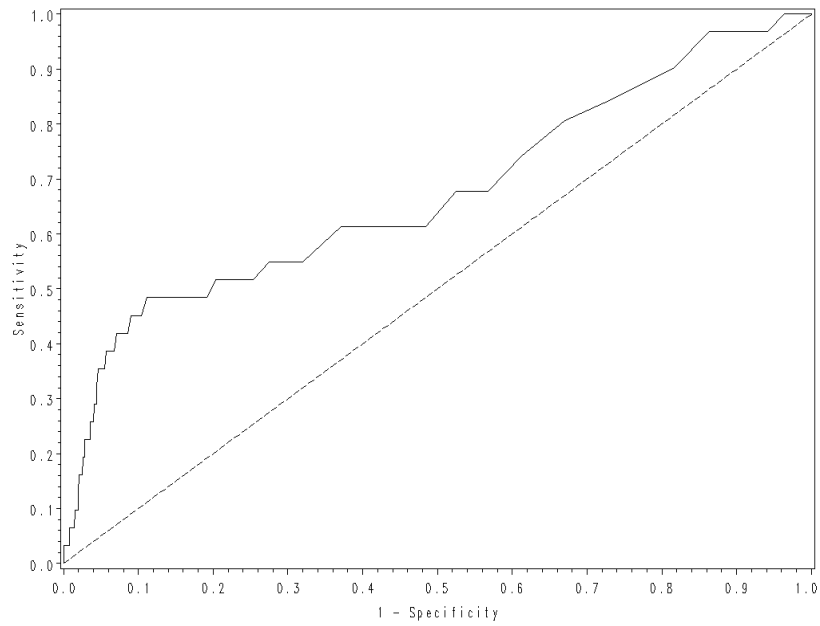
Figure 40: ROC Curve for Prediction of:
Preterm Delivery <29 Weeks
All Patients
MEAN PI
AUC 0.673, SE 0.058
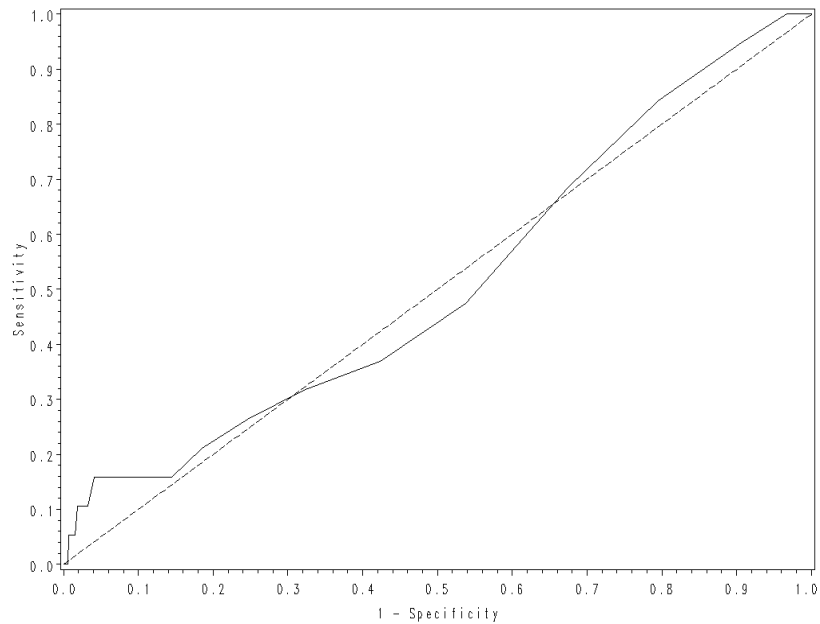
Figure 41: ROC Curve for Prediction of:
Preterm Delivery <29 Weeks
No Notch
MEAN PI
AUC 0.519, SE 0.068
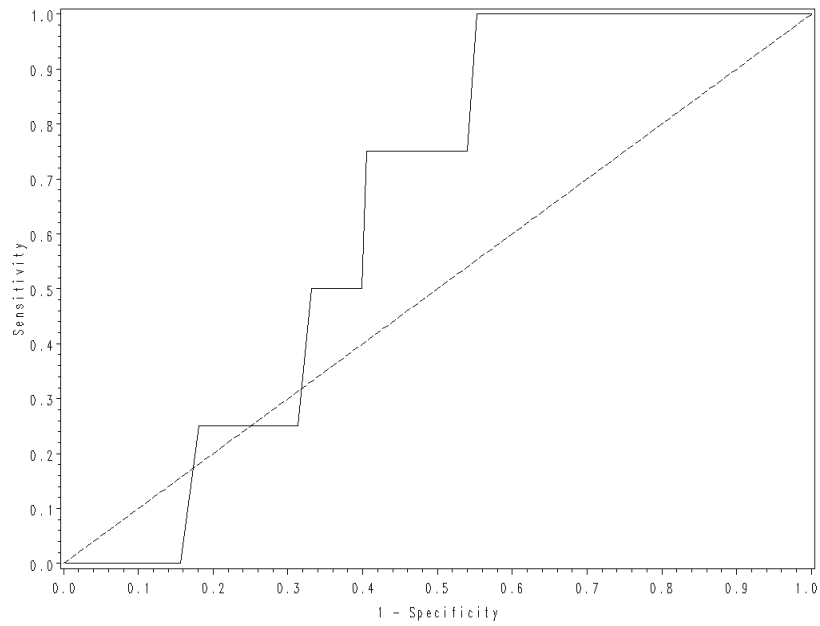
Figure 42:   ROC Curve for Prediction of:
Preterm Delivery <29 Weeks
Unilateral Notch
MEAN PI
AUC 0.638, SE 0.080
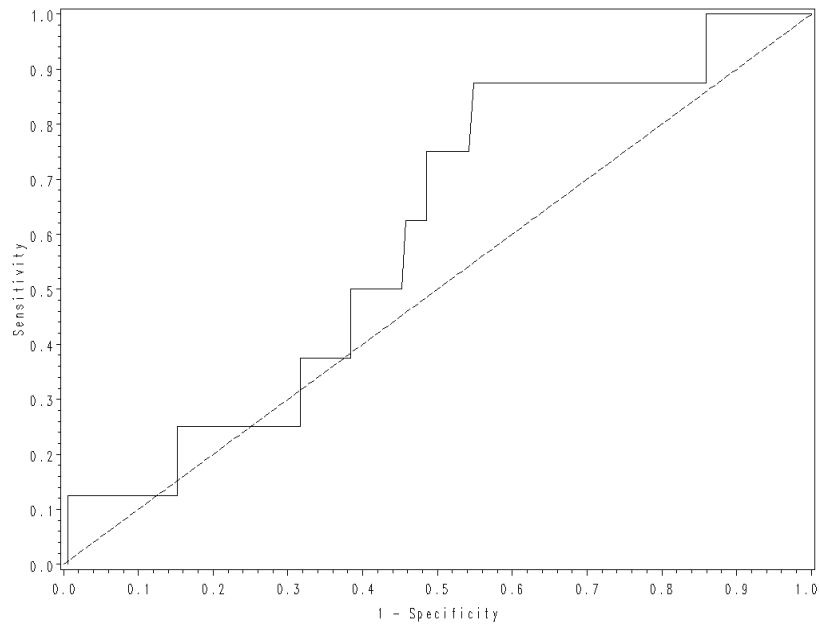
Figure 43:   ROC Curve for Prediction of:
Preterm Delivery <29 Weeks
