

ORIGINAL RESEARCH

Early Pregnancy Systolic Blood Pressure Patterns Predict Early- and Later-Onset Preeclampsia and Gestational Hypertension Among Ostensibly Low-to-Moderate Risk Groups

Erica P. Gunderson , PhD, MS, MPH; Mara Greenberg , MD; Baiyang Sun , MPH; Nancy Goler , MD; Alan S. Go , MD; James M. Roberts , MD; Mai N. Nguyen-Huynh , MD, MAS; Wei Tao , MS; Stacey E. Alexeeff , PhD

BACKGROUND: Clinical risk factors, a single blood pressure (BP) measurement, current biomarkers, and biophysical parameters can effectively identify risk of early-onset preeclampsia but have limited ability to predict later-onset preeclampsia and gestational hypertension. Clinical BP patterns hold promise to improve early risk stratification for hypertensive disorders of pregnancy.

METHODS AND RESULTS: After excluding preexisting hypertension, heart, kidney, or liver disease, or prior preeclampsia, the retrospective cohort (n=249 892) all had systolic BP <140 mm Hg and diastolic BP <90 mm Hg or a single BP elevation \leq 20 weeks' gestation, prenatal care at <14 weeks' gestation, and a still or live birth delivery at Kaiser Permanente Northern California hospitals (2009–2019). The sample was randomly split into development (N=174 925; 70%) and validation (n=74 967; 30%) data sets. Predictive performance of multinomial logistic regression models for early-onset (<34 weeks) preeclampsia, later-onset (\geq 34 weeks) preeclampsia, and gestational hypertension was evaluated in the validation data set. There were 1008 (0.4%), 10 766 (4.3%), and 11 514 (4.6%) patients with early-onset preeclampsia, later-onset preeclampsia, and gestation hypertension, respectively. Models with 6 systolic BP trajectory groups (0–20 weeks' gestation) plus standard clinical risk factors performed substantially better than risk factors alone to predict early- and later-onset preeclampsia and gestational hypertension, with C-statistics (95% CIs) of 0.747 (0.720–0.775), 0.730 (0.722–0.739), and 0.768 (0.761–0.776) versus 0.688 (0.659–0.717), 0.695 (0.686–0.704) and 0.692 (0.683–0.701), respectively, with excellent calibration (Hosmer-Lemeshow $P=0.99$, 0.99, and 0.74, respectively).

CONCLUSIONS: Early pregnancy BP patterns up to 20 weeks' gestation plus clinical, social, and behavioral factors more accurately discriminate hypertensive disorders of pregnancy risk among low-to-moderate risk pregnancies. Early pregnancy BP trajectories improve risk stratification to reveal higher-risk individuals hidden within ostensibly low-to-moderate risk groups and lower-risk individuals considered at higher risk by US Preventive Services Task Force criteria.

Key Words: blood pressure ■ hypertensive disorders ■ longitudinal trajectory analysis ■ prediction ■ preeclampsia ■ pregnancy ■ risk stratification

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Correspondence to: Erica P. Gunderson, PhD, MS, MPH, Division of Research, Kaiser Permanente Northern California, 2000 Broadway, Oakland, CA 94612. Email: erica.gunderson@kp.org

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CLINICAL PERSPECTIVE

What Is New?

- Six early pregnancy systolic blood pressure (BP) patterns based on longitudinal trajectories from routine clinical BP measurements before 20 weeks' gestation were included in prediction models in addition to standard risk factors to improve discrimination of the risk of hypertensive disorders of pregnancy among ostensibly low-to-moderate risk women after exclusion of patients considered at high risk by US Preventive Services Task Force criteria.
- The highest 3 BP trajectory groups captured 74% of preeclampsia and 82% of gestational hypertension outcomes among 52% of the cohort, and accurately identified individuals with much higher observed rates of preeclampsia (7.2% and 11.7%) and gestational hypertension (7.8% and 15.7%) for the 2 highest BP trajectory groups compared with the observed percentages within the lower BP trajectory groups (0.5% to 4.4%).

What Are the Clinical Implications?

- Classification of early pregnancy systolic BP patterns based on BP changes from 0 through 16 to 20 weeks' gestation in combination with other standard risk factors (clinical, social, and behavioral) can significantly improve individual risk stratification for early-onset and later-onset preeclampsia and gestational hypertension, allowing more targeted surveillance and potentially interventions to ameliorate hypertensive disorders of pregnancy and adverse outcomes, as well as avoidance of additional monitoring, or unnecessary interventions (ie, low-dose aspirin administration) in low-risk pregnancies.
- In the future, these findings may be translated into an automated clinical tool within the electronic health records system, or a web-based tool to classify BP pattern changes during early gestation for individual risk stratification of preeclampsia or gestational hypertension that may improve precision medicine by more accurately identifying patients who may truly benefit most from enhanced monitoring and intervention(s).

