Original Investigation

Effect of Enhanced Information, Values Clarification, and Removal of Financial Barriers on Use of Prenatal Genetic Testing
A Randomized Clinical Trial

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IMPORTANCE Prenatal genetic testing guidelines recommend providing patients with detailed information to allow informed, preference-based screening and diagnostic testing decisions. The effect of implementing these guidelines is not well understood.

OBJECTIVE To analyze the effect of a decision-support guide and elimination of financial barriers to testing on use of prenatal genetic testing and decision making among pregnant women of varying literacy and numeracy levels.

DESIGN, SETTING, AND PARTICIPANTS Randomized trial conducted from 2010-2013 at prenatal clinics at 3 county hospitals, 1 community clinic, 1 academic center, and 3 medical centers of an integrated health care delivery system in the San Francisco Bay area. Participants were English- or Spanish-speaking women who had not yet undergone screening or diagnostic testing and remained pregnant at 11 weeks' gestation (n = 710).

INTERVENTIONS A computerized, interactive decision-support guide and access to prenatal testing with no out-of-pocket expense (n = 357) or usual care as per current guidelines (n = 353).

MAIN OUTCOMES AND MEASURES The primary outcome was invasive diagnostic test use, obtained via medical record review. Secondary outcomes included testing strategy undergone, and knowledge about testing, risk comprehension, and decisional conflict and regret at 24 to 36 weeks' gestation.

RESULTS Women randomized to the intervention group, compared with those randomized to the control group, were less likely to have invasive diagnostic testing (5.9% vs 12.3%; odds ratio [OR], 0.45 [95% CI, 0.25-0.80]) and more likely to forgo testing altogether (25.6% vs 20.4%; OR, 3.30 [95% CI, 1.43-7.64], reference group screening followed by invasive testing). Women randomized to the intervention group also had higher knowledge scores (9.4 vs 8.6 on a 15-point scale; mean group difference, 0.82 [95% CI, 0.34-1.31]) and were more likely to correctly estimate the amniocentesis-related miscarriage risk (73.8% vs 59.0%; OR, 1.95 [95% CI, 1.39-2.75]) and their estimated age-adjusted chance of carrying a fetus with trisomy 21 (58.7% vs 46.1%; OR, 1.66 [95% CI, 1.22-2.28]). Significant differences did not emerge in decisional conflict or regret.

CONCLUSIONS AND RELEVANCE Full implementation of prenatal testing guidelines using a computerized, interactive decision-support guide in the absence of financial barriers to testing resulted in less test use and more informed choices. If validated in additional populations, this approach may result in more informed and preference-based prenatal testing decision making and fewer women undergoing testing.

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Since the introduction of amniocentesis,[1] prenatal genetic testing guidelines have focused on identifying women at increased risk of giving birth to an infant with Down syndrome or other chromosomal abnormalities, for whom invasive diagnostic testing should be recommended. Although initially advanced maternal age was the criterion for eligibility,[2] identification of serum and ultrasonographic markers that can quantify the risk of an affected fetus[3] led to incorporation of screening into routine prenatal care for women of all ages. The recent introduction of cell-free DNA testing has intensified the complexity of prenatal testing decision making, generating concerns about the potential for erosion of informed choice.[4]

Studies have questioned the "routinization" of prenatal screening and whether women understand its voluntary nature,[5] and documented substantial variation in how women view the outcomes of decisions to undergo or forgo testing.[6,7] Low uptake rates of invasive testing among women who receive positive screening results also have been reported,[8] raising concerns about the extent to which the purpose and potential outcomes of screening are understood, particularly among women of lower literacy and numeracy levels.[9] Nonetheless, clinicians continue to use risk-based approaches to counseling, often simply recommending screening and deferring conversations about further testing until screen-positive results are received.[10]

In this study, a randomized clinical trial was conducted of a multifaceted approach to prenatal testing designed to promote preference-based decision making. The primary goal was to assess the prenatal testing choices women make in the context of being fully informed about testing options, including having the option to forgo testing, the opportunity to engage in values-clarification exercises, and not having financial barriers. Understanding was also sought as to whether these women would make decisions characterized by greater knowledge and understanding of prenatal testing and less decisional conflict and regret.

