



California Cardiovascular Screening Tool: Findings from Initial Implementation

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Am J Perinatol Rep 2020;10:e362–e368.

Abstract

Objective American College of Obstetricians and Gynecologists (ACOG) recently published the California (CA) cardiovascular disease (CVD) screening algorithm for pregnant and postpartum women. We aim to prospectively determine screen-positive and true-positive rates of CVD among women across two populations.

Study Design This is a prospective cohort study of obstetrical patients from April 2018 to July 2019 at academic medical centers in CA and New York (NY). We attempted to screen all patients at least once during their pregnancy care (prenatal or postpartum). Women who screened positive (“Red Flags,” >3–4 moderate risk factors, abnormal physical examination, and persistent symptoms) underwent further testing. The primary outcome was the screen-positive rate. Secondary outcomes included the true-positive rate and the strength of each moderate factor in predicting a positive CVD screen.

Results We screened 846 women. The overall screen-positive rate was 8% (5% in CA vs. 19% in NY). The sites differed in ethnicity, that is, African American women (2.7% in CA vs. 35% in NY, $p < 0.01$) and substance use (2.7 vs. 5.6%, $p < 0.04$). The true-positive rate was 1.5% at both sites. The percentage of screen-positive patients who did not complete follow-up studies was higher in NY (70%) than in CA (27%). CVD was confirmed in 30% with positive screens with complete follow-up. Combinations of moderate factors were the main driver of screen-positive rates in both populations.

Conclusion This is the first data describing the performance of the CVD screening algorithm in a general obstetric population. Factors, such as proportion of African American women affect the likelihood of a positive screen. The screening algorithm highlights patients at higher lifetime risk of CVD and may identify a group that could be targeted for more direct care transitions postpartum. Data may be used to design a larger validation study.

Keywords

- ▶ cardiovascular disease in pregnancy
- ▶ cardiovascular screening in pregnancy
- ▶ cardiovascular disease prediction in pregnancy
- ▶ maternal mortality

Cardiovascular disease (CVD) has emerged as the leading cause of maternal mortality in the United States, accounting for almost 30% of all pregnancy-related deaths.^{1,2} In a review of pregnancy-related cardiovascular deaths in California (CA), only a small fraction of these women (3.1%) had known,

previously diagnosed CVD even though most women who died had presented with symptoms either during pregnancy or postpartum.³ The top three contributing provider factors identified in these deaths included delayed response, ineffective care, and misdiagnosis.³ CVD is also a leading cause of

received
February 20, 2020
accepted after revision
May 13, 2020

DOI <https://doi.org/10.1055/s-0040-1718382>.
ISSN 2157-6998.

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death for women in their lifetime and pregnancy as a window for future cardiovascular health has emerged as an important opportunity.^{4,5} These findings all highlight the potential opportunity for a standardized screening algorithm, performed during pregnancy, to identify women at higher risk, elevate provider consciousness regarding potential CVD and cardiovascular evaluation, and help prioritize how quickly and with whom patients have appropriate postpartum care.

In addition, African American women have a three- to four-fold greater risk of maternal mortality than women of other racial groups, as well as a higher rate of both preexisting CVD, and peripartum cardiomyopathy.³ The CDC has advocated standardized assessments as one modality to attempt to reduce this disparity.⁶

To this end, the California Maternal Quality Care Collaborative (CMQCC) released a CVD screening algorithm as a resource for obstetric providers to help stratify and guide the initial evaluation of symptomatic or high-risk pregnant or postpartum women (→ Fig. 1).⁷ This screening algorithm was retrospectively validated within a cohort of women who died of pregnancy-related CVD, estimating that the algorithm would have identified 88% of cases⁷; however we describe its use in a broader population of pregnant women. We piloted the screening algorithm in two academic medical centers: University of California (UCI), Irvine and Einstein/Montefiore Medical Center (MMC), the Bronx, NY. Our primary outcome was the rate of positive screens in these two populations. Secondary outcomes included the rate of “true-positive” CVD confirmed by follow-up testing (echocardiogram, telemetry, or cardiology assessments). We investigate the algorithm’s moderate factors to determine which were most predictive of positive screens and true-positive results.

