

# Association of first-trimester maternal serum PAPP-A, free-beta subunit human chorionic gonadotropin concentration, nuchal translucency and the combined risk measurement for Down's Syndrome with adverse pregnancy outcomes.

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## Aim

To determine whether maternal serum levels of pregnancy-associated plasma protein A (PAPP-A), free-beta subunit human chorionic gonadotropin (fβHCG), nuchal translucency (NT) or the combined risk (CR) as calculated for Down's Syndrome screening were associated with adverse pregnancy outcomes.



## Method

Data were obtained from the Statewide evaluation of first trimester screening for Down syndrome and other fetal anomalies in Western Australia. PAPP-A, fβHCG and NT were measured between 10 weeks 3 days and 13 weeks 6 days of gestation for 22,695 pregnancies between August 2001 and October 2003. Screening data were linked with pregnancy outcome information from the Hospital Morbidity Database and the Birth Defects Registry. A pregnancy at high risk of adverse outcomes was defined according to different percentile cut-offs for each indicator: lowest 1%, 4% and 10% for the combined risk, PAPP-A and free βhCG and the highest 1% and 5% also for free βhCG and nuchal translucency. Cut-off values for each analyte are given in the table. Current screening practice for Down's syndrome in WA is to consider the lowest 4% as high risk (risk of 1:300 or less). Logistic regression analysis was used to calculate the odds of the specified adverse event occurring in the high risk group compared to a control group where none of the specified outcomes were identified.

## Selected Results

Effect	Cut-off values	Down's Syndrome			Birth Defects			Pregnancy loss after 24 weeks			False Positive Rate
		OR#	DR	PPV	OR#	DR	PPV	OR#	DR	PPV	
Comb. risk 1%	1:56	<b>358.8</b>	65.5	30.6	<b>27.3</b>	12.6	48.8	<b>7.0</b>	3.6	2.3	0.5
Comb. risk 4%	1:302	<b>145.6</b>	82.8	8.4	<b>8.5</b>	21.9	21.4	2.3	7.1	0.8	3.2
Comb. risk 10%	1:787	<b>92.5</b>	89.7	3.6	<b>4.6</b>	30.3	12.3	<b>2.6</b>	19.6	0.8	8.6
PAPP-A 1%	0.25 MoM	<b>24.7</b>	13.8	7.1	<b>12.9</b>	7.7	32.3	<b>5.8</b>	3.6	1.9	0.6
PAPP-A 4%	0.37 MoM	<b>7.8</b>	20.7	2.2	<b>4.3</b>	12.5	13.3	<b>5.0</b>	14.3	1.5	3.2
PAPP-A 10%	0.49 MoM	<b>9.3</b>	46.6	1.9	<b>3.0</b>	22.0	9.3	<b>2.9</b>	21.4	0.9	8.6
FβHCG 1%	0.24 MoM	0	-	-	<b>7.1</b>	5.2	21.3	2.3	1.8	0.8	0.8
FβHCG 4%	0.35 MoM	0	-	-	<b>2.4</b>	8.3	8.4	0.5	-	0.3	3.6
FβHCG 10%	0.45 MoM	0	-	-	<b>1.4</b>	12.8	5.1	1.2	10.7	0.4	9.5
Nuchal trans. 95%	1.5 MoM	<b>38.4</b>	65.5	4.7	<b>5.1</b>	65.5	14.6	1.6	7.1	0.5	4.7
Nuchal trans. 99% <sup>a</sup>	2.0 MoM	<b>94.4</b>	37.9	17.3	<b>19.9</b>	37.9	41.3	2.8	1.8	0.9	0.6

OR = odds ratio, DR = detection rate, FPR = false positive rate, PPV = Positive predictive value, MoM = Multiples of Median.

†Complete results table available on separate handout.

#Significant results shown in bold (p < 0.01), Confidence intervals available on separate handout.

## Discussion

The study shows that while there is a relationship between many of the first trimester screening markers and adverse pregnancy outcomes, the tests are not suitable for screening purposes as low detection rates are coupled with high false positive rates. This is in contrast to the combined risk test for Down's Syndrome at the 4% cut-off which gives a detection rate of 83% and false positive rate of 3.2%. The results of these tests could indicate where close monitoring might benefit the patient.