

Psychological outcomes following maternal serum screening: a cohort study

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Abstract

Background: Maternal serum screening is used to assist in the prenatal detection of congenital anomalies. Its use is controversial, and one concern that has been expressed is its psychological effects on women. The authors examined whether this test leads to an increase in anxiety and depression among women who have a false-positive result as compared with those who have a true-negative result or do not undergo testing.

Methods: A prospective cohort study with baseline assessment at 15 to 18 weeks' gestation and follow-up at 24 weeks' gestation was conducted. Pregnant women at 8 geographically diverse sites across Ontario were recruited. The main outcome measures were the state portion of the State-Trait Anxiety Inventory and the Center for Epidemiologic Studies Depression Scale.

Results: Of the 2418 potential subjects 2020 (83.5%) were enrolled and eligible; 1741 (86.2%) completed the follow-up. A total of 1177 women (67.6%) underwent maternal serum screening. No overall adverse psychological effects as a result of testing were found at 24 weeks' gestation. Women with a false-positive result had a mean increase in anxiety score of 1.6 (95% confidence interval [CI] -1.7 to 4.9), whereas women with a true-negative result had a mean decrease of 1.1 (95% CI -1.8 to -0.3) and those not tested had a mean decrease of 0.4 (95% CI -1.3 to 0.5). The mean depression score increased by 0.5 (95% CI -0.9 to 2.0) in the false-positive group, was unchanged (95% CI -0.3 to 0.4) in the true-negative group and increased by 0.2 (95% CI -1.7 to 1.2) in the not tested group. Of the women who underwent testing, 87 (7.6%) were unsure of their result at the time of follow-up.

Interpretation: The results suggest that maternal serum screening in Ontario is not causing serious psychological harm to women. Communication regarding test results could be improved, since a substantial proportion of women were unsure of their test result.

Résumé

Contexte : L'analyse du sérum maternel aide à détecter des anomalies congénitales avant la naissance. Son utilisation est controversée et ses effets psychologiques sur les femmes préoccupent. Les auteurs ont cherché à déterminer si ce test augmente l'anxiété et la dépression chez les femmes qui obtiennent un résultat faussement positif comparativement à celles qui obtiennent un résultat vraiment négatif ou qui ne subissent pas de test de dépistage.

Méthodes : On a procédé à une étude prospective de cohorte comportant une évaluation de référence après 15 à 18 semaines de grossesse et un suivi à 24 semaines. On a recruté des femmes enceintes de huit régions géographiques différentes en Ontario. Les principales mesures de résultats ont été le volet relatif à l'état du State-Trait Anxiety Inventory et la Center for Epidemiologic Studies Depression Scale.

Résultats : Des 2418 sujets possibles, 2020 (83,5 %) ont été inscrites et étaient admissibles; 1741 (86,2 %) ont terminé le suivi. Au total, 1177 femmes



Evidence

Études

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‡ See pages 663 and 677 for other articles on antenatal health



(67,6 %) se sont soumises à un test de dépistage par le sérum maternel. On n'a constaté aucun effet psychologique indésirable dans l'ensemble à la suite des tests effectués à 24 semaines de grossesse. L'indice d'anxiété a augmenté en moyenne de 1,6 (intervalle de confiance [IC] à 95 % de -1,7 à 4,9) chez les femmes qui ont obtenu un résultat faussement positif tandis qu'il a diminué en moyenne de 1,1 (IC à 95 % de -1,8 à -0,3) chez celles qui ont obtenu un résultat vraiment négatif et diminué en moyenne de 0,4 (IC à 95 % de -1,3 à 0,5) chez celles qui n'ont pas subi de test. L'indice moyen de dépression a augmenté de 0,5 (IC à 95 % de -0,9 à 2,0) chez les femmes qui ont obtenu un résultat faussement positif, n'a pas changé (IC à 95 % de -0,3 à 0,4) chez celles qui ont obtenu un résultat vraiment négatif et a augmenté de 0,2 (IC à 95 % de -1,7 à 1,2) chez celles qui n'ont pas subi de test. Parmi les femmes qui se sont soumises à un test, 87 (7,6 %) n'étaient pas sûres des résultats au moment du suivi.