Methods

Patients were prospectively screened with the algorithm at UCI from April 2018 and July 2019 and at Einstein/MMC from September 2018 to December 2018. The studies at each site were institutional review board (IRB) approved at their respective institution. The only exclusion criterion was a history of CVD known prior to pregnancy. At UCI, the coinvestigators trained clinicians in the use of the algorithm and instructed them to consecutively screen all pregnant or postpartum patients receiving care at least once during their pregnancy or postpartum course. Screening occurred at outpatient prenatal clinics, on labor and delivery, triage, antepartum and postpartum units, and providers were instructed to document the screen for all women under their care within the computer-based medical record.

At Einstein/MMC, the coinvestigators trained two research associates to administer the screening at an outpatient general obstetric prenatal practice consecutively screening all initial obstetrics or postpartum patients, as well as eligible patients, in triage and postpartum wards depending on associate availability.

At both institutions, additional assessments or consultations were ordered based on the algorithm. In CA, patient providers conducted the screening and ordered the follow-up testing. In New York (NY), the research associates conducted the screening and subsequently ordered initial testing on all screen-positive patients. In addition, in NY, all screen-positive patients were referred to a joint Maternal Fetal Medicine (MFM)/cardiology clinic for testing beyond electrocardiogram (ECG) and brain natriuretic peptide (BNP). The study did not provide additional follow-up to assist participants in pursuing recommended care; however, in

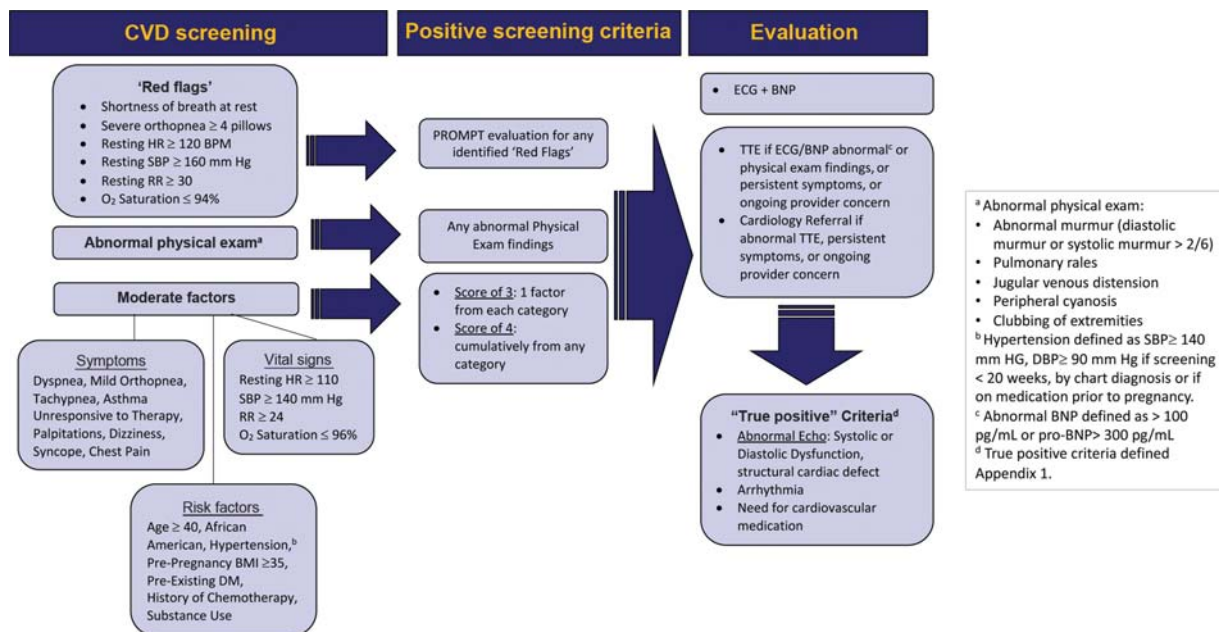


Fig. 1 CVD screening, evaluation, and initial management Toolkit. BNP, brain natriuretic peptide; CVD, cardiovascular disease; DBP, diastolic blood pressure; DM, diabetes mellitus; ECG, echocardiogram; HR, heart rate; RR, respiratory rate; SBP, systolic blood pressure; TTE, transthoracic echocardiogram.

NY, patients were reminded at least once regarding testing that had been ordered.