Nonstandard Abbreviations and Acronyms

BPT	blood pressure trajectory
HDP	hypertensive disorders of pregnancy
KPNC	Kaiser Permanente Northern California
LDASA	low-dose aspirin administration
TRIPOD	Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis
USPSTF	US Preventive Services Task Force

Hypertensive disorders of pregnancy (HDP) and, in particular, preeclampsia are a leading cause of maternal and fetal morbidity and mortality worldwide.¹ Screening for risk of preeclampsia during early pregnancy is currently recommended by the American College of Obstetrics and Gynecology and the US Preventive Services Task Force (USPSTF) to determine risk status and to direct management.^{2–5} Risk stratification involves taking a detailed medical history to identify individuals considered clinically “high risk,” defined by having history of preeclampsia or obstetric complications, chronic hypertension, cardiovascular disease, liver or kidney dysfunction, and diabetes,⁴ or having ≥ 2 moderate factors (ie, first pregnancy [nulliparous], maternal age of ≥ 35 years, body mass index [BMI] >30 kg/m² [obesity], family history of preeclampsia, Black race, low income, and smoking).^{6,7} Any individuals meeting these criteria are considered of sufficiently high risk to benefit from low-dose aspirin administration (LDASA) to prevent preeclampsia.^{5–8} The USPSTF additionally advises that LDASA may be considered for individuals with any single moderate risk factor, including Black race or low income.⁶ An analysis of the 2019 US birth certificates found that according to the current guidelines, 85.7% of pregnant individuals would be eligible for LDASA.⁹ The USPSTF also recommends repeated blood pressure (BP) measurements throughout pregnancy to detect elevations for timely diagnosis and treatment of preeclampsia, including increased maternal and fetal surveillance, antihypertensive medications, and magnesium sulfate for eclampsia prophylaxis.² Early and accurate risk stratification is critically important to mitigate serious perinatal morbidity. Thus, a new approach, based on routine clinical BP measurements during the first and early second trimesters (<16 – 20 weeks), holds promise to improve early prediction of HDP by effectively discriminating risk, especially in ostensibly low-to-moderate risk people.¹⁰

Previous prediction models incorporate clinical screening criteria plus a single BP measurement, as well as biomarkers and biophysical tests to discriminate risk.^{11–14} However, confidence in models' performance and validity has diminished because of ubiquitous methodologic weaknesses. A systematic review of 40 qualified prediction models for HDP stated that 77% incorporated maternal characteristics (eg, BMI and first-trimester BP) and biophysical and biomarker tests,¹⁵ but few fully followed the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis (TRIPOD) guidelines.¹⁶ A meta-analysis of 11 UK cohorts found C-statistics of 0.6 to 0.7, poor model calibration (overfitting <1), and substantial inter-study heterogeneity, diminishing predicted risk across external populations.¹⁷ Although the models including biomarkers and biophysical measures effectively discerned $\approx 75\%$ to 95% of early-onset preeclampsia¹⁸ that comprised $<10\%$ of all preeclampsia cases,

performance was less robust for later-onset preeclampsia.^{15,19–21} Furthermore, inclusion of chronic medical conditions (ie, hypertension and heart, liver, or kidney disease) or prior preeclampsia pinpointed high-risk status, but HDP prediction models among ostensibly low-to-moderate risk individuals proved challenging.

To address this knowledge gap, we aimed to develop and validate predictive models using the early pregnancy BP trajectory (BPT) patterns before 20 weeks' gestation, previously identified by our team from electronic health record (EHR) data, for improved risk stratification for early- and later-onset preeclampsia, and gestational hypertension among a racially and ethnically diverse cohort of low-to-moderate risk pregnant women.¹⁰ We hypothesized that early pregnancy systolic BPT groups plus standard clinical, demographic, social, and lifestyle risk factors will yield more accurate prediction of HDP outcomes compared with standard risk factors alone, or plus a single initial BP measurement. If successful, electronic health records or web-based tools incorporating early pregnancy BP patterns routinely measured in clinical settings could facilitate enhanced individual risk stratification for HDP early in pregnancy by discriminating low from high risk within an ostensibly low-risk population, and implementing targeted surveillance and interventions to ameliorate adverse outcomes, as well as avoid additional monitoring or unnecessary interventions during pregnancy among truly low-risk individuals.^{22,23}

METHODS

Transparency and Openness Promotion Guidelines

Requests to access the data set from qualified researchers trained in human subjects' confidentiality protocols may be sent to Dr Erica P. Gunderson, principal investigator, at the Division of Research, email: erica.gunderson@kp.org. The patient data are owned by the Kaiser Foundation Health Plan, Inc, Kaiser Foundation Hospitals, Inc, and The Permanente Medical Group, Inc. Because of their third-party rights, it is not possible to make the data publicly available without restriction.