Interprétation : Les résultats indiquent que le dépistage par le sérum maternel en Ontario ne cause pas de préjudice psychologique grave aux femmes. On pourrait améliorer les communications au sujet des résultats de tests puisqu'un pourcentage important de femmes n'étaient pas sûres de leurs résultats.

Concern about anxiety is often reported by physicians as a reason for not offering prenatal screening to women.¹⁻³ Although such effects have been shown to occur for some tests in some settings,⁴ the results are not consistent.⁵ Most previous studies have lacked adequate power to demonstrate clinical effects or have not included baseline data, involving only women who had already received a positive test result. With the ongoing development of new screening techniques, such as those based on genetic markers, it is important that the potential psychological effects of screening tests be confirmed in large studies.

Maternal serum screening (also referred to as the triple-marker test) is a technique for estimating the risk for fetal trisomy 21 and trisomy 18 and neural tube defects.⁶⁻¹¹ The sensitivity and specificity of this test are 70% and 92% respectively for Down's syndrome, 60% and 99.8% respectively for trisomy 18, and 80% and 98% respectively for neural tube defects.⁶⁻¹¹ Ideally, women undergoing screening should understand the implications of both a positive and a negative result as well as the full cascade of events that may follow a positive result.

The psychological consequences of other prenatal screening tests, particularly maternal serum α -fetoprotein, amniocentesis and chorionic villus sampling, have been studied extensively, with mixed results.^{12,13} Studies on amniocentesis have tended to show minimal psychological consequences, perhaps because women referred for amniocentesis already have raised levels of anxiety and the results thus tend predominantly to be reassuring. Since amniocentesis poses some risk to the fetus, such results may not be generalizable to serum tests. Similarly, the results of studies of maternal serum α -fetoprotein testing may not be generalizable to maternal

serum screening, since the latter test is available to a much broader and younger population.

In Ontario all providers of prenatal care are able to offer maternal serum screening to pregnant women at 15 to 19 weeks of gestation. We carried out an observational cohort study of the process of informed choice, patient factors related to the use of maternal serum screening, satisfaction, knowledge of the test and its implications, and the psychological effects associated with screening. In this report we present the findings on the psychological effects of testing, specifically, whether having a false-positive result leads to increased anxiety or depression.

Methods

Subject recruitment

The main study site was North York General Hospital, North York, Ont. We selected 7 additional sites across Ontario to reflect a combination of teaching and community hospitals and urban and rural settings. We also wished to ensure that a variety of population demographic characteristics, such as place of birth, language and education, were represented in the sample. The study received ethics approval from the University of Toronto and each site.

Study enrolment took place between January and June 1994 at North York General Hospital and from November 1994 to June 1995 at the other sites. Subjects were recruited by research nurses at providers' offices, prenatal clinics and ultrasonography facilities. Research nurses were trained by the research coordinator, who also visited each site on a regular basis. Potentially eligible patients were identified by physicians or by office or clinic staff, or both, and were approached by the research nurse. Pre- and post-



test counselling were provided by the usual health care provider and were not influenced by the study design.

The criterion for inclusion was gestational age of 15 to 18 weeks, with or without ultrasound confirmation. Both women undergoing and those not undergoing maternal serum screening were included. Women with a personal or family history of pregnancies involving neural tube defects, fetal malformations or genetic disorders were excluded. We also excluded women who were carrying more than one fetus and those who did not understand sufficient English to give informed consent. Women were not eligible if they had already undergone maternal serum screening in the current pregnancy and knew the result. Those who were found to have a pregnancy affected by one of the target conditions (true-positive result) were excluded from further follow-up. It was not felt appropriate to contact women who had recently learned that their fetus might have a congenital anomaly or who had terminated their pregnancy. Furthermore, the study would have accrued only 1 or 2 such women, making any inferences about this group impossible.

Data collection instruments

At the time of enrolment, women gave written consent and completed booklet 1. This booklet elicited responses about the course of the current pregnancy as well as demographic characteristics and standardized scales measuring anxiety (the state portion of the State-Trait Anxiety Inventory¹⁴) and depression (the Center for Epidemiologic Studies Depression Scale¹⁵). A standardized scale measuring knowledge of maternal serum screening, the Maternal Serum Screening Knowledge Questionnaire,¹⁶ was developed and validated for this study and was included in booklet 1.