Demographic and comorbidity data, as well as the results of follow-up testing, in screen-positive patients were collected retrospectively from the electronic health records. Data sets were deidentified for analysis.

The primary outcome was the proportion of women identified as a positive screen either by red flag criteria such as resting heart rate (HR) > 120 beats per minute (BPM) or O₂ saturation < 94% (►Fig. 1), abnormal physical exam findings, persistent self-reported symptoms, or combinations of moderate factors (a score of three with one point in each category: risk factors, vital signs, symptom, or a score of four moderate factors in any category; ►Fig. 1). Patients with prior CVD under the care of a cardiologist were excluded. A total of 15 risk factors (►Fig. 1) were recorded for every patient.

We recorded whether a screen-positive patient had studies as recommended by the algorithm and whether “true cardiac disease” was uncovered. Criteria for true cardiac disease included systolic or diastolic dysfunction, ventricular dilation, or hypertrophy, pathologic arrhythmia confirmed by cardiology, pulmonary hypertension, valvular abnormality, or the initiation of a cardiac medication which would not have been indicated by blood pressure criteria alone (►Supplementary Table S1, available online only).

Univariate regression was performed among positive screen patients to determine the strength of association of the predictor variables with a positive screen. Patients with positive screens who did not have sufficient follow-up to determine if they had true CVD were excluded from this analysis.

Multivariate logistic regression using stepwise selection was performed to determine which moderate factors were most predictive of a positive screening result.

Demographics, comorbidity data, and screen-positive rates between the two sites were compared by the paired *t*-test for continuous variables (age) and Chi-square testing or Fisher’s exact test for categorical variables.

Results

A total of 846 women (648 in CA and 198 in NY) were screened with the algorithm throughout the study period (►Fig. 2). At both sites, this represented approximately 30% of the target population during the screening period. The overall screen-positive rate was 8.3%; however, differed by site (CA, 5.2% vs. NY, 18.5%; *p* < 0.01). The overall true-positive rate was 1 to 1.5% at each site; however, 70% of screen-positive patients in NY did not have sufficient study follow-up to determine if they had true-positive cardiac results (vs. 27% in CA). Among screen-positive patients who had sufficient follow-up, true CVD was found in 41.7% of screen-positive patients in CA and 18.2% in NY. Cardiac testing including ECGs, BNP assessment, and either ECG, Holter monitoring, or cardiology assessments were performed in 62, 54, and 28% of the positive screens (*n* = 69), respectively (►Table 1). Almost 60% of the ECGs were ordered in cases where either the ECG or BNP was abnormal; however, the remainder were ordered in cases of ongoing provider concern despite otherwise normal testing. Likewise, 50% of cardiology consultations were performed based on ongoing provider concern despite normal ECG or BNP.