Methods

Participants

Pregnant women who were English- or Spanish-speaking were recruited from prenatal clinics affiliated with 3 county hospitals (San Francisco General Hospital, Santa Clara Valley Medical Center, Highland Hospital [a member of the Alameda Health System]); 1 community clinic serving primarily low-income women (La Clínica de la Raza); 1 academic center (the University of California, San Francisco); and 3 medical centers of an integrated health care delivery system (Kaiser Permanente Northern California). Eligibility criteria included being less than or equal to 20 weeks of gestation with a singleton or twins and not having undergone any prenatal testing for fetal aneuploidy in the current pregnancy.

Procedures

At 2 of the sites, potentially eligible participants were sent letters describing the study with postage-paid cards offering the choice to opt in or to opt out. A bilingual research associate phoned women who did not return the opt-out card and screened those who indicated interest. At the other sites, patients were referred to an on-site bilingual interviewer who assessed interest and eligibility. After providing written informed consent, participants completed an interviewer-administered baseline questionnaire and were randomized to the intervention or control group.

A computer-generated random allocation sequence assigned participants to experimental groups within permuted blocks of random size, with a 1:1 allocation ratio, stratified by age (<35 years vs ≥35 years), clinical site, parity (nulliparous vs parous), and interviewer. Women randomized to the intervention group were provided access by the interviewer to a computerized, interactive, prenatal testing decision-support guide in their preferred language (English or Spanish) located at the interview site, and were told that after using it, the study would pay for any tests discussed for which they lacked insurance coverage. Women who were randomized to the control group received no study intervention or financial support to cover prenatal genetic testing. The protocol involved no specified interaction with any clinicians.

At 24 to 36 weeks' gestation, patient-reported outcomes were measured during a 20-minute telephone interview. Prenatal test use was assessed postpartum via medical record review. Different research associates facilitated baseline and follow-up interviews and medical record review to ensure blinding to the randomization assignment. The randomization code was not available to any study-related personnel until data analysis was complete.

This study was approved by the institutional review boards for each site. All participants were enrolled between January 2010 and June 2012 and followed up through their deliveries, the last of which occurred in January 2013. Participants were given $40 as remuneration after each of the 2 interviews.

Experimental Intervention and Control Group

The goal of this study was to determine what women of varying literacy levels and sociodemographic backgrounds would choose after being fully informed about the benefits and risks of differing prenatal testing strategies and having the opportunity to clarify their values around these options, without the disincentive of having to pay for tests not covered by their insurance.

Women randomized to the experimental group were provided access to Prenatal Testing: Exploring Your Options, a decision-support guide created with input from a wide range of clinicians (including perinatologists, geneticists, obstetricians, nurse midwives, genetic counselors, and nurses), decision scientists, and communication and literacy experts,[11] and adapted for use by women of varying literacy levels. This decision-support guide is formatted as an audio-, video-, and text-based interactive computer program narrated by a bilingual actress who speaks in a style that emulates a warm and knowledgeable friend. She emphasizes the personal nature of prenatal testing decisions, noting that the choices of forgoing testing altogether, starting with a screening test, or undergoing invasive diag-

nostic testing without first having a screening test, are all reasonable options, and that the goal of the program is to help the user decide on which option would be best to undertake.

Completion of the program takes approximately 45 to 60 minutes. It begins with an educational module that provides general information about prenatal testing and the role of values and preferences in prenatal testing decisions, a description of Down syndrome over the life course, more abbreviated descriptions of trisomies 13 and 18 and structural defects, and details on the diagnostic accuracy and other features of the various screening and diagnostic tests. Optional sections containing more information (titled Learn More) are included throughout this component. In the second part of the program, the user is presented with her personalized, age-related chances of carrying a fetus with aneuploidy. She is then asked to complete values clarification questions focusing on 3 decisions: (1) whether or not to have any testing; (2) if testing is desired, whether to start with screening or with invasive diagnostic testing; and (3) which specific screening and/or diagnostic test(s) to undergo. Afterwards, the user can receive graphic highlights of the testing strategy that is most consistent with the her responses, as well as click to obtain detailed information on the features of that strategy or any of the other strategies. The program concludes by encouraging the user to discuss questions with her clinician, while emphasizing that the testing strategy to undergo is her choice (see eAppendix 1 in Supplement 1 for screen shots and values clarification questions).

