

Prenatal aneuploidy screening in a low-risk Hispanic population: price elasticity and cost-effectiveness



Caitlin M. Clifford, MD; Neil Askew, MS; Diane Smith, MD; Jesus Iniguez, MD; Andrew Smith, MD; Michael D. House, MD; Ashley A. Leech, PhD, MS

BACKGROUND: In October 2015, the Massachusetts Medicaid program temporarily stopped reimbursement for procedures in which the International Classification of Diseases, Tenth Edition, code for serum aneuploidy screening used by certain communities was stipulated. This change led to a substantial number of patients who went without aneuploidy screening for approximately 3 years.

OBJECTIVE: This study aimed to determine the change in use and cost-effectiveness of prenatal aneuploidy serum screening in a low-risk Hispanic Medicaid population in Massachusetts.

STUDY DESIGN: We conducted a retrospective chart review of Spanish-speaking pregnant patients younger than 35 years of age who underwent aneuploidy serum screening at a Massachusetts community health center. The study compared the aneuploidy serum screening rates for the periods before and after May 2016 when the Massachusetts Medicaid program, MassHealth, temporarily discontinued reimbursement for the screening. Based on these rates, we developed a Markov cohort simulation model to assess the economic value of reimbursed aneuploidy screening vs nonreimbursed or limited screening. Clinical outcomes included trisomy 21, live births, and therapeutic abortions for a trisomy 21 diagnosis. Economic outcomes included discounted quality-adjusted life years and lifetime medical costs, net health benefit, and incremental cost-effectiveness ratios.

RESULTS: Before the MassHealth policy change, 69% (55/80) of pregnant individuals selected quad or sequential screens in comparison with only 9% (10/112) who selected screens after the policy change. Traditional aneuploidy serum screening in a low-risk (aged <35 years) Hispanic population was considered to be cost-saving (ie, led to lower incremental costs and higher incremental benefits when compared with nonreimbursed or limited screening).

CONCLUSION: From a United States healthcare payer perspective, aneuploidy serum screening for Hispanic pregnant individuals under 35 years of age is economically advantageous when compared with limited screening.

Key words: aneuploidy screening, community health center, cost-effectiveness, ICD-10, low-risk pregnancy, Medicaid, price elasticity, public payer, serum screening, trisomy 21

Introduction

Prenatal screening has been used since the early 1980s to estimate the risks for carrying a pregnancy complicated by a fetal aneuploidy, such as trisomy 21 (T21). The American College of

Obstetricians and Gynecologists recommends discussing and offering aneuploidy screening for genetic disorders to all individuals early in pregnancy, irrespective of the age or risk for chromosomal abnormality.¹ Screening results

can provide patients with valuable information for present and future decision-making, including anticipatory counseling, ongoing pregnancy management, future planning, or pregnancy termination. Alternatively, for some

From the Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, Tufts Medical Center, Boston, MA (Dr Clifford); Department of Health Policy, Vanderbilt University School of Medicine, Nashville, TN (Mr Askew and Dr Leech); Greater Lawrence Family Health Center, Lawrence, MA (Drs Smith and Iniguez); Vanderbilt Center for Child Health Policy, Vanderbilt University Medical Center, Nashville, TN (Drs Smith and Leech); Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, University of Michigan, Ann Arbor, MI (Drs Clifford and House); Department of Family Medicine, University of Washington, Seattle, WA (Dr Iniguez).

M.D.H. and A.A.L. are joint senior authors.

The authors report no conflict of interest.

The research reported in this publication was supported by the National Institute on Drug Abuse of the National Institutes of Health (NIH) under award number [K01 DA050740](#) (to A.A.L.). The NIH played no role in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the article for publication.

Cite this article as: Clifford CM, Askew N, Smith D, et al. Prenatal aneuploidy screening in a low-risk Hispanic population: price elasticity and cost-effectiveness. *Am J Obstet Gynecol Glob Rep* 2023;XX:x:ex–x.ex.

Corresponding author: Caitlin M. Clifford, MD. cmcliff@med.umich.edu

2666-5778/\$36.00

© 2023 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)
<http://dx.doi.org/10.1016/j.xagr.2023.100293>

AJOG Global Reports at a Glance

Why was this study conducted?

Although we know that noninvasive prenatal testing is not cost-effective in low-risk populations insured by public payers, it remains uncertain for other types of prenatal screening.

Key findings

This study revealed that aneuploidy screening rates in a low-risk population were influenced by cost, but it remained price inelastic. Our findings indicate that traditional aneuploidy screening in a low-risk Hispanic population insured through a public payer is cost-saving (ie, led to lower incremental costs and higher incremental benefits when compared with limited screening), regardless of the age (18, 25, or 34 years) of the pregnant individuals.

What does this add to what is known?

Unintentional policy changes can lead to marked changes in patient choice, leading to long-term costs that may exceed short-term savings for a public payer.

individuals, screening may be associated with undue stress.^{2,3}

In October 2015, during the implementation of the International Classification of Diseases, 10th Revision (ICD-10) diseases and related health problems classification system, a natural experiment emerged in Massachusetts for serum aneuploidy screening. During this period, the Massachusetts Medicaid program, MassHealth, temporarily discontinued reimbursement for the “multianalyte assays with algorithmic analyses” code that was used by certain communities to bill for serum aneuploidy screening. Because of this change, and particularly applicable to small health centers that process screens in-house, patients bore the direct cost of the screening. In 1 community health center (CHC) that was affected by this change in northeastern Massachusetts, patients were required to pay an upfront out-of-pocket cost of \$105 for aneuploidy screening (previously, \$0 out-of-pocket cost). This change left a substantial number of patients without aneuploidy screening for approximately 3 years.

