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Effect of deviation of nuchal translucency measurements on the performance of screening for trisomy 21

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KEYWORDS: first trimester; nuchal translucency; quality assurance; screening; trisomy 21

ABSTRACT

Objectives *To examine the effect of deviations in median nuchal translucency thickness (NT) and the spread in measurements on the performance of screening for trisomy 21 by maternal age and fetal NT, and by maternal age, fetal NT and maternal serum biochemistry.*

Methods *We simulated the NT and multiples of the median values for pregnancy-associated plasma protein-A (PAPP-A) and free β-human chorionic gonadotropin (β-hCG) for 500 000 euploid and 500 000 trisomy 21 pregnancies at 12 weeks of gestation. Detection rates for trisomy 21 and false-positive rates were calculated without adjustments in NT and by adding or subtracting values ranging from 0.1 to 1.0 mm to each observed measurement. In addition, the effects of variation in the scatter of NT measurements were examined by applying a multiplicative factor ranging from 0.5 to 2 to the SD.*

Results *The detection rate of trisomy 21 for a fixed false-positive rate of 3% in screening by maternal age and fetal NT was 72%, and in screening by maternal age, fetal NT and serum free β-hCG and PAPP-A it was 86%. A consistent underestimate or overestimate in the measured NT reduced the detection rate of trisomy 21 for a fixed-false positive rate. At a fixed screen-positive cut-off an underestimate in fetal NT reduced the detection rate whereas an overestimate in NT increased the false-positive rate. A widening in the scatter of measurements had only a small impact on the detection rate but it caused a major increase in the false-positive rate.*

Conclusions *High performance of screening necessitates appropriate measurement of fetal NT. This paper demonstrates the effect of deviations in the median and SD of NT from the expected on the performance of screening and can form the basis of audit of results of individual sonographers. Copyright © 2009 ISUOG. Published by John Wiley & Sons, Ltd.*

INTRODUCTION

Fetal nuchal translucency thickness (NT) is the single most effective marker for trisomy 21 and all other major chromosomal defects[1,2].

We have recently presented data on the measurement of NT by sonographers who had obtained The Fetal Medicine Foundation (FMF) Certificate of Competence in carrying out such an ultrasound scan[3]. The dataset included 37 079 euploid pregnancies, 264 with trisomy 21, 81 with trisomy 18, 38 with trisomy 13 and 27 with Turner syndrome[3]. We proposed a model in which fetal NT follows two distributions, one in which NT increases with crown–rump length (CRL) and another that is CRL independent. The distribution in which NT increases with CRL is the same for chromosomally abnormal and euploid pregnancies, but the proportion that follows this distribution is large in the euploid group (about 95%) and small in the abnormal group, being about 5%, 30%, 15% and 20% for trisomies 21, 18, 13 and Turner syndrome, respectively. In contrast, the proportion of cases in which NT does not change with gestation is small for euploid pregnancies and large for the abnormal group. Furthermore, the median NT of the CRL-independent portion is different, being 2.0 mm for the euploid group, and 3.4 mm, 5.5 mm, 4.0 mm and 9.2 mm for trisomies 21, 18, 13 and Turner syndrome, respectively.

This mixture model of NT distributions, which is compatible with our understanding of the pathophysiology of increased NT in both euploid and chromosomally abnormal fetuses, provided accurate patient-specific risks and a high performance in screening for aneuploidies. The detection rate for trisomy 21, at a false-positive rate of 3%, was about 70% in screening by a combination of maternal age and fetal NT, and this increased to about 85% with the inclusion of maternal serum free pregnancy-associated plasma protein A (PAPP-A) and free β-human chorionic gonadotropin (β-hCG)[1,4].

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Effective screening necessitates accurate measurement of NT by appropriately trained sonographers, because an underestimate in the measurement would reduce risks and the overall screen-positive rate, whereas an overestimate would increase the risk and the screen-positive rate. In this study we examine the effect of deviations in the median NT and the spread in measurements on the performance of screening by maternal age and fetal NT, and by maternal age, fetal NT and maternal serum biochemistry.