Women randomized to the control group received no study intervention beyond completion of the baseline and follow-up questionnaires. Consistent with current guidelines,[12,13] the official policy at all recruitment sites was to offer all women, regardless of age, information on both screening and diagnostic tests and to inform them that testing was optional. However, discussions with clinicians at these sites suggested variable adherence to these guidelines, and all reported a greater focus on counseling and diagnostic testing for women aged 35 years or older.

Outcomes and Measures

The primary outcome, obtained from review of participants' medical records, was use of invasive prenatal diagnostic testing. Secondary outcomes (also obtained from the medical record) included testing strategy undergone, as well as knowledge, risk comprehension, decisional conflict, and decision regret, measured during the follow-up telephone interview. To measure knowledge, a 15-item measure adapted from the Maternal Serum Screening Knowledge Questionnaire (eAppendix 2, Supplement 1) was used.[14] Risk comprehension was assessed by asking participants to estimate, out of 1000 pregnant women who undergo amniocentesis, how many would experience a miscarriage (women reporting the risk to be >0 but ≤10 received a score of correct), and out of 1000 pregnant women their age, how many are carrying a fetus affected by Down syndrome (risks consistent with the participant's age-related risk of Down syndrome received a score of correct). Decisional conflict and regret were assessed using 15 items from the Decisional Conflict Scale,[15] and the 5-item Decision Regret Scale.[16]

Statistical Analysis

The primary hypothesis of this study was that women who were randomized to the intervention group would undergo invasive diagnostic testing at a lower rate than women randomized to the control group, due to better understanding of the likelihood that their fetus was affected by a chromosomal disorder and the chance that an invasive diagnostic test will cause a miscarriage, along with a greater appreciation that declining use of testing altogether is a reasonable choice.

Power analyses were conducted, partially informed by our prior research, to estimate the appropriate sample size to test this hypothesis. In assessing trends in the use of invasive diagnostic testing among women who delivered at an integrated health care system in California, this study found that the number of amniocenteses or chorionic villus sampling procedures performed as a percentage of the number of deliveries in 2006 was 12%.[17] A minimal detectable difference of 6% was selected (half of the rate in the control group), corresponding to an odds ratio (OR) of 0.47 (a small to medium effect size). To achieve 80% power (2-tailed $\alpha = .05$; 90% retention at follow-up), the required sample size was 396 per group or 792 in total.

Secondary hypotheses focused on patient-reported outcomes: compared with women randomized to the the control group, women randomized to the intervention group would have better testing knowledge and risk comprehension, as well as reduced decisional conflict and decision regret. The design was capable of detecting a minimum group mean difference equal to 0.21 standard deviations.

All reported analyses were based on a modified intention-to-treat sample that excluded women who reported (or whose medical record indicated) a pregnancy loss prior to 11 weeks (the earliest gestational age at which prenatal testing was available at the participating sites; none of those women were yet eligible to undergo testing). Group comparisons of 24-week outcomes were tested via linear and logistic regression, as appropriate. Analyses were reported using ORs or linear regression coefficients (b) with 95% CIs and *P* values. All models were fit to 20 multiple-imputed data sets created via a Markov Chain Monte Carlo method[18] using SAS PROC MI version 9.3 (SAS Institute Inc). Imputation models were stratified by randomization group and included all variables represented in **Table 1**, **Table 2**, and **Table 3**, as well as participants' median ZIP code income (US Census Bureau data, 2000). All parameter estimates, standard error estimates, and test statistics were calculated by combining results across the imputed data sets (2-tailed $\alpha = .05$ throughout).[21,22]

Results

A total of 1932 women were screened for eligibility; 635 did not meet inclusion criteria (**Figure**). Of the 1297 eligible women, 744 enrolled in the study, a 57.3% participation

Table 1. Baseline Characteristics of Study Participants by Randomization Group (n=710)