Given this event, our study objectives were twofold, namely (1) to measure the uptake rates of prenatal aneuploidy serum screening in a low-risk population at a Massachusetts community health center before and after the MassHealth policy change; and (2) to assess the cost-effectiveness of reimbursed screening with

that of nonreimbursed or limited screening for a similar hypothetical patient population. We hypothesized that the uptake of prenatal aneuploidy serum screening would decline following the MassHealth reimbursement changes. Furthermore, we expected that nonreimbursed or limited screening for aneuploidy in low-risk pregnant individuals would be considered cost-ineffective. Despite the longevity and ubiquity of prenatal screening for fetal aneuploidy in the United States, no previous studies have evaluated the change in uptake of aneuploidy screening as it relates to insurance reimbursement changes. Furthermore, no studies, apart from those evaluating subsequent noninvasive prenatal testing (NIPT), have determined the cost-effectiveness of aneuploidy screening in low-risk pregnant individuals.

Materials and Methods
Aneuploidy screening rates

Options for aneuploidy screening included multiple serum-based screens, such as the sequential or quad screen, and ultrasonography, including nuchal translucency measurements and anatomic surveys. To determine the rates of prenatal aneuploidy serum screening before and after the temporary discontinuation of MassHealth coverage for aneuploidy serum screening, we conducted a retrospective review of electronic medical records of Hispanic pregnant patients aged <35 years at an

academic CHC in northeastern Massachusetts that serves a 90% racial and/or ethnic minority population (88% Hispanic, primarily of Dominican origin) with 84% of that population living at or below the federal poverty level. Most individuals were best served by a language other than English and the majority preferred Spanish.

We did not include patients aged ≥ 35 years because alternative aneuploidy billing codes are used for this demographic. Although the ICD-10 classification system was implemented in October 2015 when the Medicaid reimbursement change for serum aneuploidy screening took effect, the health center did not immediately stop covering the costs of the screens until May 2016. We examined records of pregnant individuals with estimated delivery dates in September and October 2015 and September and October 2017 to ensure stability of practice patterns before and after the reimbursement change. A 2-month pre- and postpolicy change time period was selected given the month-to-month stability in frequency of new obstetrical visits and corresponding opportunities for prenatal screening. The insurance reimbursement gap lasted approximately 3 years. We collected patient information on age, gravidity, parity, aneuploidy screening uptake for the quad and sequential screens, invasive testing uptake, aneuploidy diagnoses, and insurance status (Table 1). All patients at this center were offered either a 2-part sequential screen or a quad screen as serum aneuploidy screening options. We assumed that patients underwent screening if they completed at least 1 of the 2 sequential screens or a quad screen.

We estimated the change in screening uptake relative to the change in out-of-pocket costs before and after the insurance reimbursement change by calculating the arc elasticity of demand. We subsequently incorporated the screening rates from this natural experiment into a decision-analytical model (described below) to assess the long-term tradeoffs of reimbursed aneuploidy screening (the screening rate

TABLE 1
Study site demographics

Characteristic	September and October 2015 cohort (n=80)	September and October 2017 cohort (n=112)
Age (y), mean±SD	25±4.8	25±4.8
Spanish-speaking	80 (100)	112 (100)
Medicaid insurance	80 (100)	112 (100)
Aneuploidy screening		
No	25 (31)	102 (91)
Yes	55 (69)	10 (9)
Sequential screen	42 (53)	7 (6)
Quad screen	13 (16)	3 (3)

The data are presented as number (percentage) except where noted.

SD, standard deviation.

Clifford. Aneuploidy screening: price elasticity and cost-effectiveness. *Am J Obstet Gynecol* 2023.

when MassHealth reimbursed this service) vs nonreimbursed or limited screening (the screening rate when MassHealth temporarily discontinued coverage of this service).

Markov model overview

Given the potential short- and long-term tradeoffs of covering aneuploidy screening for all individuals in early pregnancy, we created a Markov cohort simulation model that considered the long-term health and cost outcomes of aneuploidy screening in comparison with limited screening for a similar Hispanic pregnant population at a CHC. We chose a Markov model based on its flexibility to model repeated and longitudinal clinical events, its computational efficiency, and its interpretability. We varied the values for all variables, conducting both deterministic and probabilistic sensitivity analyses, and paid notable attention to the screening age, probability of elective abortion, and maternal health-related quality of life values. Clinical outcomes included T21 live births and therapeutic abortions for T21 diagnoses. Economic outcomes included discounted quality-adjusted life years, discounted lifetime medical costs (2020 US dollars), net health benefit, and incremental cost-effectiveness ratios.

Simulated individuals carried singleton pregnancies and were engaged in care throughout the duration of the model. We assumed that all euploid pregnancies were desired with no euploid pregnancies ending in termination. No pregnancies affected by T21 were terminated after an abnormal sequential or quad screening alone. Individuals in our model carried all pregnancies to term, and we did not allow individuals to re-enter the model during subsequent gestations. We discounted the costs and benefits using a 3% annual discount rate.