METHODS

The effects of deviations in median fetal NT and SD in the distribution of measurements were investigated by simulating the NT and multiples of the median (MoM) values for PAPP-A and free β-hCG for 500 000 euploid and 500 000 trisomy 21 pregnancies at 12 weeks of gestation. NT values were simulated with the addition of the effect of bias and changes in the SD. Likelihoods were calculated using the mixture model for NT[3] and the standard Gaussian model for log MoM PAPP-A and free β-hCG values[5]. The maternal age distribution of pregnancies in England and Wales in 2000–2002 was used and maternal age-related risks for trisomy 21 at term were adjusted according to the gestational age at the time of screening[6–8]. Likelihoods were obtained from the mixture model using the original parameters. Detection and false-positive rates were calculated without adjustments in NT, and for overestimating and underestimating the measurement of NT by adding or subtracting values ranging from 0.1 to 1.0 mm to each observed measurement. In addition, the effects of variation in the scatter of NT measurements were examined by applying a multiplicative factor f ranging from 0.5 to 2 to the SD of the CRL-dependent process of the mixture model[3]. The SD (σ) of the CRL-dependent process was replaced by $f\sigma$. Thus the component $(f^2 - 1)\sigma^2$ was added to the variance of the CRL-dependent process. With $f < 1$, this component is negative, reflecting improvements in measurement precision. With $f > 1$, it is positive, reflecting deterioration in precision. The same component of variance was added to the CRL-independent processes. It should be emphasized that these biases and changes in measurement precision were applied to the simulated NT data. Risks were produced under the original model.

RESULTS

The detection rate of trisomy 21 for a fixed false-positive rate of 3% in screening by maternal age and fetal NT was 72%, and in screening by maternal age, fetal NT and serum free β-hCG and PAPP-A it was 86%. If a fixed risk cut-off of one in 100 was used, the false-positive and detection rates were 3.3% and 73% in screening by maternal age and fetal NT, and 2.7% and 84% in screening by maternal age, fetal NT and maternal serum biochemistry.

The effect of a consistent underestimate or overestimate in the measurement of fetal NT by 0.1 to 1.0 mm on the performance of screening is shown in Figure 1. If NT is underestimated by 0.6 mm, the detection rate for a 3% false-positive rate is reduced from 71% to 68% in screening by maternal age and fetal NT, and from 86% to 83% in screening by maternal age, fetal NT and maternal serum biochemistry. The effect of an increased or decreased scatter of the NT measurements on the performance of screening is shown in Figure 2. If the scatter of the NT measurements is increased by 50% the detection rate for a 3% false-positive rate is reduced from 71% to 62% in screening by maternal age and fetal NT, and from 86% to 81% in screening by maternal age, fetal NT and maternal serum biochemistry.

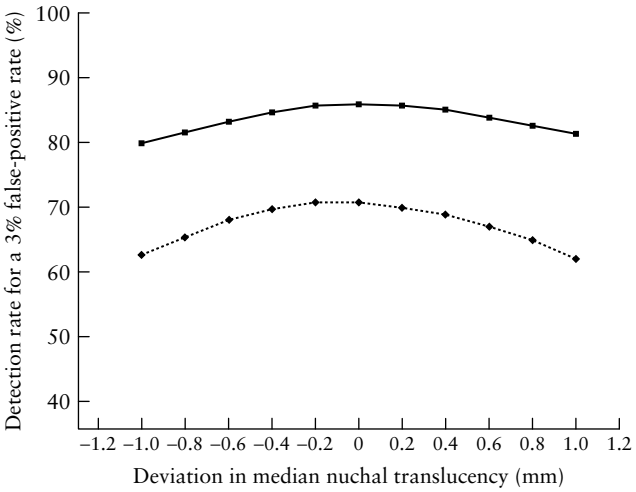

Figure 1 Estimated detection rates for a 3% false-positive rate in screening for trisomy 21 by maternal age and fetal nuchal translucency (NT) (·····), and by maternal age, fetal NT and maternal serum biochemistry (———), in case of deviations in the measurements of NT from the expected distribution obtained by experts[3].

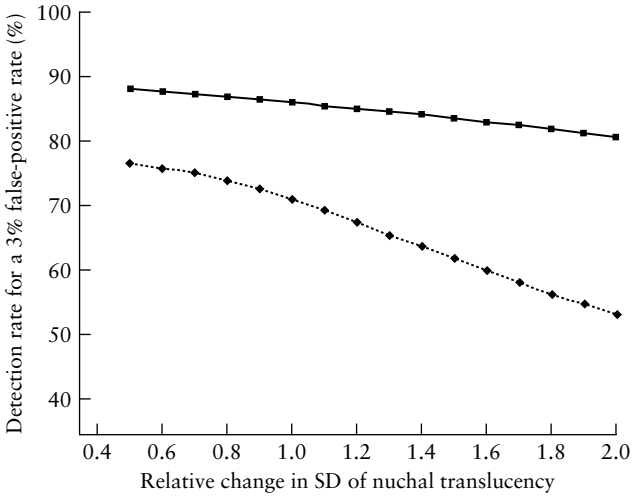

Figure 2 Estimated detection rates for a 3% false-positive rate in screening for trisomy 21 by maternal age and fetal nuchal translucency (NT) (·····), and by maternal age, fetal NT and maternal serum biochemistry (———), in case of deviations in the SD of NT expressed as factors multiplied by the SD of the NT measurement of experts[3]. A relative change in SD of, for example, 1.2, means a 20% increase in the SD.