Sociodemographic Characteristics	No. (%) in Group[a] Intervention (n = 357)	Control (n = 353)
Age, mean (SD), y	29.2 (6.0)	29.3 (6.3)
≥35 y	77 (21.6)	75 (21.2)
Married or living with partner	267 (74.8)	253 (71.6)
Race/ethnicity		
Latina, Latin American	174 (48.7)	148 (41.9)
White	93 (26.1)	89 (25.2)
Black, African American	54 (15.1)	58 (16.4)
Asian	27 (7.6)	38 (10.8)
Other[b]	9 (2.5)	20 (5.7)
Spanish-language interview	136 (38.1)	116 (32.9)
Educational attainment		
Some high school or less	105 (29.4)	94 (26.8)
High school graduate	65 (18.2)	61 (17.4)
Some college	69 (19.3)	84 (23.7)
College graduate	59 (16.5)	55 (15.6)
Graduate degree	59 (16.5)	58 (16.5)
Literacy and numeracy		
Less than adequate literacy[c]	94 (26.4)	86 (24.4)
Low numeracy[d]	161 (45.0)	155 (43.9)
Annual household income, $		
≤25 000	160 (44.9)	178 (50.3)
25 001-50 000	60 (16.9)	51 (14.6)
50 001-100 000	62 (17.4)	47 (13.2)
100 001-150 000	39 (11.1)	40 (11.3)
>150 000	35 (9.8)	38 (10.7)
Recruitment site		
Sites serving primarily women of lower-socioeconomic status		
San Francisco General Hospital	113 (31.7)	111 (31.4)
Santa Clara Valley Medical Center (San Jose)	57 (16.0)	60 (17.0)
Alameda County Medical Center-Highland Hospital (Oakland)	14 (3.9)	16 (4.5)
La Clínica de la Raza (Oakland)	24 (6.7)	23 (6.5)
Other sites		
University of California, San Francisco	81 (22.7)	78 (22.1)
Kaiser Permanente Northern California (San Francisco, Oakland, Richmond)	68 (19.0)	65 (18.4)
Reproductive history		
Prior pregnancy	253 (70.9)	247 (70.0)
Prior live birth	203 (56.9)	202 (57.2)
Had prenatal testing in a previous pregnancy	109 (30.5)	122 (34.5)
Had genetic counseling in a previous pregnancy	49 (13.7)	53 (15.1)
Gestational age at first prenatal visit, mean (SD), wk[e]	9.4 (3.3)	9.3 (3.1)

[a] Data are reported as No. (%) unless otherwise indicated.

[b] Includes Native American and participants who self-reported as mixed.

[c] Rapid Estimate of Adult Literacy in Medicine-Revised score of less than or equal to 6 on a scale of 0 to 8 (which is considered as being at risk for poor literacy).[19]

[d] Two or fewer correct responses on a 5-item numeracy scale.[20]

[e] Estimated from self-reported first prenatal visit date and last menstrual period.

rate. There were 375 women randomized to the intervention group and 369 randomized to the control group. After randomization, 34 women experienced pregnancy losses before 11 weeks' gestation. The 710 remaining women (357 randomized to the intervention group and 353 to the control group) comprised the modified intention-to-treat sample from which the data used in this analysis were obtained.

This sample constituted a sociodemographically diverse cohort of pregnant women; 45.4% of the participants self-identified as Latina, 25.6% as white, 15.8% as black or African American, and 9.2% as Asian or Pacific Islander. Approximately one-third (35.5%) opted to participate in the Spanish-language version of the study. Nearly half (45.9%) had a high school education or less, one-fourth (25.4%) had less than adequate literacy, and 44.5% had low numeracy (Table 1).

As hypothesized, significantly fewer women who were randomized to the intervention group underwent invasive diagnostic testing compared with women randomized to the control group (Table 2; 5.9% vs 12.3%; OR, 0.45 [95% CI, 0.25-0.80]; P = .005). The overall prenatal testing strategy used by the 2 groups also differed: women randomized to

Table 2. Prenatal Tests and Testing Strategies Undergone by Randomization Group (n=710)

	No. (%) in Group			
	Intervention (n = 357)	Control (n = 353)	OR (95% CI)	*P* Value
Had invasive diagnostic testing				
Amniocentesis	14 (3.9)	29 (8.2)	0.45 (0.22-0.92)	.02
CVS	9 (2.4)	15 (4.1)	0.57 (0.23-1.42)	.22
Any diagnostic testing[a]	21 (5.9)	43 (12.3)	0.45 (0.25-0.80)	.005
Testing strategy undergone				.03[b]
No testing	92 (25.6)	72 (20.4)	3.30 (1.43-7.64)	.005
Screening test only	244 (68.5)	238 (67.3)	2.67 (1.19-5.97)	.02
Invasive diagnostic testing without first having a screening test	11 (3.0)	16 (4.6)	1.67 (0.54-5.21)	.37
Screening test followed by invasive diagnostic test	10 (2.9)	27 (7.7)	1 [Reference]	

Abbreviations: CVS, chorionic villus sampling, OR, odds ratio.