We constructed the model and performed analyses in TreeAgePro 2020 (TreeAge Software, LLC, Williamstown, MA). The model assumed a yearly time cycle, lifetime horizon, and a healthcare payer perspective on costs. We converted all cost data into 2020 US dollars using the US Bureau of Labor Statistics consumer price index.⁴

Model structure

Demography and cohort characteristics. We initiated a cohort of 10,000 pregnant individuals who established prenatal care in the first or second trimester, starting at an age of 25 years. This age corresponds to the average patient age observed at the CHC. We included cohorts of 18- and

34-year-old pregnant individuals in subsequent sensitivity analyses. The cohort experienced mortality as a function of age for each year in the model. Because our goal was to simulate a population that closely resembled the demographic characteristics of the CHC, we used US life tables for a Hispanic population (Appendix A).⁵

Serum aneuploidy screening. The base case model assumed a screening rate of 69% (the screening uptake at the CHC before the MassHealth policy change) and used 9% as the limited screening comparator (representing the screening rate postpolicy change). We assumed that despite differing rates of serum screening (ie, the sequential screen on quad-screen uptake) across the pre- and postpolicy screening interventions, all pregnant individuals underwent universal aneuploidy screening during a routine ultrasound. We further assumed that if serum screening or ultrasound findings were concerning for a diagnosis of T21, all individuals were offered follow-up with either an NIPT, invasive testing, or expectant management. Any patient with a false positive sequential screen or quad screen was also modeled to have the option for follow-up evaluation. We used a subsequent NIPT uptake probability of 0.43 specific to Hispanic women.⁶ Given the published sensitivity and specificity of NIPT for the detection of T21 of 100% and 99.9% respectively, we assumed both values were 100% and thus were not varied.⁷ All high-risk NIPT results were confirmed with either chorionic villus sampling or an amniocentesis as dictated by the gestational age. Procedure-related loss rates for chorionic villus sampling and amniocentesis^{8,9} and miscarriage and stillbirth rates for both euploid and T21 fetuses^{10–13} are listed in Table 2. Termination of pregnancy was only modeled after confirmation of T21 with chorionic villus sampling or amniocentesis.

Caring for a child affected by trisomy 21. To model the impact of caring for a child affected by T21, we incorporated the incremental maternal health-related

TABLE 2
Markov model inputs

Variable	Base case value	Range in sensitivity analysis	Distribution	Sources
Screening test probabilities ^a				
Sequential 1 sensitivity	0.85	0.8–0.9	Beta	14
Sequential 1 specificity	0.95	0.905–0.974	Beta	14
Sequential 2 sensitivity	0.95	0.91–0.97	Beta	14
Sequential 2 specificity	0.951	0.902–0.98	Beta	14
Quad screen sensitivity	0.81	0.74–0.9	Beta	14
Quad screen specificity	0.95	0.881–0.97	Beta	14
Ultrasound sensitivity	0.69	0.3–0.9	Beta	10
Ultrasound specificity	0.92	—	Beta	10
Procedure-related loss probabilities ^a				
Amniocentesis loss	0.0011	0.0011–0.0026	Beta	8,9
Chorionic villus sampling loss	0.0022	0.002–0.0116	Beta	8,9
Pregnancy outcome probabilities ^a				
Euploid spontaneous abortion (10–14 wk)	0.01	—	Beta	10
Euploid stillbirth	0.01	—	Beta	10
T21 SAB (CVS-amnio) age 18 & 25 y	0.04	0.02–0.04	Beta	11
T21 Stillbirth (amnio-term) age 18 & 25 y	0.19	0.14–0.27	Beta	11
T21 SAB (CVS-amnio) age 34 y	0.07	—	Beta	11
T21 Stillbirth (amnio-term) age 34 y	0.24	—	Beta	11
Spontaneous vaginal delivery	0.681	—	Beta	12
Cesarean delivery	0.319	—	Beta	12
Therapeutic abortion	0.3	0.13–0.3	Beta	13
Pregnancy outcome utility values				
Spontaneous abortion	0.76	0.590–0.930	Beta	15,16
Procedure-related loss	0.76	0.590–0.930	Beta	15,16
Therapeutic abortion	0.841	0.771–0.910	Beta	15,16
Stillbirth	0.76	0.590–0.930	Beta	15,16
T21 birth	0.645	0.480–0.810	Beta	15,16
Euploid birth	1.0	1.0–1.0	Beta	15,16
Screens and tests ^b				
Amniocentesis	\$625.16	—	Gamma	17,18
Anatomy scan physician fee	\$195.58	—	Gamma	17,18
Maternal-fetal medicine consultation physician fee	\$174.22	—	Gamma	17,18
Chorionic villus sampling	\$395.44	—	Gamma	17,18
Noninvasive prenatal testing	\$789.99	—	Gamma	18
Quad screen	\$91.99	—	Gamma	18
Sequential screen #1	\$169.08	—	Gamma	18
Sequential screen #2	\$91.99	—	Gamma	18
Procedures ^b				

Clifford. Aneuploidy screening: price elasticity and cost-effectiveness. *Am J Obstet Gynecol* 2023.