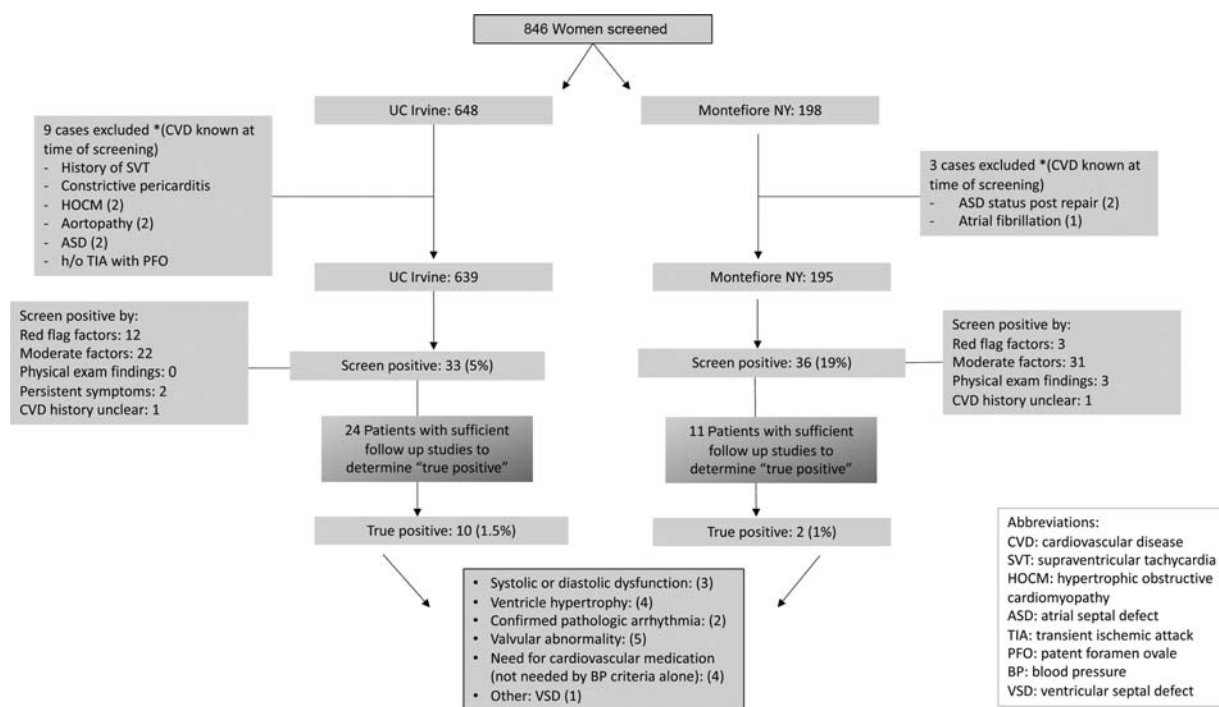


Fig. 2 Case selection. ASD, atrial septal defect; BP, blood pressure; CVD, cardiovascular disease; HOCM, hypertrophic obstructive cardiomyopathy; NY, New York; PFO, patent foramen ovale; SVT, supraventricular tachycardia; TIA, transient ischemic attack; UC, University of California; VSD, ventricular septal defect.

Table 1 List of follow-up studies performed on patients with a positive cardiovascular screen ($n = 69$)

Follow-up study	Tests performed
ECG	(43/69) 62.3%
BNP	(37/69) 53.6%
ECG + BNP	(31/69) 44.9%
Echocardiogram ^a	(19/69) 27.5%
Cardiology consultation ^a	(10/69) 14.5%

Abbreviations: BNP, brain natriuretic peptide; ECG, electrocardiogram.
^aSee ►**Fig. 1** (screening algorithm). If ECG and BNP were within normal limits, no additional testing was recommended unless there were physical exam findings, persistent symptoms, or ongoing provider concern.

Demographic and comorbidity data are shown in ►**Table 2**. NY had significantly more African American women in the screening population (35% in NY vs. 2.7% in CA, $p < 0.01$). NY also had more patients with active substance use at the time of screening (5.6 vs. 2.7%, $p < 0.04$). CA had higher rates of obesity than NY (33 vs. 24%, $p = 0.02$). There were differences between the sites in terms of when the screening was conducted. In CA, 61% of the screens were conducted in the antepartum setting versus 39% in NY. Additionally, 25% of NY screens were conducted in patients over 1 week postpartum (vs. 7% in CA). This difference was also substantial within the group of patients with positive screens. In CA, 12% (4/33) women with positive screens were in the intrapartum/postpartum period versus 56% (20/36) of women with positive screens in NY.

Red flags made up 20% of screen-positive patients (►**Fig. 3**); however, over 50% of these cases would have been screen positive by moderate factors as well. The majority of screen-positive results overall came from combinations of moderate factors, the large majority being from a score of 4 or more. Multivariate regression revealed that O_2 saturation less than 97% and symptoms of dyspnea were the two strongest factors associated with a positive CVD screen (►**Table 3**). Using stepwise selection including demographic variables, among all moderate factors and institution, 12 moderate factors were identified as most predictive of a positive CVD screen (C statistic = 0.98). True-positive cardiac results found in the course of the study are listed in ►**Table 4**. No factors were found to be associated with false-positive screens within the cohort of screen-positive patients who had sufficient follow-up to determine true versus false-positive CVD status.