[a] Two women had both CVS and amniocentesis.

[b] *P* value from omnibus 3-degree of freedom test from multinomial logistic regression.

Table 3. Knowledge About Prenatal Testing, Risk Comprehension, Decisional Conflict, and Decision Regret at 24 to 36 Weeks' Gestation

	No. (%) in Group			
	Intervention (n = 357)	Control (n = 353)	Intervention Effect	*P* Value
Continuous Outcomes, Mean (SD)			**b (95% CI)[a]**	
Knowledge[b]	9.4 (3.2)	8.6 (3.2)	0.82 (0.34 to 1.31)	<.001
Decisional conflict[c]	12.9 (14.1)	13.8 (15.6)	−0.89 (−3.27 to 1.50)	.47
Decision regret[d]	8.29 (12.5)	6.83 (10.8)	1.46 (−0.36 to 3.29)	.12
Categorical Outcomes, No. (%)			**OR (95% CI)[a]**	
Correct estimate of amniocentesis miscarriage risk[e]	263 (73.8)	208 (59.0)	1.95 (1.39 to 2.75)	<.001
Correct estimate of Down syndrome risk[f]	210 (58.7)	163 (46.1)	1.66 (1.22 to 2.28)	.001

Abbreviation: b, linear regression coefficient; OR, odds ratio.

[a] Data are reported as point estimates of the intervention effect representing unstandardized linear regression coefficients (b) or odds ratios, 95% CIs of point estimates, and *P* values of point estimates.

[b] Number of correct responses on a 15-item knowledge questionnaire adapted from the Maternal Serum Knowledge Questionnaire[14] (score range, 0 [no correct answers] to 15 [all answers correct]).

[c] Fifteen items from the 16-item Decisional Conflict Scale[15] (score range, 0-100 with higher scores indicating more conflict).

[d] Mean score on the Decision Regret Scale[16] (score range, 0-100 with higher scores indicating more regret).

[e] Correct responses (defined as replies of >0 to ≤10 of 1000 pregnancies).

[f] Replies were considered correct if the estimate provided was within the age-specific range for the participant.

the intervention group were more likely to have no testing (25.6% vs 20.4%; OR, 3.30 [95% CI, 1.43-7.64]; *P* = .005) or screening alone (68.5% vs 67.3%; OR, 2.67 [95% CI, 1.19-5.97]; *P* = .02; reference group screening followed by invasive diagnostic testing).