(continued)

TABLE 2
Markov model inputs (continued)

Variable	Base case value	Range in sensitivity analysis	Distribution	Sources
Spontaneous abortion	\$549.39	—	Gamma	19
Therapeutic abortion 14–20 wk	\$722.76	—	Gamma	19
Therapeutic abortion >20 wk	\$3395.26	—	Gamma	19
Stillbirth induction of labor	\$7206.24	—	Gamma	20
Delivery (weighted)	\$7910.73	—	Gamma	20
Insurance ^b				
Incremental payer costs of T21 care over 18 years	\$196,908.67	—	Gamma	21

Amnio, amniocentesis; *CVS*, chorionic villus sampling; *SAB*, spontaneous abortion; *T21*, trisomy 21.

^a Probabilities were defined as the false-positive rate and false-negative rate of Seq 1 and Seq 2 and Quad screens also varied in the sensitivity analysis; ^b Costs in 2020 US dollars, range probabilistic Clifford. *Aneuploidy screening: price elasticity and cost-effectiveness. Am J Obstet Gynecol* 2023.

quality of life impacts^{15,16} and added the present value of excess healthcare costs attributable to a baby born with T21 in the model.²¹ We added the latter cost value onto the mother's overall costs, which was a conservative estimate spanning up to 18 years of costs borne, derived from a United States public payer expenditure for cohorts of children with T21 and matched controls.²¹

We obtained a lower bound T21 utility value using a time tradeoff metric obtained from a diverse group of pregnant individuals presenting for care at the University of California, San Francisco prenatal care clinic and prenatal diagnosis center and the San Francisco General Hospital prenatal care clinic¹⁶ and a higher bound value using a standard gamble metric taken from a diverse group of 1084 individuals presenting for care in the San Francisco Bay Area.¹⁵ The 0.645 value used in the base case was the median of these 2 values. We assumed live-term euploid births had a utility value of 1 (utility of 1 = perfect health).

Model data

Probabilities. We obtained model input probabilities for aneuploidy screens and tests,^{10,14} procedure-related losses,^{8,9} and pregnancy outcomes from published literature,^{10–13} including meta-analyses and cohort studies (Table 2). We varied the age-related risk for T21

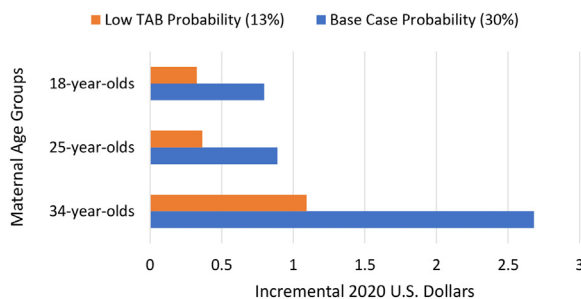
by maternal age cutoff points of 18, 25, and 34 years, the latter of which is the last year before a woman is considered to be of advanced maternal age and at higher risk for aneuploidy. Our base case model included probabilities corresponding to 25-year-olds; therefore, the risk for T21 included in the base case was 1 per 1030 (for 18 year-olds, 1 per 1150; and for 34 year-olds, 1 per 310).²² Given the difference in spontaneous loss rates observed in euploid and T21 pregnancies, we also incorporated these rates into the model.^{10,11} We chose a termination probability of 30% for our base case, which represents the estimated T21 termination rate in the Northeast region of the United States, and varied this in the sensitivity analyses.¹³

Quality of life values. We assigned utility values for the health states in the model, which were estimated from both direct and indirect utility measures, including time tradeoff and standard gamble measures. We applied utilities associated with pregnancy events including spontaneous abortions, procedure-related losses, therapeutic abortions, stillbirths, and euploid births.^{15,16} We employed the EuroQoL–5 Dimension scale for general age-based utility decrements over time. In every simulation year, the cohort experienced mortality as a function of age, weighted for increased comorbidity over time.²³ For

mothers delivering an infant with T21, we multiplied the T21 utility, as detailed above, by the non-T21 maternal age-related utilities for 18 years before transitioning to solely maternal age-related utilities (Appendix B). We varied the application of the T21 utility in sensitivity analyses from 1 to 56 years (Figure 1).

Costs. We derived healthcare costs from a healthcare payer perspective to reflect the temporary Medicaid coverage disruption at the CHC. We modeled costs that would differ across interventions, which were mostly incurred within the initial model cycle (during pregnancy) and included those associated with screening, ultrasound, maternal-fetal medicine physician fees, invasive testing, termination procedures, and delivery fees (Table 2).^{17–20} We included costs of tests or procedures with multiple components by summing individual cost components (eg, we obtained the cost of a quad screen by summing the cost of the individual component analytes, namely alpha-fetoprotein, total beta-human chorionic gonadotropin, estriol, and inhibin A). We calculated the total delivery costs by adding the weighted cost of vaginal delivery with the weighted cost of a cesarean section given that vaginal deliveries account for approximately two-thirds of total deliveries in the United States.¹² We added excess

FIGURE 1
Sensitivity analysis of the incremental effectiveness of screening



The horizontal axis displays the incremental effectiveness of screening when compared with limited screening. The vertical axis displays the maternal age groups that were evaluated. Combinations of varied trisomy 21 utility values and applied duration of the utility values were plotted. The base case analysis included the utility value of 0.645 applied to the mother's life years for 18 years.