Bilateral Notch
MEAN PI
AUC 0.600, SE 0.094
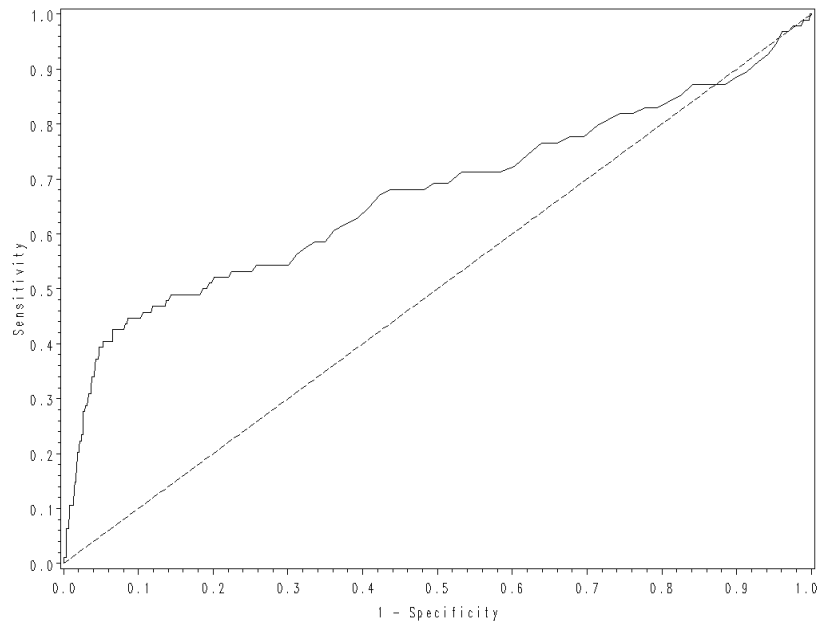
Figure 44: ROC Curve for Prediction of:
**Preterm Delivery <33 Weeks
All Patients**
MEAN PI
AUC 0.670, SE 0.036
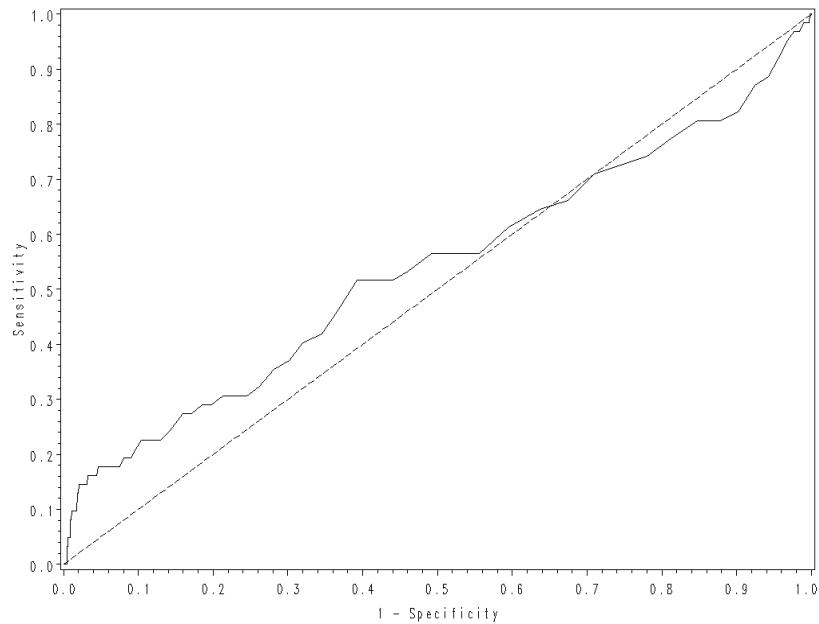
Figure 45: ROC Curve for Prediction of:
Preterm Delivery <33 Weeks
No Notch
MEAN PI
AUC 0.538, SE 0.043
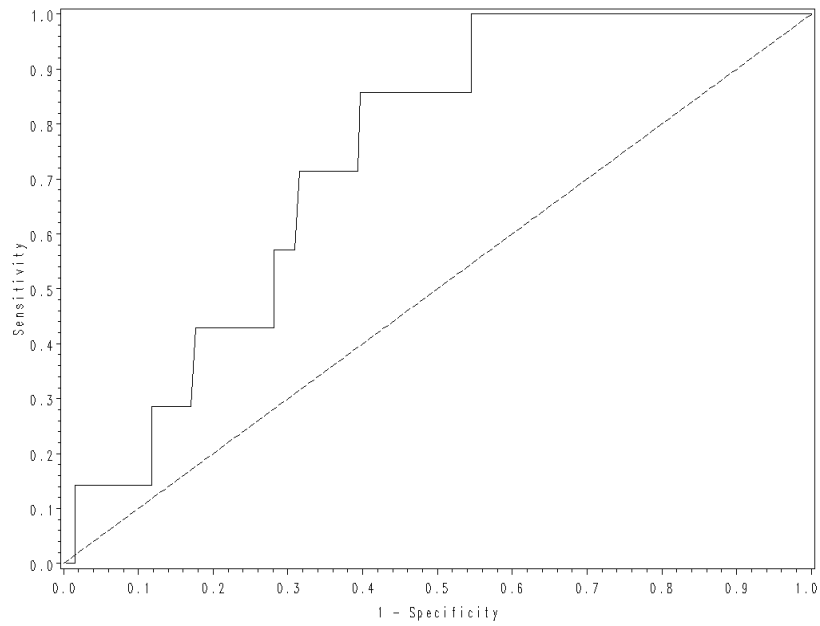
Figure 46: ROC Curve for Prediction of:
Preterm Delivery <33 Weeks
Unilateral Notch
MEAN PI
AUC 0.737, SE 0.070
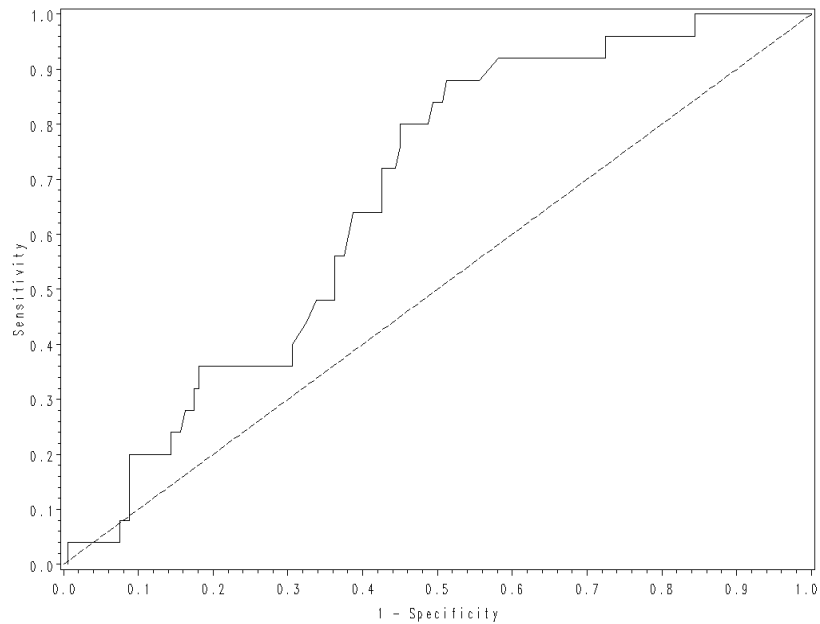
Figure 47: ROC Curve for Prediction of:
Preterm Delivery <33 Weeks
Bilateral Notch
MEAN PI
AUC 0.667, SE 0.049
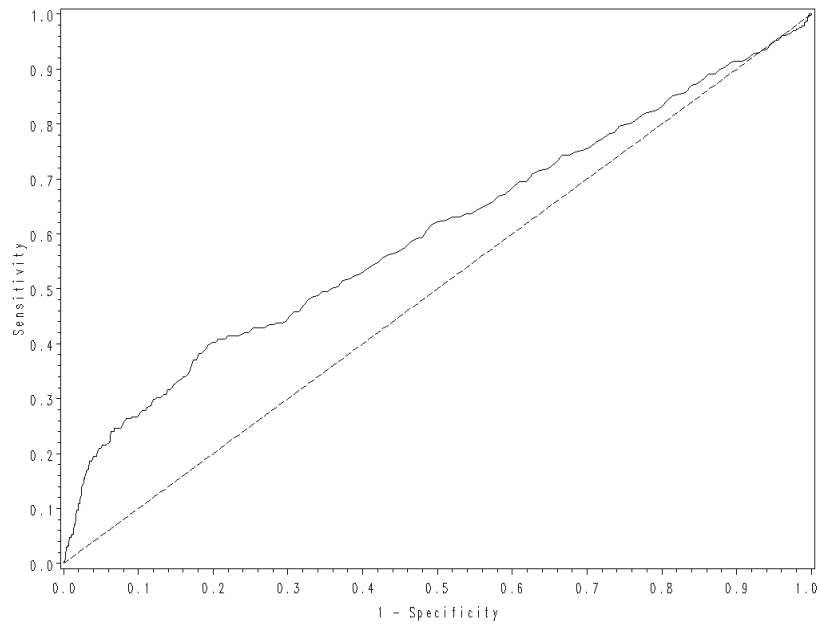
Figure 48:   ROC Curve for Prediction of:
Preterm Delivery <37 Weeks
All Patients
MEAN PI
AUC 0.600, SE 0.018
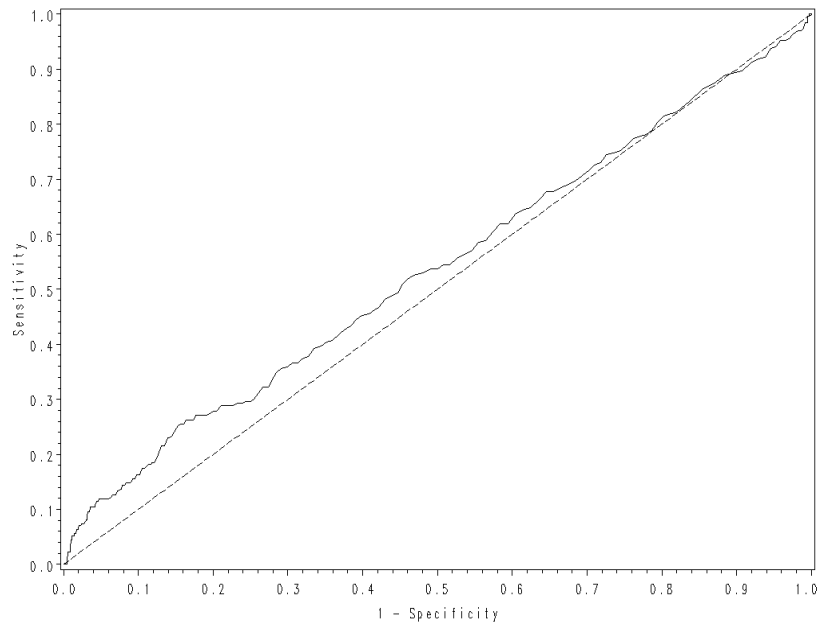
Figure 49:   ROC Curve for Prediction of:
Preterm Delivery <37 Weeks
No Notch
MEAN PI
AUC 0.535, SE 0.019
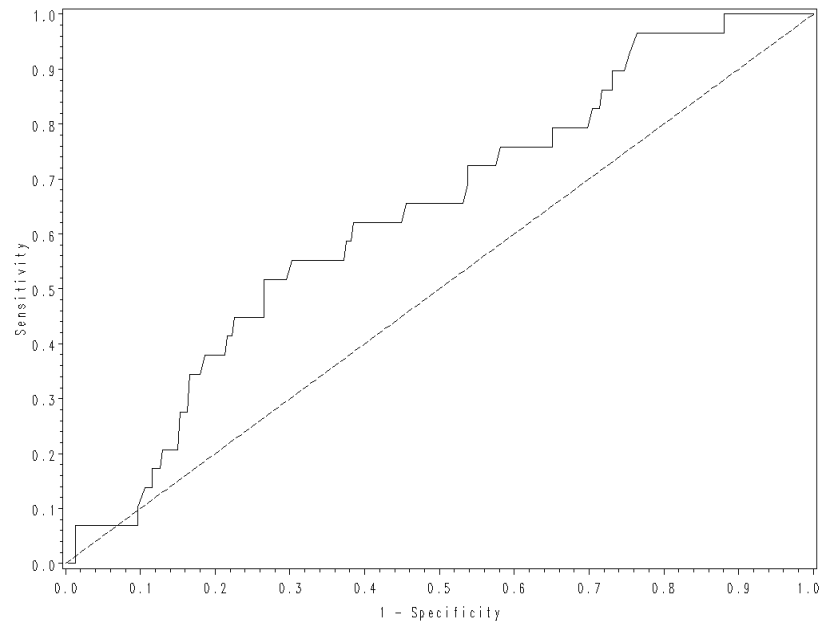
Figure 50: ROC Curve for Prediction of:
Preterm Delivery <37 Weeks
Unilateral Notch
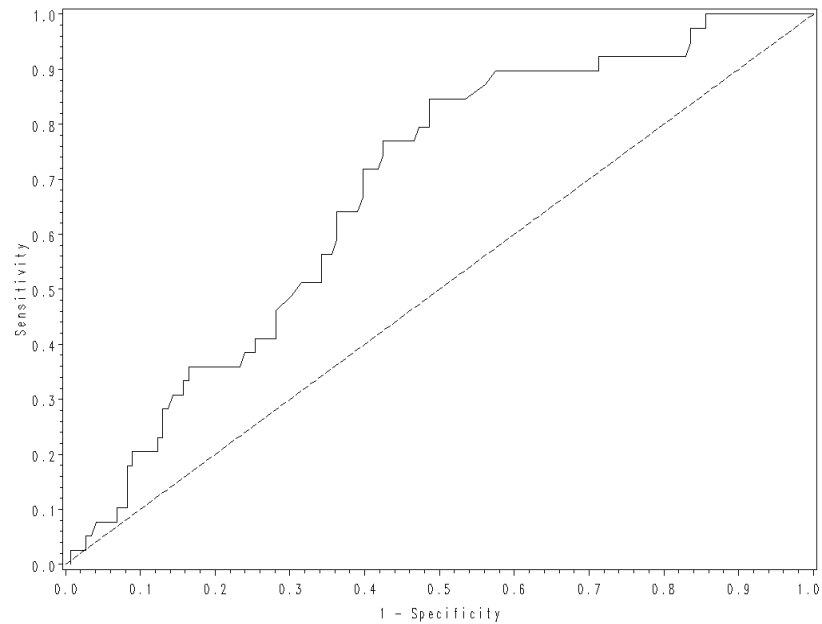MEAN PI