Study Design and Setting

The Kaiser Permanente Northern California (KPNC) is an integrated health care delivery system providing care to >4.5 million members through >10 000 physicians, >255 medical facilities, and 21 hospitals. The KPNC service area spans 22 counties of the greater Bay Area, and the California central valley from Sacramento to Fresno,

including urban and rural areas. The membership is sociodemographically diverse and highly representative of the surrounding region and statewide population.²⁴ Sixteen KPNC delivery hospitals deliver ≈45 000 births per year with prenatal care standardized across centers, and 90% to 95% of women enter prenatal care before 14 weeks' gestation. This retrospective cohort study used the EHR data to obtain BP measurements, prepregnancy information, sociodemographic, clinical, and social factors, lifestyle behaviors, and perinatal outcomes for pregnancies >20 weeks delivered from January 1, 2009, to December 31, 2019. This data-only project was approved by the KPNC Institutional Review Board, which waived the requirement for informed consent from patients, given the retrospective, data-only, minimal risk study design.

Eligibility Criteria

As previously detailed, we selected the first index singleton live or still birth delivered at a KPNC hospital with EHR BP measurements (N=308 775) for each person.¹⁰ After exclusion for prenatal care entry after 14 weeks' gestation, membership gap ≥4 months or no prenatal care, delivery at a non-KPNC hospital, or prior serious medical conditions (ie, cancer, kidney, liver, or cardiovascular disease, by *International Classification of Diseases, Ninth Revision [ICD-9]* or *International Classification of Diseases, Tenth Revision [ICD-10]*, codes), 267 887 individuals remained. Next, we excluded individuals who met criteria for prior chronic hypertension within 2 years before conception of the index birth using a validated algorithm²⁵: (1) *ICD-9/ICD-10* codes for hypertension identified on 2 separate dates, (2) stage 2 BP elevations (systolic ≥140 mmHg or diastolic ≥90 mmHg) from outpatient records on 2 separate consecutive days at least 3 months apart, or (3) *ICD-9/ICD-10* codes for hypertension plus a dispensed prescription for antihypertensive therapy. We also excluded those identified individuals with chronic hypertension during 0 to 20 weeks' gestation based on criteria for stage 2 BP elevations, with or without use of antihypertensive medications, or a diagnosis of chronic hypertension before pregnancy via *ICD-9/ICD-10* codes, as previously described.¹⁰

Thus, we excluded 13 626 women (5.1%) with prior chronic hypertension or hypertension during the index pregnancy up to 20 weeks' gestation, 47 missing all BP measurements before 20 weeks' gestation, and 4322 parous women with a history of preeclampsia (Figure S1). Among the final cohort of 249 892 eligible pregnant women, we randomly selected 70% (N=174 925) for the development data set and 30% (N=74 967) for the internal validation data set,¹⁰ across all study years (2009–2019) because HDP diagnostic criteria were modified in 2013.²⁶

Covariates

From the EHR, we obtained outpatient prenatal visit BP measurements, pregnancy outcomes from the delivery hospitalization record (*ICD-9/ICD-10* codes), and standard clinical and sociodemographic risk factors: maternal age, self-reported race and ethnicity (Asian, Black, Hispanic, White, or mixed/Native/unknown that combines groups of small size such as American Indian or Alaskan Native, Native Hawaiian or Other Pacific Islander), parity, height, measured prepregnancy weight within 1 year before conception or weight ≤ 14 weeks' gestation to calculate BMI (kg/m^2), gestational age at delivery, and pregestational diabetes status. We also obtained lifestyle behaviors, including tobacco smoking habit during pregnancy (never, current, or former) and last weight measured ≤ 20 weeks' gestation to estimate rate of gestational weight gain from 0 to 20 weeks' gestation (kg per week). Social factors included government health insurance (ie, Medicaid, MediCal, or state subsidized) and the neighborhood deprivation index, calculated on the basis of the Census Bureau's American Community Survey data (<https://www.census.gov/programs-surveys/acs/>). The racial and ethnic diversity represents characteristics, such as shared "history, language, beliefs, and customs" that may be influenced by social determinants of health (education, socioeconomic disadvantage, structural racism, and discrimination).²⁷ Jointly, these factors may contribute to disparities in racial and ethnic health outcomes.²⁸ These groups have broad importance in health research for not only identifying, but "monitoring, understanding and intervening" to ameliorate health inequities.²⁹

Primary Outcomes: Early- and Later-Onset Preeclampsia and Gestational Hypertension