TAB, therapeutic abortion; T21, trisomy 21.

Clifford. Aneuploidy screening: price elasticity and cost-effectiveness. *Am J Obstet Gynecol* 2023.

healthcare costs attributable to caring for a child with T21 to the mothers' overall costs in the model.

Analyses

We simulated the lifetime progression of each cohort of pregnant individuals. We assessed key clinical outcomes and calculated the incremental cost-effectiveness ratios by dividing the incremental cost of the limited screening option in comparison with screening by their incremental effectiveness for each age group. We deemed an intervention to be cost-effective if it fell below the conventional United States willingness to pay a threshold of \$100,000 per quality-adjusted life year gained. We considered an intervention to be cost-saving if an intervention both reduced the costs and proved to be more effective than the alternative. We calculated the net health benefit of screening by taking the incremental cost divided by the opportunity cost threshold of \$100,000 and subtracting this from the incremental gain in quality-adjusted life years. A positive net health benefit value corresponds to an increase in overall population health owing to the intervention.

Sensitivity analyses

To test model robustness, we performed sensitivity analyses by varying values for all variables in our model, notably focusing on screening age, elective

abortion probability, and maternal health-related quality of life values. In 1-way sensitivity analyses, we varied screening test sensitivities and specificities, pregnancy outcome probabilities, and utilities. Specifically, we varied the sensitivity and specificity of sequential screens, quad screens, NIPT, ultrasound, chorionic villus sampling loss rates, amniocentesis loss rates, and T21 loss rates. In addition, we varied utilities associated with procedure losses, spontaneous abortions, stillbirths, and therapeutic abortions.

Of note, we varied the utility associated with the birth of an infant affected by T21 to the extremes of published ranges, namely from 0.48 to 0.81,^{15,16} and applied those utilities to the mother's life years for 18 years before transitioning to maternal age-related utilities not impacted by T21. We further varied the duration of time that we applied the utility value to the mother's life tables. For example, we applied a utility decrement for caring for a child with T21 in the first year of life (0.645, derived by time tradeoff and standard gamble metrics), which is often medically intensive.²¹ Next, we applied this same utility for 56 years (our higher-end estimate), which is the average life expectancy of a person affected by T21.

Lastly, we performed probabilistic sensitivity analyses using a beta distribution to define probability density

functions around all probability parameters and a gamma distribution for all cost variables in our model.

Local institutional review board (IRB) approval was obtained before initiation of the study, which conforms to recognized standards contained in the US Federal Policy for the Protection of Human Subjects. The IRB granted a waiver of informed consent because of the retrospective nature of the initial portion of the study.

Results

Family health center cohort

A total of 80 individuals with estimated delivery dates in September and October 2015 and 112 individuals with delivery dates in September and October 2017 received prenatal care at the CHC. All pregnant individuals were Spanish-speaking and insured through Medicaid. The mean age of the pregnant individuals who presented for care in 2015 and 2017 did not differ and was 25 ± 4.8 years. A total of 55 individuals (69%) underwent a quad or sequential screen in 2015 before the MassHealth policy change in comparison with 10 individuals (9%) in 2017 after the policy change (Table 1). Those who underwent screening postpolicy change had to pay \$105 out-of-pocket at the time of laboratory sample collection. Estimating the average percentage change in both quantity and price from before and after the reimbursement change, for every 10% change in price, the demand for screening was reduced by 7.7%, indicating general price inelasticity.

Simulation model (base case)

Because the change in Medicaid reimbursement inspired our cost-effectiveness analysis, 25 years was selected as the base case age. The base case model assumed a screening rate of 69% and a limited screening comparator of 9%. In our base case analysis, there were fewer T21 live births and more therapeutic abortions for a T21 diagnosis in the screening strategy when compared with the limited screening strategy period (Table 3). The screening strategy provided better overall outcomes at a lower cost per quality-

TABLE 3**The base case model selected clinical and economic outcomes by age group**

Age	Strategy	T21 live births per 10,000 individuals	T21 therapeutic abortions per 10,000 individuals	Discounted cost per individual ^a	Effectiveness per individual	Incremental cost-effectiveness ratio	Net health benefit
18	Screening	5.69	1.00	\$8348.34	24.892768	N/A	N/A
	Limited screening	6.00	0.95	\$8349.14	24.892750	N/A	N/A
	Incremental	N/A	N/A	\$0.80	0.000018	Cost-saving	0.000026
25	Screening	6.66	1.12	\$8361.91	23.522149	N/A	N/A
	Limited screening	6.70	1.06	\$8362.80	23.522129	N/A	N/A
	Incremental	N/A	N/A	\$0.89	0.000020	Cost-saving	0.000029
34	Screening	20.09	3.66	\$8620.91	21.439041	N/A	N/A
	Limited screening	20.23	3.48	\$8623.60	21.438982	N/A	N/A
	Incremental	N/A	N/A	\$2.68	0.000059	Cost-saving	0.000085

N/A, not applicable; T21, trisomy 21.

^a 2020 US dollars.

Clifford. Aneuploidy screening: price elasticity and cost-effectiveness. *Am J Obstet Gynecol* 2023.

adjusted life year gained than the limited screening strategy (Table 3). The screening strategy extended quality-adjusted life expectancy by 0.2 per 10,000 individuals and saved an incremental cost of \$0.89 per woman (or \$8900 total cost-savings for 10,000 individuals in our cohort). Therefore, screening was considered cost-saving (Figure 2) when compared with limited screening and was associated with a net health benefit of 0.000029 (Table 3).