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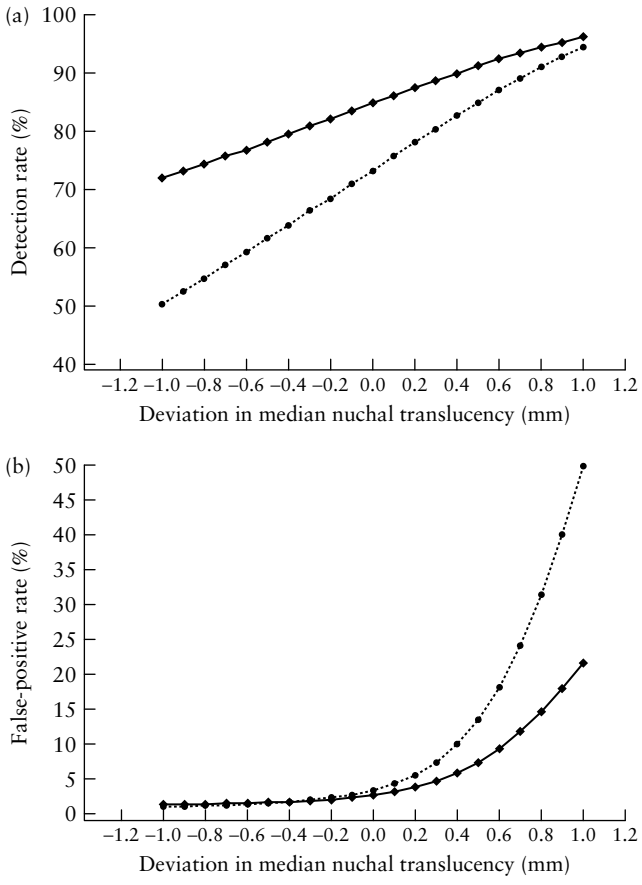

Figure 3 Estimated detection rate (a) and false-positive rate (b) for a risk cut-off of 1 in 100 in screening for trisomy 21 by maternal age and fetal nuchal translucency (NT) (·····), and by maternal age, fetal NT and maternal serum biochemistry (———), in case of deviations in the measurements of NT thickness from the expected distribution obtained by experts[3].

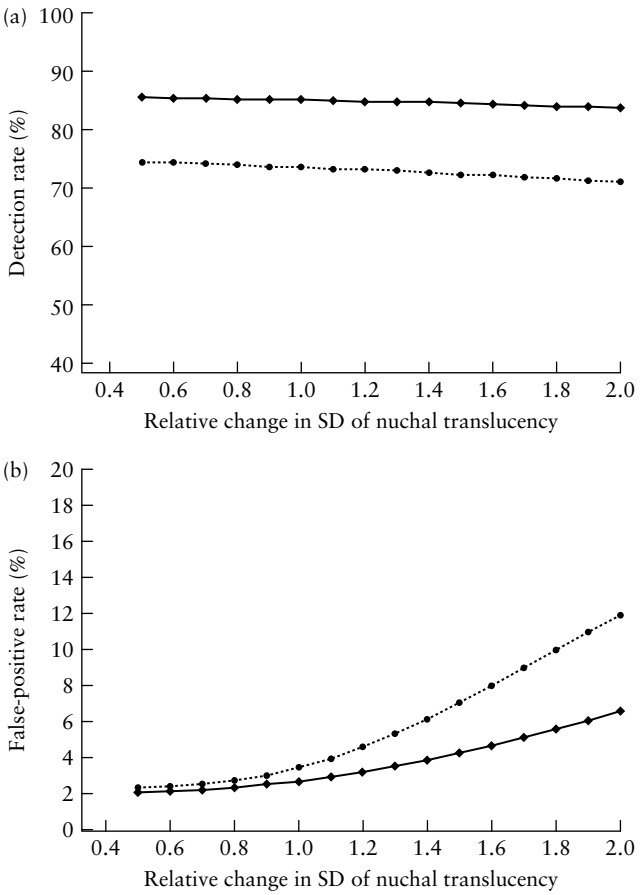

Figure 4 Estimated detection rate (a) and false-positive rate (b) for a risk cut-off of 1 in 100 in screening for trisomy 21 by maternal age and fetal nuchal translucency (NT) (·····), and by maternal age, fetal NT and maternal serum biochemistry (———), in case of deviations in the SD of NT expressed as factors multiplied by the SD of the NT measurement of experts[3]. A relative change in SD of, for example, 1.2, means a 20% increase in the SD.