Booklet 2 was mailed to all subjects eligible for follow-up at approximately 24 weeks' gestation. This booklet contained the same questions as booklet 1, except the knowledge scale. Questions were added about the results of ultrasonography, maternal serum screening and amniocentesis, satisfaction with testing and the way in which results were given, perception of maternal health, smoking, and use of alcohol or drugs. Booklet 2 also contained standardized measures of social support and life events¹⁷ and locus of control and open-ended questions to elicit additional concerns.

Data analysis

We analysed the data using SAS software (SAS Institute Inc., Cary, NC). Verification of the accuracy of data entry for a random 10% sample showed an error rate of less than 0.1%.

The subjects were classified into 4 groups: those who did not undergo maternal serum screening, those who underwent testing and reported a negative result at follow-up, those who underwent testing and reported a false-positive result, and those who underwent testing and were not sure of the result.

We compared demographic characteristics across sites and groups using contingency tables and analysis of variance. Distributions of outcome measures and their changes were assessed to ensure that parametric tests could be used. Paired *t*-tests were used to compare mean anxiety and depression scores between the groups at baseline and at 24 weeks' gestation. We compared the mean change in anxiety and depression scores between baseline and 24 weeks across the 4 groups by means of analysis of variance. Change in anxiety level was also dichotomized (with a cutoff of 5 points or more), and contingency tables were used to assess significance. The mean change in anxiety score and the mean change in depression score were then used as the dependent variables in multiple linear regression modelling, with the 4 groups as well as demographic factors, baseline anxiety score and factors correlated with anxiety (medical complications, social support, life events, and alcohol or drug abuse) as independent variables.

The sample size was designed to include at least 80 women with a false-positive result and to have a power of 80% to detect a mean difference of 5 points (which we considered to be clinically significant) in the anxiety score between women with a false-positive result and those with a negative result (2-tailed $\alpha = 0.05$).

Results

During the recruitment periods 2418 women were eligible for enrolment. Of the 2418, 2052 (84.9%) were enrolled in the study, 95 (3.9%) were missed by the research nurse, and 271 (11.2%) declined to participate. Thirty-two women were later found to be ineligible or to have given incomplete data, leaving 2020 subjects. Of the 2020, 1741 (86.2%) responded to booklet 2.

The characteristics of the subjects who did or did not complete follow-up are shown in Table 1. Although the 2 groups were similar on most factors, the respondents were more likely to be Canadian born, to be aware of maternal serum screening and to have a higher score on the Maternal Serum Screening Knowledge Questionnaire.

Self-reported test status at 24 weeks' gestation is shown in Table 2. A total of 75 women (4.3%) reported being told there was something unusual on their test: 31 reported Down's syndrome, 22 reported open neural tube defects, and 16 reported both or a finding compatible with a positive result of screening. For the 6 remaining

women their written comments suggested that the unusual result was actually for a test other than maternal serum screening. These 6 women, as well as 23 who did not report their test result, were excluded from the analysis. We therefore considered 69 women (4.0%) as reporting that they had a false-positive result. Of the remaining 1643 women 564 (34.3%) did not undergo testing, 87 (5.3%) reported being unsure of their test result, and 992 (60.4%) reported receiving a negative result. The women who were unsure of the result accounted for 7.6% of those tested.

Table 2 also shows the baseline characteristics of the women by test result. The women in the false-positive group were older than those in the other groups. The women who were unsure of their result appeared to form a demographically distinct group who were more likely to be not Canadian born, to have a lower level of education and household income and to have lower knowledge of maternal serum screening.

The relation between the test result and psychological effects is shown in Table 3. No differences in depression

scores were found between the subjects with a false-positive result and those with a negative result. Only small, nonsignificant differences in anxiety scores were found between the 2 groups. Based on the distribution of anxiety scores, the study had a power of 90% to detect a mean difference of 5 points between the 2 groups (post hoc analysis).