Using 2016 American College of Obstetrics and Gynecology criteria, we classified early-onset preeclampsia (diagnosis 20 to <34 weeks' gestation), later-onset preeclampsia (diagnosis ≥ 34 weeks' gestation), gestational hypertension after 20 weeks' gestation, and no HDP (referent group). The study methods and validation study for classification of HDP have been previously described.¹⁰ Briefly, we classified early- and later-onset preeclampsia subgroups and gestational hypertension via *ICD-9/ICD-10* codes and gestational age at diagnosis in the EHR hospital discharge summary. Our chart validation study showed excellent accuracy for the *ICD-9/ICD-10* codes to classify the occurrence of each HDP with sensitivity and specificity both equal to 94% for preeclampsia, and the sensitivity $>85\%$ and specificity of 91% for gestational hypertension.¹⁰

Development of 6 Systolic BPT Groups

As previously described, we developed longitudinal BP patterns using the BP measurements from prenatal outpatient visits from 0 to 20 weeks' gestation.¹⁰ The BP measurements were obtained by trained medical assistants using automated oscillometers to capture BP under routine conditions rather than during an acute illness. On average, there were 4 BP measurements per person, with a range of 1 to 10 measurements on separate days during 0 to 20 weeks' gestation. The longitudinal systolic BP measurements were included in the group-based trajectory modeling (latent class growth modeling) to identify distinct pregnancy BPT groups up to 20 weeks' gestation, under the assumption that latent classes held parameter values that determine the underlying distribution and vary by class membership.³⁰ We fit each trajectory curve with third-order polynomial terms to allow for curvature, and tested for statistical significance of quadratic and cubic terms to determine the appropriate shape of each trajectory pattern, as previously detailed.¹⁰ The BPT groups were chosen to most accurately represent differences in systolic BP changes from early to mid gestation, including a steady decrease characterizing normal pregnancy, and shallower declines for a somewhat more elevated BP level linked to preeclampsia.³¹ The trajectory group statistical modeling was conducted in SAS using PROC TRAJ.³² Each woman was then assigned to the BPT group that best reflected her profile of change using a maximum probability assignment rule for the posterior probabilities for group membership obtained from the model.³³ Six early pregnancy systolic BPT groups were identified on the basis of the best fit,¹⁰ and ordered by increasing risk of HDP: (1) ultra-low declining, (2) low declining, (3) moderate-fast decline, (4) low increasing, (5) moderate stable, and (6) elevated stable (Figure 1).

Statistical Analysis: Prediction of HDP

We followed TRIPOD guidelines for the methods and reporting of predictive models (Table S1).¹⁶ We used a split-sample design to randomly partition the study cohort into model development (70%) and validation (30%) data sets. The development data set was used to develop risk prediction models, and the validation data set was only used to validate the predictions from the final models. We fit multinomial logit regression using the model development data set with 4 outcomes: early-onset preeclampsia, later-onset preeclampsia, gestational hypertension, and no HDP (referent).

To select relevant predictors, we used the least absolute shrinkage and selection operator, a machine learning statistical method that imposes a shrinkage penalty term on the regression coefficients, treating variable selection as a continuous process.³⁴ Least

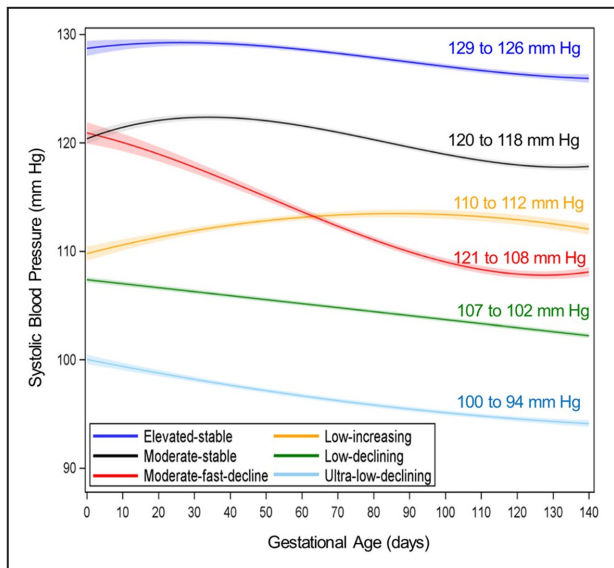


Figure 1. Six early pregnancy systolic blood pressure trajectory (BPT) groups from 0 to 20 weeks' gestation (from initial to last average blood pressure measurement in mm Hg for each BPT group).