In practice, it is unlikely that the cut-off would be adjusted to maintain a false-positive rate of 3% so, from a practical perspective, it is important to examine the effects at a fixed risk cut-off. Figures 3 and 4 show the effects on the detection rate of trisomy 21 and the false-positive rate at a risk cut-off of 1 in 100 of a deviation in the median NT and SD, respectively. An underestimation of NT by 0.6 mm leads to false-positive and detection rates of 1.3% and 58%, respectively, in screening by maternal age and fetal NT, and 1.5% and 76% in screening by maternal age, fetal NT and maternal serum biochemistry (Figure 3). If the scatter of the NT measurements is increased by 50% the false-positive and detection rates are 7.0% and 71%, respectively, in screening by maternal age and fetal NT, and 4.3% and 85% in screening by maternal age, fetal NT and maternal serum biochemistry (Figure 4).

Tables 1–4 show the estimated effects on screening performance of a combination of deviations in median and spread of NT measurements.

DISCUSSION

This study has shown the importance of quality assurance of operators undertaking measurement of fetal NT based on the median and SD of the distribution of their NT measurements. The findings of the study demonstrate the effect of deviations in the measurements of fetal NT on the performance of early screening for trisomy 21 by fetal NT with and without maternal serum free β-hCG and PAPP-A.

A consistent underestimate or overestimate in the measured NT reduces the detection rate of trisomy 21 for a fixed false-positive rate. At a fixed screen-positive cut-off, an underestimate in fetal NT reduces the detection rate whereas an overestimate in NT increases the false-positive rate. A widening in the scatter of measurements has only a small impact on the detection rate but it causes a major increase in the false-positive rate. As expected, when the factor applied to the SD is < 1.0, reflecting improved precision, performance of screening improves. However, this result needs to be interpreted with caution. First, the capacity to reduce variation in measurements is limited by the inherent variation in NT between pregnancies and it is unlikely that reductions as extreme as halving could be achieved in practice. Second, the results assume that reductions in variation reflect true improvements in measurement precision and not, for example, a tendency for operators to mismeasure in a way that reduces

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Table 1 Estimated detection rates (%) for a 3% false-positive rate in screening for trisomy 21 by maternal age and fetal nuchal translucency thickness (NT) in case of deviations in the measurements of NT from the expected distribution obtained by experts[3]

Deviation in median NT (mm)	*Relative changes in the SD of NT*															
	0.5	*0.6*	*0.7*	*0.8*	*0.9*	*1.0*	*1.1*	*1.2*	*1.3*	*1.4*	*1.5*	*1.6*	*1.7*	*1.8*	*1.9*	*2.0*
−1.0	64	64	65	65	65	63	63	62	61	61	59	58	56	54	53	51
−0.9	66	65	66	67	67	65	64	63	62	62	60	58	56	55	53	51
−0.8	67	68	67	67	67	66	65	64	63	62	60	59	57	56	53	51
−0.7	68	69	68	68	68	67	66	66	64	62	61	59	58	56	54	51
−0.6	70	70	69	69	69	68	67	66	65	63	61	59	58	56	54	52
−0.5	71	71	70	70	70	69	67	67	65	64	61	59	58	56	54	52
−0.4	73	73	72	72	71	70	68	67	66	64	62	59	58	56	54	52
−0.3	74	74	73	73	72	71	69	67	66	64	62	59	58	56	54	52
−0.2	75	75	74	73	72	71	69	68	66	64	62	60	58	56	54	53
−0.1	76	76	75	74	73	72	69	68	66	64	62	60	58	56	54	53
0	76	76	76	74	73	72	70	68	65	64	62	60	58	56	55	54
0.1	77	76	76	74	73	71	69	67	65	63	61	60	57	56	54	54
0.2	77	75	75	74	72	70	68	66	65	62	61	59	56	55	54	53
0.3	76	75	75	73	72	69	68	66	64	62	60	58	56	55	54	52
0.4	75	74	73	71	70	69	67	66	63	62	60	58	56	55	54	52
0.5	74	73	72	71	70	68	66	65	63	62	59	58	56	55	54	52
0.6	73	72	71	69	69	67	65	63	62	61	59	58	56	54	54	52
0.7	72	71	70	69	68	66	64	63	61	60	58	58	56	54	53	52
0.8	71	69	68	67	66	65	63	61	60	59	57	57	56	54	53	52
0.9	68	68	67	65	64	63	62	61	59	58	57	56	54	53	53	52
1.0	68	66	65	64	63	62	61	60	59	57	57	56	54	53	52	51

On the vertical axis are changes in the median measurement of NT away from the expected value and on the horizontal axis are changes in the SD of NT expressed as factors multiplied by the SD of the NT measurement of experts.