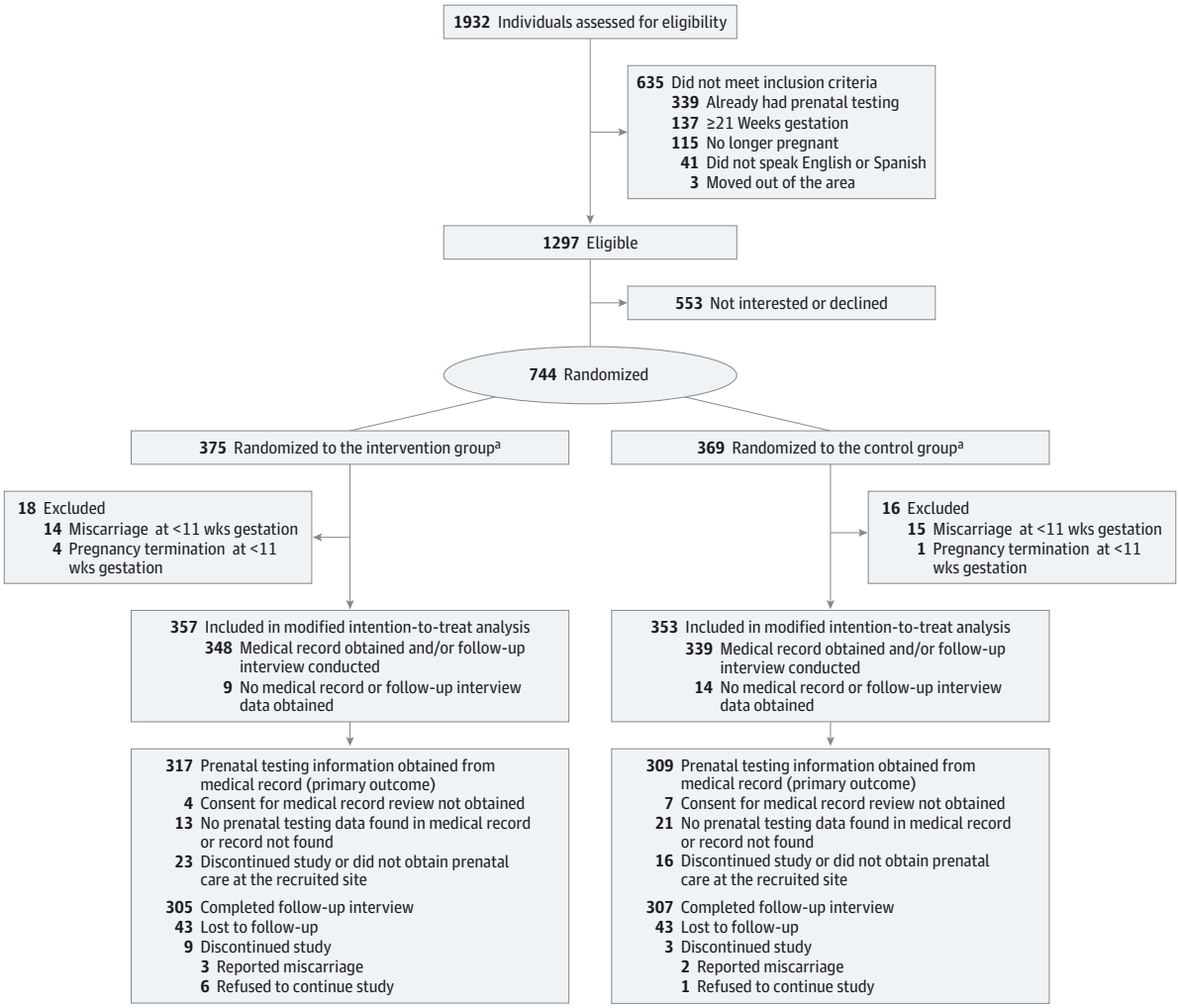
Also as hypothesized, women randomized to the intervention group had significantly higher knowledge scores (Table 3; 9.4 vs 8.6 on a 15-point scale; b = 0.82 [95% CI, 0.34-1.31]; *P* < .001), were more likely to correctly report both the miscarriage risk of amniocentesis (73.8% vs 59.0% correct; OR, 1.95 [95% CI, 1.39-2.75]; *P* < .001), and their age-adjusted likelihood of carrying a fetus with trisomy 21 (58.7% vs 46.1% correct; OR, 1.66 [95% CI, 1.22-2.28]; *P* = .001). Although it was hypothesized that women randomized to the intervention group would have lower decisional conflict and decision regret, significant differences did not emerge on these outcomes.

This study accessed usage data from the decision-support guide for 325 of 357 women who were randomized to the intervention group; 309 of those women completed all sections of the program and obtained data on the testing strategy the program suggested might be most aligned with their values. For 72.2% of these women, the suggested approach was to start with a screening test; 9.7% were told that invasive testing might be the best initial approach. The remaining 18.1% were informed that their values indicated a preference for no testing. When use of the recommended testing strategy was compared with the strategy undergone among the 264 women who completed all sections of the program and for whom we had testing data, the majority (75.0%) underwent the recommended strategy.

Discussion

In a diverse population of women receiving care in a variety of settings, these findings show that after receiving complete prenatal testing information and the opportunity to explicitly consider their values and preferences via an interactive decision-support tool and having financial barriers to testing re-

Figure. Study Participants and Flow



[a] Participants in the intervention group used a computerized, interactive, decision-support guide and had access to prenatal testing with no out-of-pocket expense; those in the control group received usual care per current guidelines.

moved, participants were less likely to opt for invasive testing and more likely to forgo testing for aneuploidy altogether. This suggests that expanding coverage of amniocentesis and chorionic villus sampling to women of all risk levels may not result in increased use of these procedures. The findings also show that this approach improved patient knowledge regarding prenatal testing and understanding of amniocentesis-related miscarriage and age-adjusted risk of Down syndrome, suggesting that this intervention resulted in more informed patient decision-making.