Six early pregnancy BPT groups: ultra-low declining (light blue), low declining (green), moderate-fast decline (red), low increasing (yellow), moderate stable (black), and elevated stable (purple). Adapted from Gunderson et al¹⁰ with permission. Copyright ©2022 Wolters Kluwer Health, Inc.

absolute shrinkage and selection operator has desirable asymptotic properties, including estimation consistency in choosing the correct subset of predictors, providing an advantage over alternative variable-selection procedures.³⁵

We fit predictive models with different combinations of variables included sequentially to quantify and evaluate the predictive value of the BPT groups and other risk factors. Model 1 includes standard risk factors only (prepregnancy BMI, parity, age, race and ethnicity, and diabetes); models 2.0 to 2.2 include initial BP only, or plus some or all standard risk factors; and models 3.0 to 3.3 include the 6 BPT groups only, or BPT groups plus standard risk factors, and additionally, lifestyle behaviors and social factors. In extended models, we also used least absolute shrinkage and selection operator to assess inclusion of interaction terms for prepregnancy BMI, parity, racial and ethnic groups, or group probabilities for BPT groups. We also report the adjusted odds ratios (aORs) and 95% CIs for each HDP outcome for model 3.3 among 6 BPT groups (ultra-low declining, referent) and standard risk factors (clinical prenatal, sociodemographic, and diabetes), lifestyle behaviors, and social factors. We also evaluated C-statistics for models that included interaction terms for prepregnancy BMI, parity, racial and ethnic groups, and with the addition of group probabilities for the BPT group assignments to model 3.3.

For each model, we obtained estimates of the predicted probabilities for each outcome in the validation data set. We evaluated predictive performance by examining predictive model discrimination and calibration. Discrimination in the validation data set was quantified using the C-statistic (ie, area under the receiver operating characteristic curve) and 95% CIs.³⁶ Calibration of model predictions was assessed by comparing the model's predicted risk of each outcome with the observed incidence of each outcome in the validation data set using calibration plots and the Hosmer-Lemeshow statistics ($P > 0.05$ is consistent with good calibration).³⁷

Using model 3.3, we further compared the predicted probabilities to the observed incidence of overall preeclampsia and gestational hypertension to assess the model performance for stratification by risk factors. We stratified by the number of moderate risk factors and diabetes from the 2021 USPSTF recommendations: 0, 1, 2, and >2 risk factors.⁶ We display the predicted and observed numbers and percentages of each HDP among racial and ethnic groups (Black race, Asian race, Hispanic ethnicity, and White race), parity groups, prepregnancy BMI categories, and risk factor combinations. In a sensitivity analysis, we restricted the number of BP measurements to ≤ 2 , ≤ 3 , or ≤ 4 measurements and recomputed the BPT group for each woman. We assessed how many women were reassigned to a different BPT group, and then we refit separate prediction models and recomputed C-statistics to assess the change in accuracy. Finally, we conducted a sensitivity analysis by limiting BP measurements up to 16 weeks' gestation to evaluate predictive performance within the recommended time frame to initiate LDASA among high-risk individuals.⁸

RESULTS

Among the study cohort of 249 892 low-to-moderate risk women with one eligible singleton birth, 242 200 (96.9%) had at least 1 BP measurement before 12 weeks' gestation, and 159 206 (63.7%) had ≥ 3 BP measurements (on different days) by 16 weeks. By 20 weeks' gestation, 216 792 (86.8%) patients had ≥ 3 , and 142 504 (57.0%) had ≥ 4 BP measurements (on different days). The mean (SD) gestational age at entry into prenatal care was 8.2 (2.0) weeks (range, 0–14 weeks), and maternal age at delivery was 30.9 years (SD, 5.3 years). Of the group, 57% were nulliparous, 20.4% were classified with obesity, 7.4% received government health insurance, and 5.6% were current smokers; and racial and ethnic groups included 7.2% Black, 26.4% Hispanic, 25.4% Asian, 36.6% White, and 4.4% mixed/Native/unknown.

In the development data set ($n=174\,925$), 700 (0.4%), 7571 (4.3%), and 7981 (4.6%) of pregnancies developed

Table 1. Maternal Characteristics for Early-Onset Preeclampsia, Later-Onset Preeclampsia, Gestational Hypertension, and No HDP for the Model Development (N=174925) and Validation (N=74967) Data Sets (One Singleton Gestation; Live or Still Birth Among Low-to-Moderate Risk Women; 2009–2019)