AUC 0.634, SE 0.051

Figure 51: ROC Curve for Prediction of:
Preterm Delivery <37 Weeks
Bilateral Notch
MEAN PI
AUC 0.678, SE 0.044

The comparison of the diagnostic capacity of the four methods as seen in Tables 4 – 12 shows, that in the prediction of pre-eclampsia, "Combination 1" performed equally well compared to the use of notching alone. In the prediction of intrauterine growth retardation, "Combination 1" performed equally well when compared to the use of elevated impedance alone. In the prediction of IUD / NND, preterm delivery prior to 29 or 33 weeks and the prediction of "any complication", the performance of "Combination 1" appeared to be better than when using elevated impedance alone, notching alone or using the alternative combination ("Combination 2").

Figures 8-51 show the ROC curves for all forms of pathological pregnancy outcome comparing all patients, patients with no, unilateral or bilateral notching. In Figures 8-11 and 24-51, the comparison is performed using Mean PI. In addition, a comparison of the diagnostic capacity of MEAN-, MAX- and MIN PI is given in Figures 11 – 13, 14 – 16, 17 – 19 and 20 – 22 and Tables 4 – 10. The difference between the diagnostic capacities of these three definitions is small with a slight advantage for the use of MEAN PI.

Figures 7, 12, 24, 28, 32, 36, 40, 44 and 48 demonstrate the diagnostic capacity of elevated impedance (MEAN PI) for all patients regarding different definitions of pathological pregnancy outcome. Accepting a specificity of 90%, the sensitivity for the evaluated problems lies in the range of 30 – 40% with a worse performance for adverse pregnancy outcomes including preterm delivery <37 weeks.