Table 2 Estimated detection rates (%) for a 3% false-positive rate in screening for trisomy 21 by maternal age, fetal nuchal translucency thickness (NT) and maternal serum biochemistry in case of deviations in the measurements of NT from the expected distribution obtained by experts[3]

Deviation in median NT (mm)	*Relative changes in the SD of NT*															
	0.5	*0.6*	*0.7*	*0.8*	*0.9*	*1.0*	*1.1*	*1.2*	*1.3*	*1.4*	*1.5*	*1.6*	*1.7*	*1.8*	*1.9*	*2.0*
−1.0	80	80	79	78	80	80	79	79	78	78	79	78	78	77	75	75
−0.9	80	81	80	79	80	81	80	80	80	79	79	78	78	77	75	75
−0.8	80	81	80	81	81	81	81	81	81	81	80	79	78	77	76	76
−0.7	82	82	82	82	82	82	82	82	81	81	80	79	78	78	77	76
−0.6	83	84	84	84	83	83	83	82	82	81	80	79	78	78	77	76
−0.5	85	85	84	84	84	83	83	83	82	82	81	80	79	78	77	76
−0.4	85	85	85	85	85	84	84	84	83	82	81	80	79	78	77	76
−0.3	86	86	85	85	85	86	85	84	83	82	81	80	79	78	77	76
−0.2	87	87	87	86	86	86	85	84	83	82	81	80	79	78	77	76
−0.1	89	87	87	86	86	86	85	84	84	83	81	80	79	79	77	76
0	89	88	88	87	86	86	85	85	83	83	81	79	79	79	77	76
0.1	88	89	88	88	87	86	85	84	83	83	81	79	79	78	76	76
0.2	88	89	88	88	86	86	85	83	82	82	81	79	79	78	76	75
0.3	88	88	87	87	85	85	84	83	82	82	81	79	78	77	76	75
0.4	88	88	87	86	85	84	83	83	82	81	80	79	78	77	76	75
0.5	87	87	87	86	85	84	83	83	82	80	80	79	78	77	76	75
0.6	87	87	87	86	85	84	83	82	82	80	79	79	78	76	76	75
0.7	87	85	86	85	84	83	82	82	81	80	79	78	77	76	76	75
0.8	86	85	84	84	84	83	82	82	80	80	79	78	77	76	76	75
0.9	85	85	84	84	83	82	82	81	80	80	79	78	76	76	76	75
1.0	84	83	83	82	81	81	81	80	80	80	77	78	75	76	75	74

On the vertical axis are changes in the median measurement of NT away from the expected value and on the horizontal axis are changes in the SD of NT expressed as factors multiplied by the SD of the NT measurement of experts.

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Table 3 Estimated false-positive rate (FPR) and detection rate (DR) for a risk cut-off of 1 in 100 in screening for trisomy 21 by maternal age and fetal nuchal translucency thickness (NT) in case of deviations in the measurements of NT from the expected distribution obtained by experts[3]