Characteristics	Model development data set (N=174 925)				Validation data set (N=74 967)			
	Early-onset preeclampsia (N=700 [0.4%])	Later-onset preeclampsia (N=7571 [4.3%])	Gestational hypertension (N=7981 [4.6%])	No HDP (N=158 673 [90.7%])	Early-onset preeclampsia (N=308 [0.4%])	Later-onset preeclampsia (N=3195 [4.3%])	Gestational hypertension (N=3533 [4.7%])	No HDP (N=67 931 [90.6%])
Maternal age, mean (SD) y	30.8 (5.8)	30.6 (5.8)	31.1 (5.4)	30.9 (5.3)	30.9 (5.7)	30.6 (5.7)	31.2 (5.4)	31.0 (5.3)
Age categories, n (%)								
18–25 y	155 (22)	1695 (22)	1458 (18)	28 854 (18)	58 (19)	722 (23)	647 (18)	12 162 (18)
26–30 y	200 (29)	2184 (29)	2453 (31)	49 780 (31)	97 (31)	887 (28)	1040 (29)	21 195 (31)
31–35 y	210 (30)	2282 (30)	2603 (33)	52 965 (33)	97 (31)	1009 (32)	1186 (34)	22 989 (34)
36–40 y	106 (15)	1162 (15)	1210 (15)	23 063 (15)	47 (15)	478 (15)	531 (15)	9869 (15)
41–45 y	29 (4)	247 (3)	257 (3)	4011 (3)	9 (3)	99 (3)	129 (4)	1716 (3)
Race or ethnicity, n (%)								
Asian	172 (25)	1664 (22)	1569 (20)	40 811 (26)	71 (23)	738 (23)	653 (18)	17 732 (26)
Black	91 (13)	722 (10)	671 (8)	11 224 (7)	40 (13)	302 (9)	301 (9)	4715 (7)
Hispanic	195 (28)	2218 (29)	1711 (21)	42 165 (27)	86 (28)	902 (28)	768 (22)	17 958 (26)
Mixed/Native/unknown	26 (4)	338 (4)	366 (5)	7055 (4)	16 (5)	118 (4)	182 (5)	2983 (4)
White	216 (31)	2629 (35)	3664 (46)	57 418 (36)	95 (31)	1135 (36)	1629 (46)	24 543 (36)
Prenatal parity, n (%)								
Nulliparous, 0 prior births	534 (76)	6027 (80)	6019 (75)	87 392 (55)	235 (76)	2549 (80)	2659 (75)	37 457 (55)
Primiparous, 1 prior birth	114 (16)	969 (13)	1236 (15)	44 896 (28)	40 (13)	421 (13)	573 (16)	18 945 (28)
Biparous, 2 prior births	40 (6)	384 (5)	499 (6)	18 024 (11)	25 (8)	160 (5)	206 (6)	7887 (12)
Multiparous, ≥3 prior births	12 (2)	191 (3)	227 (3)	8361 (5)	8 (3)	65 (2)	95 (3)	3642 (5)
Diabetes, pregestational, n (%)	22 (3)	143 (2)	80 (1)	833 (1)	8 (3)	59 (2)	44 (1)	369 (1)
Pregnancy weight, mean (SD), kg	73.3 (17.8)	72.8 (18.9)	76.8 (19.9)	68.3 (16.1)	73.3 (17.7)	73.7 (19.3)	76.2 (19.4)	68.1 (16.0)
Height, mean (SD), cm	161.7 (7.1)	161.8 (7.0)	163.6 (7.2)	162.5 (7.0)	161.2 (6.7)	161.9 (7.0)	163.5 (7.3)	162.4 (7.0)
Pregnancy BMI, mean (SD), kg/m ²	28.0 (6.4)	27.7 (6.6)	28.6 (6.9)	25.8 (5.7)	28.1 (6.3)	28.0 (6.7)	28.4 (6.8)	25.8 (5.6)
Pregnancy BMI categories, n (%)								
Underweight (<18.5 kg/m ²)	12 (2)	144 (2)	84 (1)	4426 (3)	6 (2)	60 (2)	56 (2)	1973 (3)
Normal weight (18.5–24.9 kg/m ²)	254 (37)	2944 (39)	2790 (35)	80 184 (51)	102 (33)	1204 (38)	1218 (35)	34 502 (51)

(Continued)