What do the findings of this study suggest for patient counseling and decision making in an era of rapidly expanding options for prenatal testing, including cell-free DNA testing and chromosomal microarray analysis?[23,24] First, this study has generated evidence that using an interactive decision-support guide that presents systematic information and an opportunity to engage in values-clarification exercises can help women of varying literacy levels make informed prenatal decisions reflective of their own preferences and goals. In addition to enabling women to consider the various options at their own pace, having such a decision guide available in clinical settings can provide a consistent and accurate message regarding the risks and benefits of testing.

This study's finding that women who were randomized to the intervention group were less likely to undergo testing than those who received usual care adds support to the contention that women may not be receiving adequate counseling about their options. This underscores the need for clinicians to be clear that prenatal testing is not appropriate for everyone, and to present forgoing testing as a reasonable choice. With the advent of cell-free DNA testing for aneuploidy, it is particularly important that women understand the purpose and potential consequences of undergoing testing, as without adequate counseling, this new test may easily come to be viewed as simply another blood test in the large panel of routine prenatal laboratories.

Although this study was strengthened by its use of a randomized design, its focus on outcomes obtained from medical records as well as those reported by patients, and participation of English- and Spanish-speaking women of varying literacy levels receiving care in a variety of settings, several limitations deserve comment. First, while a diverse sample was successfully recruited, all participants resided in the San Francisco Bay area and the participation rate was 57.3%, potentially limiting the study's generalizability. Participants' knowledge and values were not measured until 24 weeks' gestation because having women respond to those questions prior to making decisions about prenatal screening would, in itself, constitute an intervention. Therefore, this study cannot assess mechanisms of action via those potential mediators. Although a significant difference in knowledge scores emerged at this time point, the clinical significance is unclear. However, differences in knowledge scores have been shown to be strongest in the first 2 weeks after using decision tools and to dissipate over time,[11] suggesting that the intergroup difference in this score may have heen higher at the time testing utilitization decisions were made. Moreover, substantive differences in the percent of women who correctly reported their likelihood of carrying an affected fetus and experiencing a procedure-related miscarriage suggests that the tool improved knowledge in these domains.

In addition, because chromosomal disorders are relatively rare (5 cases of trisomy were detected, all of which were identified via prenatal testing and resulted in terminations), there was not a sufficient sample to conduct a subanalysis of women who were found to be carrying an affected fetus. Because of the focus on observing what women would do in the context of complete information about all prenatal testing options without financial barriers, participants were told they could undergo testing without any out-of-pocket expense. How to effectively implement guides in clinical settings without such guaranteed access remains to be determined.

Importantly, this study was largely conducted before the introduction of cell-free DNA testing. As a result, no information on this new screening test was included in the decision-support guide and this option was not available to study participants. However, the general features of cell-free DNA testing and the conditions for which it screens are similar to the tests covered in this study, and the implications for counseling and informed patient decision making remain the same.

Conclusions

Full implementation of prenatal testing guidelines, using a computerized, interactive decision-support guide in the absence of financial barriers to testing, resulted in less prenatal test use and more informed choices. If validated in additional populations, this approach may result in more informed and preference-based prenatal testing decision making and fewer women undergoing testing.

ARTICLE INFORMATION

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Author Contributions: Drs Kuppermann and Gregorich had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
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Study supervision: Kuppermann, Pena, Gregorich, Norton.

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REFERENCES

1. Nadler HL, Gerbie A. Present status of amniocentesis in intrauterine diagnosis of genetic defects. *Obstet Gynecol*. 1971;38(5):789-799.

2. National Institutes of Health. Antenatal diagnosis. NIH Consens Statement. 1979;2(2):11-15. http://consensus.nih.gov/1979/1979AntenatalDx012html.htm. Accessed September 8, 2014.

3. Haddow JE, Palomaki GE, Knight GJ, Cunningham GC, Lustig LS, Boyd PA. Reducing the need for amniocentesis in women 35 years of age or older with serum markers for screening. *N Engl J Med*. 1994;330(16):1114-1118.