Sensitivity analyses

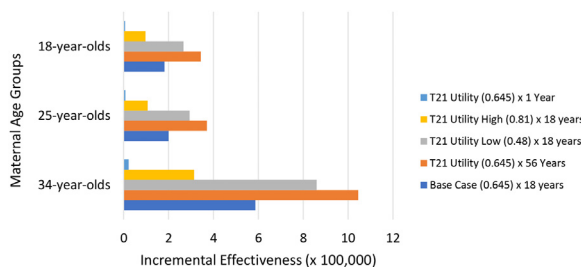
In all modeled analyses, the results remained cost-saving across all age groups. For 18-year-olds, the screening strategy yielded a slightly lower quality-adjusted life expectancy and incremental costs saved when compared with the base case (25-year-olds) but was still considered a cost-saving intervention (Table 3, Figure 2). The highest cost savings and health benefits associated with screening occurred among 34-year-olds among whom there was a

higher risk for a T21 birth, yielding an incremental 0.59 quality-adjusted life years per 10,000 individuals—a total cost-savings of \$26,800 for 10,000 individuals and a positive net health benefit of 0.000085 (Table 3, Figure 2).

When we varied the probability of a therapeutic abortion for a T21 diagnosis from 30% in the base case to 13%, the lowest reported probability in the literature,^{13,24} the lower probability decreased the incremental cost savings of the screening strategy when compared with the limited screening strategy (Figure 3). However, the result remained cost-saving across all age groups. In our sensitivity analyses of the T21 utility impact, changing both the number of years in which T21 impacted the mother and the utility value from 0.48 to 0.81 changed our conclusions minimally; in all scenarios, screening remained cost-saving (Figures 1 and 3). In our probabilistic sensitivity analyses for our base case scenario, screening was preferred in 100% of 1000 simulations at all willingness-to-pay thresholds (Figure 2, Appendix C).

FIGURE 2

Probabilistic cost-effectiveness plane for screening vs limited screening in 25-year-olds, 18-year-olds, and 34-year-olds



The horizontal axis displays incremental quality-adjusted life years. The vertical axis displays incremental costs in 2020 US dollars. Simulated incremental cost-effectiveness ratios were potted and were all cost-saving.

T21, trisomy 21.

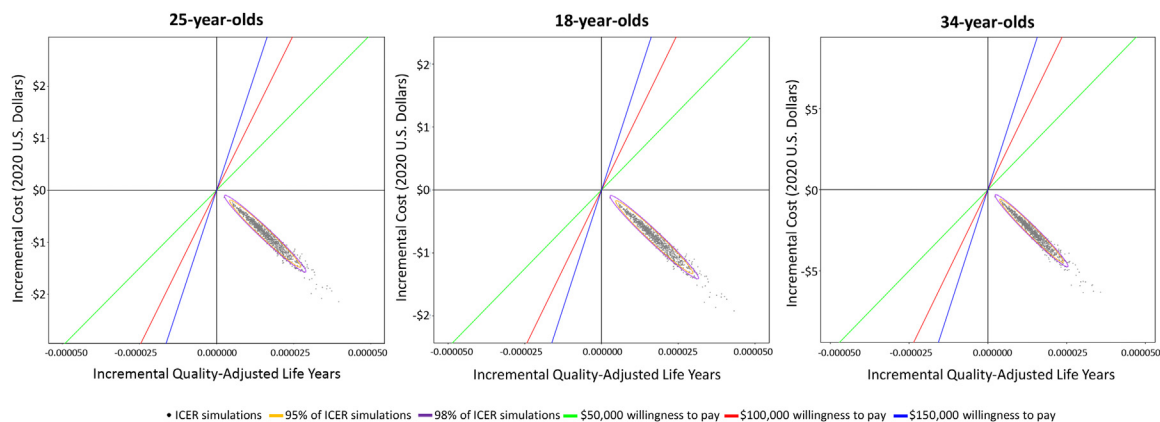
Clifford. Aneuploidy screening: price elasticity and cost-effectiveness. *Am J Obstet Gynecol* 2023.

Discussion

Principal findings

This study found that aneuploidy screening rates in a low-risk Hispanic

FIGURE 3
Incremental cost savings of screening in comparison with limited screening based on probability of therapeutic abortion for a trisomy 21 diagnosis



TAB probability for a T21 diagnosis was varied from 30-13%.

ICER, incremental cost-effectiveness ratio; TAB, therapeutic abortion.

Clifford. Aneuploidy screening: price elasticity and cost-effectiveness. *Am J Obstet Gynecol* 2023.

population were influenced by changes in cost, although it remained price inelastic overall, and that insurance reimbursement of aneuploidy screening in our modeled population is cost-saving.

Results

We found that in all modeled cohorts in our decision analytical model, insurance reimbursement for aneuploidy screening is cost-saving (ie, it is associated with lower incremental costs and higher benefits) when compared with non-reimbursement (ie, limited screening). In all sensitivity analyses, Medicaid reimbursement for screening remained cost-saving even when using the lowest published termination rate of 13% in the lowest-risk age category of 18-year-olds. This result was likely because of the low cost of aneuploidy screening and the high cost of T21 care. In nearly all instances, increasing maternal age was associated with increasing incremental effectiveness of reimbursed screening. This finding makes intuitive sense because aneuploidy risk increases with maternal age and reimbursed screening identifies more fetuses affected by T21, thereby allowing the option of termination.