	Relative changes in the SD of NT															
Deviation in median NT (mm)	*0.5*	*0.6*	*0.7*	*0.8*	*0.9*	*1.0*	*1.1*	*1.2*	*1.3*	*1.4*	*1.5*	*1.6*	*1.7*	*1.8*	*1.9*	*2.0*
	FPR/DR	*FPR/DR*	*FPR/DR*	*FPR/DR*	*FPR/DR*	*FPR/DR*	*FPR/DR*	*FPR/DR*	*FPR/DR*	*FPR/DR*	*FPR/DR*	*FPR/DR*	*FPR/DR*	*FPR/DR*	*FPR/DR*	*FPR/DR*
−1.0	0.8/50	0.9/50	1.0/50	0.8/50	0.8/50	0.8/50	1.0/50	1.0/50	1.1/49	1.2/50	1.2/50	1.6/50	1.6/50	2.0/50	2.3/49	2.8/51
−0.9	1.0/53	0.9/51	1.0/52	1.0/52	1.0/53	0.9/52	1.2/53	1.0/52	1.2/52	1.4/52	1.4/51	1.7/52	1.9/51	2.4/52	2.4/51	2.9/53
−0.8	1.0/55	1.0/54	0.9/54	1.0/54	1.1/54	1.0/54	1.1/54	1.2/54	1.2/54	1.5/54	1.6/55	2.0/54	2.3/54	2.4/54	3.0/54	3.6/53
−0.7	1.1/56	1.0/57	1.1/57	1.2/57	1.2/56	1.3/57	1.3/56	1.1/57	1.7/56	1.8/56	2.0/57	2.2/56	2.8/56	3.3/55	3.8/56	4.2/57
−0.6	1.1/59	1.3/59	1.3/59	1.4/58	1.2/59	1.3/58	1.5/59	1.5/60	1.6/58	2.1/58	2.1/58	2.5/58	3.1/59	3.5/58	3.9/57	4.9/58
−0.5	1.2/61	1.2/61	1.5/61	1.4/61	1.3/61	1.5/61	1.5/61	1.8/61	1.9/60	2.5/60	2.6/61	2.9/60	3.7/60	4.1/61	4.8/60	5.4/60
−0.4	1.4/64	1.3/65	1.6/65	1.6/63	1.6/63	1.8/64	1.7/63	2.1/63	2.3/63	2.7/63	2.7/63	3.4/63	4.1/63	5.0/62	5.4/62	6.5/62
−0.3	1.4/67	1.6/66	1.6/66	1.6/66	2.0/66	2.0/66	2.0/65	2.5/65	2.7/65	3.2/65	3.7/65	4.5/65	5.0/64	5.7/65	6.4/63	7.7/64
−0.2	1.8/69	2.1/68	1.8/68	2.0/68	2.1/69	2.3/68	2.5/69	2.9/68	3.3/68	3.8/66	4.5/68	5.0/66	6.0/67	7.1/66	7.6/66	8.1/66
−0.1	1.7/71	2.2/71	2.1/71	2.2/71	2.4/71	2.7/71	3.4/70	3.3/70	3.9/70	4.7/69	5.7/70	6.4/70	7.3/68	8.2/69	9.4/68	9.6/69
0	2.2/73	2.3/74	2.5/73	2.9/73	3.0/73	3.3/73	3.7/72	4.1/72	5.1/72	6.2/72	7.0/71	7.5/72	8.8/72	9.4/71	10.7/71	11.7/70
0.1	2.5/76	2.6/76	2.8/75	3.2/76	3.5/75	4.3/75	4.8/74	5.7/74	6.8/74	7.6/74	8.4/74	9.7/74	10.6/73	11.4/74	13.0/73	13.8/73
0.2	3.4/78	3.1/79	3.7/78	4.3/78	4.5/78	5.4/78	6.3/78	7.3/77	8.4/77	9.3/77	10.9/76	11.6/76	12.9/76	14.2/76	15.2/75	15.8/74
0.3	3.8/81	4.3/81	4.7/81	5.5/80	6.4/81	6.9/80	8.3/80	9.1/80	11.1/80	11.9/79	13.1/79	14.4/79	15.9/78	16.1/78	17.8/77	18.6/77
0.4	5.2/83	5.9/83	6.9/83	7.6/83	8.3/82	10.1/82	10.7/82	12.4/82	13.8/82	14.4/82	16.1/80	17.6/81	18.4/80	19.9/79	20.9/80	22.3/80
0.5	7.3/86	8.4/85	9.4/85	10.5/85	11.8/85	13.0/85	14.4/84	16.4/84	17.0/84	18.7/84	20.1/83	21.0/83	22.0/83	23.5/82	24.7/82	25.6/82
0.6	10.7/88	12.1/87	13.2/87	14.8/87	16.4/87	17.3/87	19.7/87	20.7/86	22.6/86	23.5/86	24.2/86	25.6/85	27.2/85	27.6/84	28.5/84	30.0/83
0.7	15.8/90	17.4/89	19.2/89	20.8/89	22.1/89	23.6/89	24.7/88	26.9/89	27.8/89	29.7/88	29.4/88	30.5/87	31.9/87	33.0/86	33.5/86	34.6/86
0.8	23.3/91	25.2/91	26.8/91	28.1/91	29.5/91	31.6/91	32.9/91	33.8/90	33.6/90	35.0/90	35.2/89	36.7/89	37.5/89	38.0/89	39.2/89	39.7/88
0.9	33.9/93	35.4/94	36.6/93	37.9/93	39.3/93	39.8/93	40.5/92	41.4/92	42.3/92	42.1/92	42.6/91	42.5/92	43.2/91	44.2/91	43.7/90	45.2/90
1.0	46.1/95	47.6/95	47.8/95	48.5/95	49.1/94	49.5/95	49.7/94	49.5/94	49.3/93	50.0/93	51.0/93	51.1/93	50.9/93	50.0/92	49.8/92	50.2/91

On the vertical axis are changes in the median measurement of NT away from the expected value and on the horizontal axis are changes in the SD of NT expressed as factors multiplied by the SD of the NT measurement of experts.