Discussion

This is the first data describing the performance of the California CVD screening algorithm in a general obstetric population. Our data suggest that the screen-positive rate can vary significantly across populations, and demographic factors, such as the proportion of African American women in the population, affect the likelihood of a positive screen. The algorithm gives additional weight to race, given that the pregnancy mortality rate for African Americans is three to

four times higher than for whites nationally⁶ and in CA, it was shown to be eight times higher in cardiovascular pregnancy mortality.³ An important limitation of our findings is the loss of follow-up testing between those with positive screening and completion of the recommended evaluation, making it difficult to draw conclusions about the true-positive rate and whether a higher proportion of African American women in a population translates into a population with truly higher disease burden versus higher rates of false positive screening. We anticipate, given the known higher rates of maternal and cardiovascular mortality among African American women, that the differences in true-positive rates between CA and NY were secondary to the significant difference in follow-up testing between the two populations; however, this remains a limitation of the study.

The lost to follow-up studies was substantially higher in NY than CA (70 vs. 27%, respectively). In both settings, initial ECG and BNP were ordered at the time of the positive screen; however, in CA, the screening and testing were conducted by the patient's routine care provider, while in NY initial screening and testing was conducted by separate research personnel, and all screen-positive patients were also referred to a joint MFM/cardiology visit for further follow-up and testing. NY had the capability of calling these patients at least once to remind them of outstanding studies or missed appointments; however, in many cases, when contacted, investigators heard that patients did not believe that they had CVD and felt too busy or overwhelmed to come in for additional testing even when further educated about the screening tool. There may have been some difference in how patient's perceived physician concern when the screening and testing was initially ordered by a provider versus other staff.

In addition, timing of screening may have been important to the follow-up rate. In CA, the majority of screens were conducted in the antepartum setting, lending more time during pregnancy care to complete the follow-up studies, and also more interaction with a health care team. In NY, over 60% of the screens were during the delivery hospitalization or postpartum (25% during the postpartum visit), and in their screen-positive population, over half of their screen-positive patients were captured in this later portion of pregnancy care when women have many competing priorities.

The algorithm applies a combination of up to four positive predictor variables for the identification of a positive screen. Our data suggest that any of the risk factors highlighted in ►**Table 2** would be highly predictive of a positive CVD screen, and may allow simplification of the screening algorithm by requiring any one of these factors. This finding would be valuable to investigate in additional studies, as simplification of the algorithm may help with adoption. In our analysis none of the variables was associated with false-positive screen; however, our sample of women with positive screens and sufficient follow-up studies ($n = 35$) was too small to draw definite conclusions.

This study also highlights that in addition to screening patients for more immediate cardiovascular risk, the algorithm also uncovers women who are at higher risk of CVD complications in their lifetime (i.e., ventricular hypertrophy or diastolic dysfunction).^{8,9} This observation contributes to

Table 2 Summary of patient characteristics at time of cardiovascular screen by intervention site

	All (n = 834)	CA (n = 639)	NY (n = 195)	p-Value ^a
Age mean ± SD	29.5 ± 6.1	29.5 ± 6.2	29.4 ± 6.0	0.91
Gravidity n (%)				0.09
1	237 (28.4)	191 (29.9)	46 (23.6)	
2+	597 (71.6)	448 (70.1)	149 (76.4)	
Parity n (%)				0.02
0	208 (24.9)	172 (26.9)	36 (18.5)	
1+	626 (75.1)	467 (73.1)	159 (81.5)	
Race-ethnicity, n (%)				<0.01
White	131 (15.7)	128 (20)	3 (1.5)	
Black	86 (10.3)	17 (2.7)	69 (35.4)	
Hispanic	435 (52.2)	358 (56)	77 (39.5)	
Asian	59 (7.1)	52 (8.1)	7 (3.6)	
Other/unknown	123 (14.8)	84 (13.1)	39 (20)	
Insurance				<0.01
Medicaid	584 (70.4)	447 (70.4)	137 (70.3)	
Private	155 (18.7)	151 (23.8)	4 (2)	
Other	51 (6.1)	17 (2.7)	34 (17.4)	
Unknown	40 (4.8)	20 (3.1)	20 (10.3)	
Screening timeframe n (%)				<0.01
Antepartum	461 (55.5)	386 (60.5)	75 (38.5)	
Intrapartum	173 (20.7)	106 (16.6)	67 (34.4)	
< 1-week postpartum	199 (23.9)	146 (22.9)	53 (27.2)	
> 1-week postpartum	92 (11.2)	43 (6.9)	49 (25.1)	
Consistent prenatal care ^b				<0.01
No	95 (12.3)	49 (7.8)	46 (29.9)	
Yes	688 (87.7)	580 (92.2)	108 (70.1)	
Comorbidities				
Substance use	28 (3.4)	17 (2.7)	11 (5.6)	0.04
Preexisting diabetes	58 (7.0)	50 (7.8)	8 (4.1)	0.07
Obesity (BMI ≥ 30 kg/m ²)	255 (30.6)	209 (32.7)	46 (23.6)	0.02
Chronic hypertension	76 (9.1)	58 (9.1)	18 (9.2)	0.95

Abbreviations: BMI, body mass index; CA, California; NY, New York; SD, standard deviation.