Clinical implications

Modifications in reimbursement policies by insurers can lead to unintended consequences for medical tests and services.^{25,26} The extent of these consequences depends, in part, on the price elasticity of these tests and services. The finding of price inelasticity in our study may suggest the value-driven nature of aneuploidy screening and its ability to provide insight into potentially life-altering changes in family structure. However, in this particular instance, the unintentional policy change had a marked impact on aneuploidy screening rates at a CHC that served a Hispanic population in northeastern Massachusetts. Although decreased insurance reimbursement may save insurers money in the short term, the long-term costs may exceed any short-term savings.

Despite the increased use of NIPT, traditional serum-based aneuploidy screening is still used because of provider familiarity with the modality, low cost, and benefit in certain clinical scenarios like vanishing twin pregnancies. In 2020, traditional serum-based screens were used for 1.1 million pregnancies, whereas NIPT was used for nearly 1.5 million pregnancies in the United States.²⁷ Although cost-

effectiveness analyses have been performed for NIPT in low-risk populations insured by public payers, NIPT is generally not cost-effective.²⁸ NIPT list prices can vary widely from \$1100 to \$1590 depending on the laboratory used, and self-pay options ranged from \$299 to \$349.²⁹ Furthermore, the cost of NIPT is perceived to be a major barrier in countries that do not offer public funding, like India and parts of China.³⁰ In India, where no public prenatal screening program exists, the cost of NIPT represents up to 10% of the average annual income per capita.³⁰ Given our finding that an out-of-pocket cost of just \$105 can alter individual screening preferences, it is important to ensure that all pregnant individuals have screening options that are either fully reimbursed or affordable.

Research implications

Given that our study was inspired by a natural experiment related to the implementation of the ICD-10 at a CHC serving a Hispanic population, additional research is needed to determine whether the price elasticity and cost-effectiveness findings apply to other populations with potentially different cultural and religious beliefs.

Strengths and limitations

Our study has limitations. First, the studied patient population is primarily of Dominican origin, potentially limiting the generalizability of the observed change in aneuploidy screening rates from 2015 to 2017. In addition, the model is limited to T21 and does not include trisomy 13 or trisomy 18, which were excluded because of the relative rarity of these disorder when compared with T21 and the severely shortened lifespans associated with these disorders. Furthermore, the utilities and metrics used in this study do not reflect the complete value of human life. Although our model did not simulate live births, we incorporated evidence-based disutility values associated with T21 from a mother's caregiving perspective. Although we varied these values in sensitivity analyses, they do not reflect the full spectrum of values that a woman might associate with a T21 birth (eg, including cases that reflect zero disutility associated with a T21 birth). Furthermore, we took a conservative approach when estimating T21 care by applying incremental care costs for up to 18 years only. Although this is likely an underestimation of the lifetime costs associated with T21 care, accounting for these incremental costs over the lifetime of an individual with T21 would lead to increased incremental cost savings in the screening strategy. Limiting our analysis to a payer perspective also underestimates the true societal costs of nonreimbursed or limited screening.

Despite these limitations, our study examined the price elasticity and cost-effectiveness of traditional modes of aneuploidy screening in low-risk pregnant individuals. We demonstrated that traditional modes of aneuploidy screening are cost-effective and that a lack of insurance reimbursement leads to decreases in screening rates in a vulnerable population at an increased cost to payers.

Conclusion

In our study, we found that aneuploidy screening rates were influenced by reimbursement changes with rates dropping from 69% before the

MassHealth reimbursement change to 9% after the change took place. Our simulation model demonstrated that reimbursing aneuploidy screening for Hispanic pregnant individuals younger than 35 years of age was cost-saving, that is, it led to lower incremental costs and higher quality of life when compared with nonreimbursement. This study serves as an example of the unintended consequences that can accompany even short-term policy changes. ■

Supplementary materials

Supplementary material associated with this article can be found in the online version at [doi:10.1016/j.xagr.2023.100293](https://doi.org/10.1016/j.xagr.2023.100293).