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Table 4 Estimated false-positive rate (FPR) and detection rate (DR) for a risk cut-off of 1 in 100 in screening for trisomy 21 by maternal age and fetal nuchal translucency (NT) and maternal serum biochemistry in case of deviations in the measurements of NT thickness from the expected distribution obtained by experts[3]

	Relative changes in the SD of NT															
	0.5	*0.6*	*0.7*	*0.8*	*0.9*	*1.0*	*1.1*	*1.2*	*1.3*	*1.4*	*1.5*	*1.6*	*1.7*	*1.8*	*1.9*	*2.0*
Deviation in median NT (mm)	*FPR/DR*	*FPR/DR*	*FPR/DR*	*FPR/DR*	*FPR/DR*	*FPR/DR*	*FPR/DR*	*FPR/DR*	*FPR/DR*	*FPR/DR*	*FPR/DR*	*FPR/DR*	*FPR/DR*	*FPR/DR*	*FPR/DR*	*FPR/DR*
−1.0	1.3/72	1.2/71	1.3/71	1.2/71	1.1/71	1.3/72	1.3/71	1.3/72	1.3/71	1.5/71	1.4/71	1.5/71	1.8/71	1.8/71	2.1/72	2.0/72
−0.9	1.3/74	1.2/73	1.2/73	1.4/73	1.1/72	1.3/73	1.4/73	1.5/73	1.3/72	1.5/72	1.6/73	1.7/73	1.8/73	2.0/73	2.0/72	2.3/72
−0.8	1.3/74	1.4/74	1.3/74	1.3/73	1.2/74	1.3/74	1.3/74	1.4/74	1.6/74	1.5/73	1.6/73	1.7/74	2.1/74	2.0/74	2.5/74	2.4/74
−0.7	1.4/75	1.5/76	1.3/76	1.3/76	1.5/75	1.4/75	1.5/75	1.5/76	1.5/75	1.6/75	1.8/75	1.7/75	1.9/75	2.5/75	2.4/76	3.1/74
−0.6	1.3/77	1.4/76	1.4/77	1.6/76	1.5/77	1.5/76	1.4/76	1.5/76	1.7/76	1.8/76	2.0/76	2.2/76	2.4/76	2.5/75	2.8/76	3.2/77
−0.5	1.4/78	1.6/78	1.6/78	1.5/78	1.5/78	1.6/78	1.7/78	1.6/78	2.0/77	2.0/78	2.2/78	2.2/78	2.6/77	2.9/78	3.0/77	3.4/78
−0.4	1.5/79	1.5/79	1.5/80	1.6/79	1.6/79	1.7/79	1.8/79	1.7/79	1.8/79	2.3/79	2.5/79	2.6/79	2.8/79	3.4/78	3.6/78	3.9/79
−0.3	1.5/81	1.8/81	1.6/81	1.8/81	1.8/81	1.8/80	2.0/80	2.0/80	2.0/80	2.4/80	2.7/80	3.2/80	3.3/80	3.5/80	4.2/80	4.2/80
−0.2	1.7/82	1.9/82	1.8/82	1.8/83	1.7/82	2.1/82	2.2/82	2.4/82	2.4/82	2.8/81	3.0/81	3.1/81	3.6/81	3.9/81	4.4/81	5.0/80
−0.1	1.8/84	2.0/84	1.7/84	1.9/83	2.0/83	2.3/83	2.2/83	2.7/83	2.9/83	3.2/82	3.7/83	3.8/83	4.2/82	4.7/82	5.4/82	5.5/81
0	1.9/85	2.0/85	2.0/85	2.5/85	2.4/84	2.7/84	2.8/84	2.9/85	3.3/84	3.8/84	4.3/85	4.7/84	5.0/84	5.5/83	5.6/84	6.6/83
0.1	2.3/87	2.3/86	2.1/86	2.5/86	2.7/86	2.8/86	3.2/86	3.7/86	4.0/85	4.3/85	5.1/85	5.6/85	5.8/85	5.9/85	6.7/84	7.1/84
0.2	2.6/87	2.7/88	2.8/87	3.0/88	3.2/87	3.4/88	4.3/87	4.7/87	4.7/87	5.3/87	5.9/86	6.5/86	6.6/86	7.4/86	7.4/86	8.2/85
0.3	3.0/88	3.3/89	3.6/89	4.1/89	4.2/89	4.5/88	5.1/88	5.6/89	6.1/88	6.6/88	7.1/88	7.4/88	8.0/88	8.4/88	9.1/87	9.6/87
0.4	3.9/90	4.2/90	4.5/90	4.9/90	5.5/90	5.7/90	6.3/90	6.6/89	7.4/89	7.4/89	8.5/89	8.8/89	9.4/88	10.2/89	10.8/88	11.6/88
0.5	5.4/91	5.5/91	5.8/91	6.2/91	6.8/92	7.0/91	7.9/91	8.2/91	8.5/91	9.4/90	9.9/90	10.7/90	11.5/90	11.5/90	12.5/90	13.0/90
0.6	6.8/92	7.0/92	7.7/93	8.6/93	8.4/92	9.0/92	9.5/92	10.1/92	11.0/92	11.3/91	11.9/92	12.2/91	12.7/91	13.8/91	14.2/91	14.5/91
0.7	9.7/94	9.8/94	9.9/94	10.5/93	11.3/93	11.7/93	12.0/93	13.1/93	13.8/93	14.1/93	14.6/93	14.7/92	15.2/92	16/92	15.6/91	16.8/92
0.8	12.2/95	12.4/95	13.2/95	13.9/95	14.1/94	14.6/94	14.6/94	15.2/94	15.6/94	15.6/94	16.9/94	17.7/94	17.8/94	18.3/93	18.3/92	19.1/93
0.9	16.0/96	16.1/96	16.4/95	16.7/96	17.2/95	17.9/95	18.0/95	18.6/95	18.6/95	18.9/95	19.7/95	19.7/94	20.1/94	20.6/94	20.9/94	21.7/94
1.0	19.9/97	20.5/96	20.6/96	21/96	20.5/96	21.5/96	21.9/96	22.2/96	22.4/95	22.2/96	22.4/95	22.8/95	23.6/95	23.4/95	24.3/95	24.6/95