4. van den Heuvel A, Chitty L, Dormandy E, et al. Will the introduction of non-invasive prenatal diagnostic testing erode informed choices? an experimental study of health care professionals. *Patient Educ Couns*. 2010;78(1):24-28.

5. Press N, Browner CH. Why women say yes to prenatal diagnosis. *Soc Sci Med*. 1997;45(7):979-989.

6. Kuppermann M, Nease RF, Learman LA, Gates E, Blumberg B, Washington AE. Procedure-related miscarriages and Down syndrome-affected births:

implications for prenatal testing based on women's preferences. *Obstet Gynecol*. 2000;96(4):511-516.

7. Grobman WA, Dooley SL, Welshman EE, Pergament E, Calhoun EA. Preference assessment of prenatal diagnosis for Down syndrome: is 35 years a rational cutoff? *Prenat Diagn*. 2002;22(13):1195-1200.

8. Jaques AM, Collins VR, Muggli EE, et al. Uptake of prenatal diagnostic testing and the effectiveness of prenatal screening for Down syndrome. *Prenat Diagn*. 2010;30(6):522-530.

9. Roter DL, Erby L, Larson S, Ellington L. Oral literacy demand of prenatal genetic counseling dialogue: predictors of learning. *Patient Educ Couns*. 2009;75(3):392-397.

10. Driscoll DA, Morgan MA, Schulkin J. Screening for Down syndrome: changing practice of obstetricians. *Am J Obstet Gynecol*. 2009;200(4):459.e1-459.e9.

11. Kuppermann M, Norton ME, Gates E, et al. Computerized prenatal genetic testing decision-assisting tool: a randomized controlled trial. *Obstet Gynecol*. 2009;113(1):53-63.

12. American College of Obstetricians and Gynecologists. ACOG practice bulletin No. 88, December 2007: invasive prenatal testing for aneuploidy. *Obstet Gynecol*. 2007;110(6):1459-1467.

13. ACOG Committee on Practice Bulletins. ACOG practice bulletin No. 77: screening for fetal chromosomal abnormalities. *Obstet Gynecol*. 2007;109(1):217-227.

14. Goel V, Glazier R, Holzapfel S, Pugh P, Summers A. Evaluating patient's knowledge of maternal serum screening. *Prenat Diagn*. 1996;16(5):425-430.

15. O'Connor AM. Validation of a decisional conflict scale. *Med Decis Making*. 1995;15(1):25-30.

16. Brehaut JC, O'Connor AM, Wood TJ, et al. Validation of a decision regret scale. *Med Decis Making*. 2003;23(4):281-292.

17. Norton ME, Nakagawa S, Norem C, Gregorich SE, Kuppermann M. Effects of changes in prenatal aneuploidy screening policies in an integrated health care system. *Obstet Gynecol*. 2013;121(2 pt 1):265-271.

18. Schafer J. *Analysis of Incomplete Multivariate Data*. London, England: Chapman & Hall; 1997.

19. Bass PF III, Wilson JF, Griffith CH. A shortened instrument for literacy screening. *J Gen Intern Med*. 2003;18(12):1036-1038.

20. Lipkus IM, Samsa G, Rimer BK. General performance on a numeracy scale among highly educated samples. *Med Decis Making*. 2001;21(1):37-44.

21. Rubin D. *Multiple Imputation for Nonresponse in Surveys*. New York, NY: John Wiley & Sons; 1987.

22. Li K-H, Meng X-L, Raghunathan TE, Rubin DB. Significance levels from repeated P values with multiply imputed data. Stat Sin. 1991;1:65-92. http://www3.stat.sinica.edu.tw/statistica/j1n1/j1n15/j1n15.htm. Accessed September 8, 2014.

23. American College of Obstetricians and Gynecologists Committee on Genetics. Committee opinion No. 545: noninvasive prenatal testing for fetal aneuploidy. *Obstet Gynecol*. 2012;120(6):1532-1534.

24. American College of Obstetricians and Gynecologists Committee on Genetics. Committee opinion No. 581: the use of chromosomal microarray analysis in prenatal diagnosis. *Obstet Gynecol*. 2013;122(6):1374-1377.