REFERENCES

1. The American College of Obstetricians and Gynecologists. Prenatal diagnostic testing for genetic disorders. 2016. Available at: <https://www.acog.org/en/clinical/clinical-guidance/practice-bulletin/articles/2016/05/prenatal-diagnostic-testing-for-genetic-disorders>. Accessed December 29, 2021.
2. Kowalcek I. Stress and anxiety associated with prenatal diagnosis. *Best Pract Res Clin Obstet Gynaecol* 2007;21:221–8.
3. Hall S, Bobrow M, Marteau TM. Psychological consequences for parents of false negative results on prenatal screening for Down's syndrome: retrospective interview study. *BMJ* 2000;320:407–12.
4. US Bureau of Labor Statistics. CPI inflation calculator. Available at: https://www.bls.gov/data/inflation_calculator.htm. Accessed December 29, 2021.
5. Arias E, Xu J. United States life tables, 2018. *Natl Vital Stat Rep* 2020;69:1–45.
6. Chetty S, Garabedian MJ, Norton ME. Uptake of noninvasive prenatal testing (NIPT) in women following positive aneuploidy screening. *Prenat Diagn* 2013;33:542–6.
7. Norton ME, Jacobsson B, Swamy GK, et al. Cell-free DNA analysis for noninvasive examination of trisomy. *N Engl J Med* 2015;372:1589–97.
8. Odibo AO, Gray DL, Dicke JM, Stamilio DM, Macones GA, Crane JP. Revisiting the fetal loss rate after second-trimester genetic amniocentesis: a single center's 16-year experience. *Obstet Gynecol* 2008;111:589–95.
9. Akolekar R, Beta J, Picciarelli G, Ogilvie C, D'Antonio F. Procedure-related risk of miscarriage following amniocentesis and chorionic villus sampling: a systematic review and meta-analysis. *Ultrasound Obstet Gynecol* 2015;45:16–26.
10. Biggio Jr JR, Morris TC, Owen J, Stringer JSA. An outcomes analysis of five prenatal screening strategies for trisomy 21 in women

younger than 35 years. *Am J Obstet Gynecol* 2004;190:721–9.

11. Savva GM, Morris JK, Mutton DE, Alberman E. Maternal age-specific fetal loss rates in Down syndrome pregnancies. *Prenat Diagn* 2006;26:499–504.
12. Martin JA, Hamilton BE, Osterman MJ, Driscoll AK. Births: final data for 2018. *Natl Vital Stat Rep* 2019;68:1–47.
13. de Graaf G, Buckley F, Skotko BG. Estimates of the live births, natural losses, and elective terminations with Down syndrome in the United States. *Am J Med Genet A* 2015;167A:756–67.
14. Ball RH, Caughey AB, Malone FD, et al. First- and second-trimester evaluation of risk for Down syndrome. *Obstet Gynecol* 2007;110:10–7.
15. 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;96:511–6.
16. Kaimal AJ, Norton ME, Kuppermann M. Prenatal testing in the genomic age: clinical outcomes, quality of life, and costs. *Obstet Gynecol* 2015;126:737–46.
17. CMS.gov. Search the physician fee schedule. Available at: <https://www.cms.gov/medicare/physician-fee-schedule/search>. Accessed December 29, 2021.
18. CMS.gov. Clinical Laboratory fee schedule. Available at: <https://www.cms.gov/medicare/medicare-fee-for-service-payment/clinical-labfeesched>. Accessed December 29, 2021.
19. Roberts SCM, Gould H, Kimport K, Weitz TA, Foster DG. Out-of-pocket costs and insurance coverage for abortion in the United States. *Womens Health Issues* 2014;24:e211–8.
20. Truven Health Analytics. The cost of having a baby in the United States. Available at: <https://www.catalyze.org/product/2013-cost-baby-united-states/>. Accessed August 16, 2021.
21. Kageleiry A, Samuelson D, Duh MS, Lefebvre P, Campbell J, Skotko BG. Out-of-pocket medical costs and third-party healthcare costs for children with Down syndrome. *Am J Med Genet A* 2017;173:627–37.
22. Messerlian GM, Palomaki GE, Wilkins-Haug SEL, Barss DEV. Down syndrome: overview of prenatal screening. UpToDate. 2021. Available at: <https://www.uptodate.com/contents/down-syndrome-overview-of-prenatal-screening/print?search=Down>. Accessed August 16, 2021.
23. Nyman JA, Barleen NA, Dowd BE, Russell DW, Coons SJ, Sullivan PW. Quality-of-life weights for the US population: self-reported health status and priority health conditions, by demographic characteristics. *Med Care* 2007;45:618–28.
24. Presson AP, Partyka G, Jensen KM, et al. Current estimate of Down syndrome

population prevalence in the United States. *J Pediatr* 2013;163:1163–8.

25. Mookherjee S, Vidyarthi AR, Ranji SR, Maselli J, Wachter RM, Baron RB. Potential unintended consequences due to Medicare's "no pay for errors" rule? A randomized controlled trial of an educational intervention with internal medicine residents. *J Gen Intern Med* 2010;25:1097–101.

26. Song Z, Ayanian JZ, Wallace J, He Y, Gibson TB, Chernew ME. Unintended consequences of eliminating medicare payments for

consultations. *JAMA Intern Med* 2013;173:15–21.

27. Lepage N, Wyatt P, Ashwood ER, Best RG, Long T, Palomaki GE. Prenatal serum screening for Down syndrome and neural tube defects in the United States: changes in utilization patterns from 2012 to 2020. *J Med Screen* 2021;28:405–10.

28. Xie X, Wang M, Goh ESY, et al. Noninvasive prenatal testing for trisomies 21, 18, and 13, sex chromosome aneuploidies, and microdeletions in average-risk

pregnancies: a cost-effectiveness analysis. *J Obstet Gynaecol Can* 2020;42:740–9. e12.

29. Benoy ME, Iruretagoyena JI, Birkeland LE, Petty EM. The impact of insurance on equitable access to non-invasive prenatal screening (NIPT): private insurance may not pay. *J Community Genet* 2021;12:185–97.

30. Ravitsky V, Roy MC, Haidar H, et al. The emergence and global spread of noninvasive prenatal testing. *Annu Rev Genomics Hum Genet* 2021;22:309–38.