On the vertical axis are changes in the median measurement of NT away from the expected value and on the horizontal axis are changes in the SD of NT expressed as factors multiplied by the SD of the NT measurement of experts.

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variability. This would lead to deterioration, rather than improvement, in screening performance.

The results presented were obtained under the assumption that all measurements were taken in the middle of week 12. When we repeated the calculations at 11 weeks and 13 weeks we found that the effects of biases and changes in precision were essentially the same as they are at 12 weeks.

Effective screening for chromosomal abnormalities utilizing the measurement of fetal NT necessitates appropriate training of sonographers, adherence to a standard ultrasound technique and regular audit of their results. In a study of about 20 000 pregnancies, in which fetal NT was measured by 60 sonographers who had obtained the FMF Certificate of Competence in this measurement, the median NT of the individual operators was within 0.1 mm of the expected in 47 (78.3%) sonographers, within 0.15 mm in 57 (95%) and within 0.2 mm in all[9]. As demonstrated by the findings of this study, such small deviations in median NT do not have a substantial adverse effect on the performance of screening. In contrast, larger deviations in median NT and/or widening in the scatter of results, with an increase in the SD of the distribution of measurements, have a substantial adverse effect on the performance of screening.

One approach to correcting for deviations in median NT is to use operator-specific medians[10,11]. Logghe *et al.* reported that by introducing center-specific medians the variance of the NT measurements could be reduced by 15%, which would lead to an improvement in the detection rate from 70% to 72% and a decrease in the false-positive rate from 3.4% to 3.2%[10]. In the Serum, Urine and Ultrasound Screening Study (SURUSS), this idea was taken further, from center-specific to operator-specific medians, which apparently improved the detection rate from 46% to 51% for a 5% false-positive rate[11]. However, the detection rate was still substantially lower than the 75% reported in other studies in which operator-specific medians were not used but the sonographers were appropriately trained and had received the FMF Certificate of Competence in the 11–13-week scan[3]. In the SURUSS, in which a quarter of the patients did not have a valid NT measurement because the scans were carried out at inappropriate gestational ages, the sonographers were unable to obtain a measurement or the quality of the images was deemed unacceptable, the median NT was about 1 mm lower than our median[11]. The only possible explanation for such a major underestimate in measurements is a poor technique in ultrasound scanning with a large overlap in NT measurements between euploid and trisomy 21 fetuses. In this respect, accepting an operator-specific error in the measurement of NT and attempting to correct it by introducing operator-specific medians does not improve the performance of screening.

As shown by our results, small deviations in median NT do not have an effect on the performance of screening and would therefore not benefit from the use of operator-specific medians which complicates the whole process of screening. Large deviations in median NT are likely to be the consequence of a faulty technique in the measurement of NT and may well be accompanied by deviations in SD, with a major adverse impact on the performance of screening. In such cases the operators will require appropriate training and continuous auditing in the correct methodology of measuring NT rather than the false reassurance provided by the calculation of operator-specific medians. The FMF auditing process examines the NT distribution of each operator and evaluates the quality of a sample of their images. Such an approach can identify deviations in the median and SD of the NT measurements from the expected values as well as errors in ultrasound technique that can be improved through feedback and advice to the individual sonographer. Snijders *et al.* assessed the quality of NT measurements and the distribution of NT from five sonographers every 6 months over a period of 18 months[12]. They demonstrated through audit, written feedback and personal training that there was improvement in the ultrasound technique and a decrease in the deviation of the measured NT from the expected distribution.

In summary, fetal NT thickness is the single most effective marker for trisomy 21. However, high performance of screening necessitates appropriate measurement of NT. This paper demonstrates the effect of deviations in the median and SD of NT from the expected on the performance of screening and can form the basis of audit of results of individual sonographers.

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