Table 1. Continued

Characteristics	Model development data set (N=174,925)				Validation data set (N=74,967)			
	Early-onset preeclampsia (N=700 [0.4%])	Later-onset preeclampsia (N=7571 [4.3%])	Gestational hypertension (N=7981 [4.6%])	No HDP (N=158,673 [90.7%])	Early-onset preeclampsia (N=308 [0.4%])	Later-onset preeclampsia (N=3195 [4.3%])	Gestational hypertension (N=3533 [4.7%])	No HDP (N=67,931 [90.6%])
Overweight (25–29.9 kg/m ²)	199 (29)	2136 (28)	2270 (29)	42441 (27)	94 (31)	887 (28)	1045 (30)	18159 (27)
Obesity class I (30–34.9 kg/m ²)	131 (19)	1254 (17)	1469 (19)	18661 (12)	61 (20)	547 (17)	621 (18)	7820 (12)
Obesity class II (35–39.9 kg/m ²)	58 (8)	643 (9)	752 (9)	7567 (5)	30 (10)	280 (9)	343 (10)	3209 (5)
Obesity class III (≥40 kg/m ²)	39 (6)	415 (6)	575 (7)	4219 (3)	14 (5)	192 (6)	232 (7)	1749 (3)
Gestational age at first prenatal care visit, mean (SD), wk	7.9 (2.0)	8.0 (2.0)	8.0 (1.9)	8.2 (2.0)	7.8 (2.0)	8.1 (2.0)	8.0 (1.9)	8.2 (2.0)
Gestational age at delivery, mean (SD), wk	32.3 (3.2)	38.8 (1.7)	39.3 (1.6)	39.3 (2.0)	32.2 (3.4)	38.8 (1.7)	39.3 (1.6)	39.3 (2.0)
Social factors, n (%)								
Neighborhood deprivation index								
≤-1 (Least deprived)	68 (10)	784 (10)	914 (11)	18369 (12)	24 (8)	316 (10)	419 (12)	7829 (12)
>-1 and ≤0	339 (49)	3732 (49)	4110 (52)	79803 (50)	156 (51)	1601 (50)	1796 (51)	34410 (51)
>0 and ≤1	194 (28)	2049 (27)	2047 (26)	41028 (26)	82 (27)	856 (27)	939 (27)	17547 (26)
>1 (Most deprived)	97 (14)	995 (13)	900 (11)	19222 (12)	46 (15)	415 (13)	374 (11)	8027 (12)
Government health insurance	51 (7)	584 (8)	590 (7)	11656 (7)	22 (7)	273 (9)	256 (7)	4969 (7)
Lifestyle behaviors								
Smoking status, n (%)								
Current	41 (6)	456 (6)	535 (7)	8886 (6)	14 (5)	178 (6)	264 (7)	3713 (5)
Former	79 (11)	1011 (13)	1185 (15)	19025 (12)	35 (11)	465 (15)	540 (15)	8069 (12)
Never	578 (83)	6058 (80)	6213 (78)	129987 (82)	255 (83)	2530 (79)	2714 (77)	55834 (82)
Unknown	2 (0)	46 (1)	48 (1)	775 (0)	4 (1)	22 (1)	15 (0)	315 (0)
Rate of gestational weight gain to 20 wk gestation, mean (SD), kg/wk	0.2 (0.3)	0.2 (0.2)	0.2 (0.3)	0.2 (0.2)	0.1 (0.3)	0.2 (0.2)	0.2 (0.3)	0.2 (0.2)

(Continued)

Table 1. (Continued)

Characteristics	Model development data set (N=174 925)			Validation data set (N=74 967)				
	Early-onset preeclampsia (N=700 [0.4%])	Later-onset preeclampsia (N=7571 [4.3%])	Gestational hypertension (N=7981 [4.6%])	No HDP (N=158 673 [90.7%])	Early-onset preeclampsia (N=308 [0.4%])	Later-onset preeclampsia (N=3195 [4.3%])	Gestational hypertension (N=3533 [4.7%])	No HDP (N=67 931 [90.6%])
Total gestational weight gain, mean (SD), kg	12.6 (7.4)	15.2 (7.1)	14.7 (7.4)	13.4 (6.4)	12.3 (8.0)	15.2 (7.2)	14.8 (7.3)	13.3 (6.3)

Early-onset preeclampsia defined as diagnosis <34 weeks' gestational age; later-onset preeclampsia defined as diagnosis ≥34 weeks' gestational age. All characteristics are significantly different according to outcomes (all $P < 0.01$), except for government insurance ($P = 0.69$ in the model development data set, and $P = 0.08$ in the validation data set). BMI indicates body mass index; and HDP, hypertensive disorders of pregnancy.

early-onset preeclampsia, later-onset preeclampsia, or gestational hypertension after 20 weeks' gestation, respectively (Table 1). These percentages of HDP outcomes were similar for the validation (n=74 967) data set; 308 (0.4%), 3195 (4.3%), and 3533 (4.7%), respectively. The risk factors within the development and validation data sets were also similar among the HDP groups (none, early-onset preeclampsia, later-onset preeclampsia, and gestational hypertension) (Table 1). A comparison of these 2 data sets (Table S2) showed no significant statistical differences among model covariates or the 6 BPT groups. Figure 2 shows the crude rates of each HDP outcome for each BPT group, illustrating gradations of increasing outcome rates from the ultra-low–declining BPT group through the elevated-stable BPT group for the development and validation data sets (Figure 2). For the 2 highest BPT groups, the observed rates of any preeclampsia (7.2% and 11.7%) and gestational hypertension (7.8% and 15.7%) were much greater than in the other BPT groups (0.5%–4.4%).

Association of BPT Groups and Risk Factors With HDP in the Model Development Data Set

The multivariable, multinomial logistic regression models, adjusted for covariates using the development data set, showed that the BPT groups were independently associated with an increasing gradient of aORs (95% CIs) for 3 HDP outcomes: early-onset preeclampsia, later-onset preeclampsia, and gestational hypertension (Table 2). The gradient increased from the low-declining to elevated-stable BPT groups compared with ultra-low–declining (referent) as follows: 1.87 (0.97–3.59) to 12.49 (6.49–24.05) for early-onset preeclampsia, 1.78 (1.48–2.15) to 8.88 (7.35–10.73) for later-onset preeclampsia, and 2.49 (1.90–3.27) to 26.31 (20.12–34.40) for gestational hypertension. Age, nulliparity, BMI, rate of gestational weight gain (0–20 weeks' gestation), pregestational diabetes, government health insurance, Black race, Asian race, and Hispanic ethnicity were independently associated with higher odds of early- and later-onset preeclampsia compared with no HDP. These risk factors, as well as former smoker, and White race only, were independently associated with higher odds of gestational hypertension compared with no HDP.