^aComparisons were evaluated using the two-sample *t*-test for age and the chi square or Fisher's exact test for all other variables.

^bFour or more prenatal visits.

the increasing body of work highlighting pregnancy as an opportunity to identify women at increased lifetime risk of CVD.¹⁰⁻¹⁴ While it is still somewhat unclear what postpartum interventions are most warranted to reduce long-term cardiovascular risk,^{12,13,15,16} recognizing the abnormal findings in this younger population may help direct our efforts at women who are most likely to benefit.

Limitations

This study had several limitations. The implementation of the screening started as a pilot study with the initial goal of educating providers about the algorithm and encouraging

their use in screening pregnant patients. This resulted in bias both in terms of which patients were screened, as well as in which patients had complete follow-up testing after a positive screen. Additional limitations included lack of a control group. Given that patients that screened negative did not have additional testing, this study cannot draw conclusions regarding the algorithm's validation characteristics (sensitivity, specificity, or overall accuracy). However, it lays the groundwork for future validation studies by establishing some understanding of the screen-positive rate, as well as an estimation of the true-positive rate, within that cohort. This information will be needed by centers planning studies to define validation characteristics. This study also lends

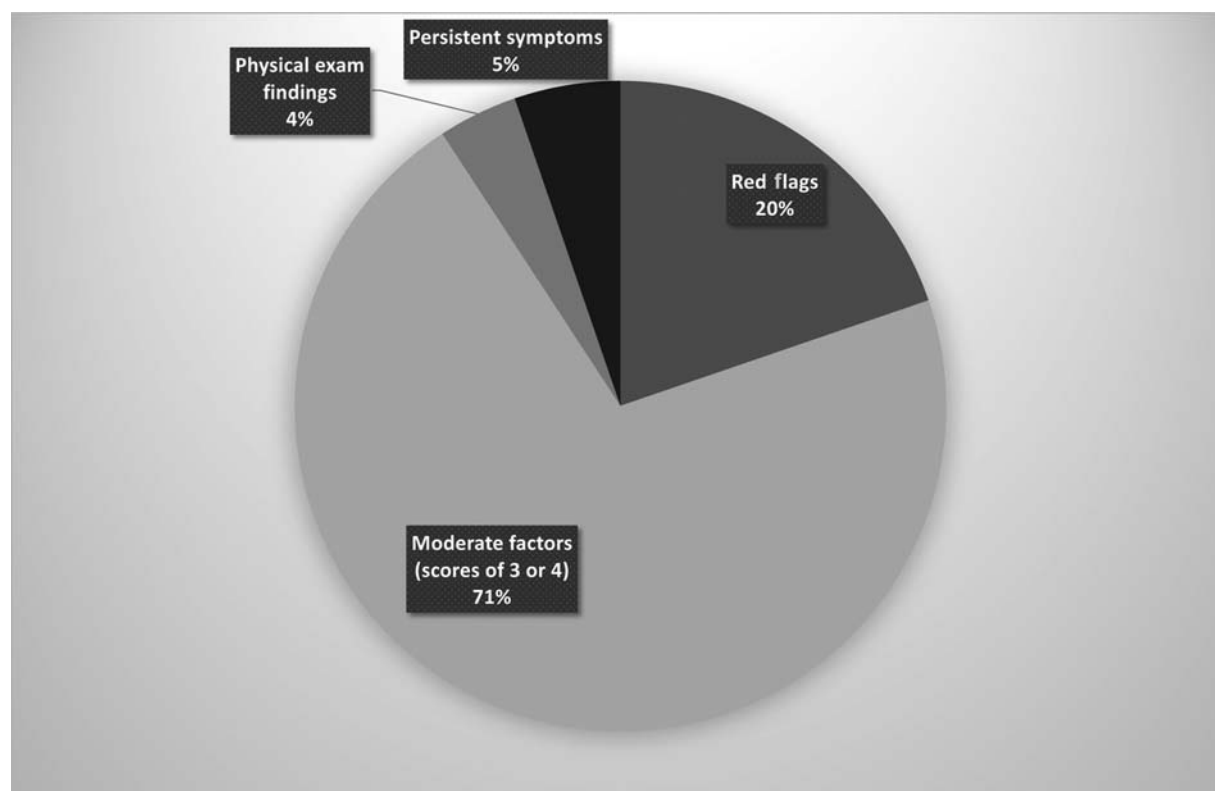


Fig. 3 Components of algorithm contributing to a positive CVD screen. CVD, cardiovascular disease.

Table 3 Moderate factors predictive of positive CVD screen using multivariate logistic regression^a

Moderate factors	Positive screen	
	Odds ratio (95% CI)	p-Value
Vital signs		
Oxygen saturation $\leq 96\%$	75.3 (12.4–457.7)	<0.01
Systolic blood pressure ≥ 140 mm Hg	34.3 (8.0–148.3)	<0.01
Respiratory rate ≥ 24	10.6 (2.2–50.3)	<0.01
Risk factors		
African American	26.1 (7.6–89.6)	<0.01
Preexisting diabetes	17.4 (4.0–76.7)	<0.01
Chronic hypertension	16.6 (4.8–57.0)	<0.01
Age ≥ 40 (y)	14.3 (3.8–54.7)	<0.01
Substance use	5.6 (1.5–21.3)	0.01
Symptoms		
Dyspnea	44.5 (12.2–161.8)	<0.01
Palpitations	28.2 (7.4–107.7)	<0.01
Asthma unresponsive to therapy	17.6 (1.5–202.4)	0.02
Mild orthopnea	5.2 (1.3–21.1)	0.02

Abbreviations: CI, confidence interval; CVD, cardiovascular disease.

^aStepwise selection was used (full model included demographic variables, all moderate factors and institution). Final model C statistic was 0.98 for positive CVD screen.