Table 3 also shows the proportion of subjects who had an increase in anxiety score of 5 points or more. The overall χ^2 test for the 4-way comparison was nonsignificant ($p = 0.061$). A greater proportion of women with a false-positive result than with a negative result had an increase of 5 points or more ($p = 0.028$). The population-attributable risk was 3.0%. This is the proportion of the tested population that will have an increase in anxiety score of 5 points or more attributable to a false-positive result.

There was no association between test result status and either change in anxiety score or change in depression score in multivariate linear regression models, even after adjustment for factors related to these outcomes, such as significant life events.

Table 1: Characteristics of women at selected sites across Ontario enrolled in a study of maternal serum screening, by response group

Characteristic*	Respondents <i>n</i> = 1741	Nonrespondents to follow-up <i>n</i> = 279	<i>p</i> value†
No. (and %) aged > 35 yr	205 (11.8)	40 (14.9)	NS
No. (and %) spoke English at home	1489 (86.3)	229 (82.3)	NS
No. (and %) born in Canada	1161 (67.4)	142 (51.8)	< 0.001
No. (and %) completed college/university	925 (53.6)	136 (49.6)	NS
No. (and %) employed	1185 (68.8)	186 (68.1)	NS
No. (and %) with family income > \$70 000	630 (38.2)	100 (38.8)	NS
No. (and %) married or living common-law	1596 (92.5)	245 (89.1)	0.051
Mean MSSKQ score (and SD)	0.57 (0.49)	0.43 (0.50)	< 0.001
Mean baseline anxiety score (and SD)	38.8 (11.5)	39.7 (11.9)	NS
Mean baseline depression score (and SD)	9.1 (7.0)	9.7 (7.0)	NS
No. (and %) had heard of maternal serum screening	1491 (86.0)	221 (79.5)	0.004

Note: MSSKQ = Maternal Serum Screening Knowledge Questionnaire,¹⁶ SD = standard deviation, NS = not significant.

*Not all subjects gave an answer to each item.

† χ^2 test for categoric variables, *t*-test for continuous variables.

Table 2: Demographic characteristics by self-reported result of maternal serum screening at 24 weeks' gestation

Characteristic*	Not tested <i>n</i> = 564	Tested			<i>p</i> value†
		Unsure of result <i>n</i> = 87	Negative <i>n</i> = 992	False-positive <i>n</i> = 69	
No (and %) aged > 35 yr	77 (13.7)	4 (4.6)	104 (10.5)	18 (26.1)	< 0.001
No. (and %) spoke English at home	485 (86.9)	69 (79.3)	860 (87.4)	61 (89.7)	NS
No. (and %) born in Canada	395 (70.9)	44 (51.2)	667 (67.8)	47 (69.1)	0.004
No. (and %) completed college/university	282 (50.5)	42 (48.3)	544 (55.2)	45 (66.2)	0.037
No. (and %) employed	354 (63.7)	63 (72.4)	705 (71.6)	49 (72.1)	0.011
No. (and %) with family income > \$70 000	145 (27.5)	23 (28.1)	426 (44.9)	32 (47.8)	< 0.001
No. (and %) married or living common-law	506 (90.7)	80 (92.0)	917 (93.1)	66 (97.1)	NS
Mean MSSKQ score (and SD)	0.52 (0.50)	0.38 (0.38)	0.62 (0.49)	0.71 (0.42)	< 0.001

*Not all subjects gave an answer to each item.

†For difference across groups. Bolded values are different from overall mean at $p < 0.05$.



Interpretation

In interpreting our findings, certain limitations should be kept in mind. Our sample included women from diverse geographic areas across Ontario, with a broad range of sociodemographic characteristics. However, we cannot say with certainty the degree to which our subjects were representative of all pregnant women in the province. For example, those who did not speak English were excluded. However, the State-Trait Anxiety Inventory scores were consistent with previously reported population averages for pregnant women.¹⁸

Only 4.3% of the women in our sample reported being told there was something unusual on their maternal serum screening test, whereas in Ontario the initial rate of a positive result at the time of our study was approximately 9% (unpublished data). Our finding of a lower rate may be attributable to selection bias owing to the exclusion of women at higher risk.