Table 4 “True-positive” cardiac results identified during screening and follow up testing

Criteria for “true-positive” result	Number of patients with qualifying findings ^a
Systolic or diastolic dysfunction on echocardiogram	3
Ventricular dilation or hypertrophy on echocardiogram	4
Pathologic arrhythmia confirmed by cardiologist	1
Valvular abnormality on echocardiogram	5
Need for cardiovascular medication (not based on BP criteria alone)	3

^a12 patients total were found to have true-positive results; however, each patient may have met more than one of the above criteria.

some information to centers that may be interested in simplifying the algorithm for implementation purposes or in decisions regarding at what time point in pregnancy to implement screening.

Lack of follow-up testing significantly limited conclusions regarding differences between CA and NY; while NY had a higher proportion of screen-positive cases, they ultimately had a lower proportion of “true-positive” cases. We presume that this may have been due to the significant loss of follow-up within the NY cohort; however, this ultimately is still unknown. While the loss of follow-up testing between those

with positive screening and completion of the recommended evaluation is a significant limitation of the study, follow-up should be prioritized by sites that are currently implementing the screening as we found a 30% rate of true CVD in women that had a positive screen and follow-up studies. In addition, screening patients during their antepartum care, may impact the likelihood of follow-up testing.

Conclusion

This study is the first to describe the initial implementation and findings of the proposed CVD screening algorithm and can help lay the groundwork for future validation studies, and potentially a simplified algorithm. If we succeed in detecting women with CVD followed by more timely interventions, we may be able to mitigate the associated morbidity and mortality related to CVD during their pregnancy. The process also sets the stage for targeting patients that may benefit from earlier and more direct care transitions (to primary care and cardiology) to help decrease the progression and burden of disease in her lifetime, as well as highlight an opportunity, for addressing racial disparities in pregnancy-related mortality.

Note

The work was presented at the Society for Maternal Fetal Medicine's 40th Annual Pregnancy Meeting February 6, 2020 in Grapevine, Texas.

Conflict of Interest

None declared.

Acknowledgments

We thank Associate Professor Heike Thiel de Bocanegra, PhD, MPH, for assistance in study interpretation and manuscript preparation.

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