Our main study question was whether maternal serum screening is associated with adverse psychological effects such as anxiety or depression. It has been suggested that some prenatal diagnosis tests are associated with acute anxiety, especially among women aged 35 years or less.¹³ At 24 weeks' gestation, when the process of testing would have been complete, we found limited evidence of adverse psychological effects of testing. When we examined the anxiety data as the proportion of subjects with a clinically significant increase in their score rather than as averages, we did note a trend toward a greater proportion in the false-positive group. However, this trend is of limited clinical and public health significance since the attributable risk is small. Although a greater proportion of women in the false-positive group than in the negative result group had an increase of 5 points or more in the anxiety score, most of the subjects with such an increase did not undergo testing or reported a negative result of test-

ing. The data also suggest that a negative result had reassurance value, since fewer women in the negative result group than in the not tested group had an increase of 5 or more points in the anxiety score. Our results show that many women have a general increase in anxiety of 5 points or more during pregnancy regardless of their maternal serum screening status. Strategies to help manage this anxiety need to be identified and made available to these women and their physicians.

One group that may have experienced an unintended effect was the 7.6% of women who underwent testing who were unsure of their result at 24 weeks' gestation. This group was larger than the false-positive group. In previous studies, uncertainty was found to be associated with poorer processing of diagnostic information.^{19,20} The uncertainty about results may have been due to lack of communication with providers, but high baseline anxiety and depression scores suggest that other characteristics of this group may have been responsible. For example, different coping styles have been shown to be associated with psychological responses to the receipt of screening test results.²¹ We also found that the women in this group were less likely to speak English at home and to have been born in Canada than those who reported receiving a negative result, which suggests that special educational efforts may be needed for some demographic groups.

Recent work has attempted to examine whether interventions can reduce the psychological consequences of screening.¹⁹ Before major resources are invested in such programs, we suggest that it would be prudent to examine who may experience such effects and what the mechanisms may be. In particular, although attention has largely focused on people who receive a false-positive result, there may be others, such as those uncertain of their results, who experience similar effects.

Our findings suggest that serious adverse psychological effects of maternal serum screening are not present at

Table 3: Mean depression and anxiety scores according to the self-reported result of maternal serum screening

Variable	Not tested	Tested		
		Unsure of result	Negative	False-positive
Mean depression score	<i>n</i> = 545	<i>n</i> = 87	<i>n</i> = 979	<i>n</i> = 67
Baseline	9.6	11.3	8.6	8.6
Follow-up	9.8	11.0	8.6	9.1
Average change (and 95% CI)	+0.2 (-1.7 to 1.2)	-0.3 (-1.7 to 1.2)	0 (-0.3 to 0.4)	0.5 (-0.9 to 2.0)
Mean anxiety score	<i>n</i> = 511	<i>n</i> = 81	<i>n</i> = 940	<i>n</i> = 65
Baseline	38.4	41.6	38.7	37.5
Follow-up	38.0	41.1	37.6	39.1
Average change (and 95% CI)	-0.4 (-1.3 to 0.5)	-0.5 (-2.7 to 1.7)	-1.1 (-1.8 to -0.3)	+1.6 (-1.7 to 4.9)
No. (and %) of subjects with increase in anxiety score \geq 5 points	152 (29.7)	27 (33.3)*	244 (26.0)	25 (38.5)*

Note: CI = confidence interval.

**p* = 0.028 (χ^2 test for pairwise comparison) for difference between negative and false-positive groups. All other comparisons were nonsignificant.



24 weeks' gestation. The findings do support the need for improved physician-patient communication before screening tests and when the patient is advised of the result. Possible strategies might include the development of tools, such as decision aids, and public education about the nature of screening tests and their limitations.

Our results show that not all women seeking prenatal care are the same. Their understanding of screening tests and their responses to them can differ depending on their past experiences and personal circumstances. Health care providers must take this diversity into account when discussing screening tests with them.

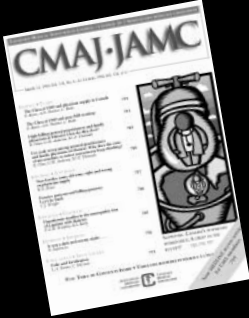
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