Prediction of HDP: Internal Validation by TRIPOD Guidelines

Table 3 displays the C-statistics (95% CIs) results from the final models in the validation data set to predict the risk of each HDP outcome: early-onset preeclampsia, later-onset preeclampsia, and gestational

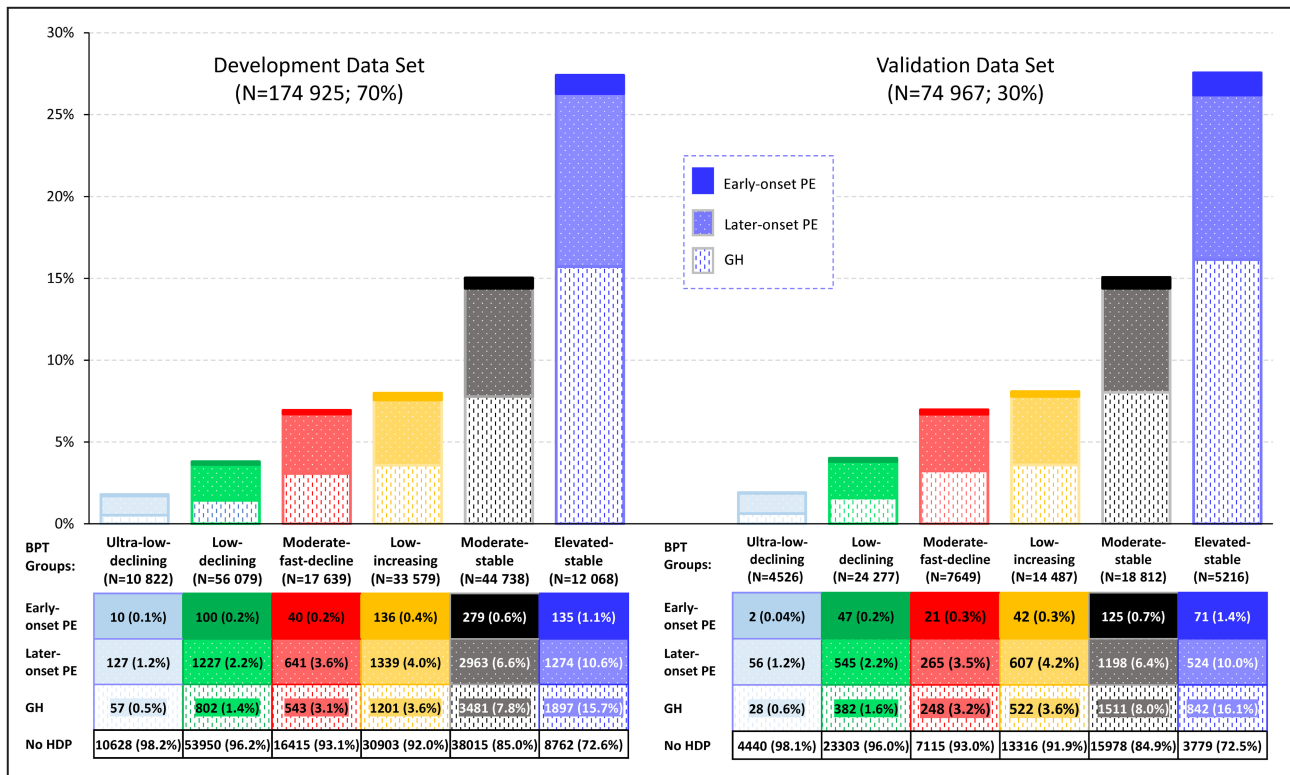


Figure 2. Number and percentages of early-onset preeclampsia (PE), later-onset PE, and gestational hypertension (GH) among systolic blood pressure trajectory (BPT) groups for the development and validation data sets. Color gradient definitions: darkest shade=early-onset PE, medium shade dots=later-onset PE, and lightest shade vertical dashes=GH. HDP indicates hypertensive disorders of pregnancy.

hypertension. Model performance C-statistics (95% CIs) for the 6 BPT groups alone (model 3) were better for early-onset preeclampsia (0.711 [0.682–0.739]), later-onset preeclampsia (0.665 [0.656–0.674]), and gestational hypertension (0.734 [0.726–0.742]) compared with initial single BP alone (model 2). The BPT groups plus BMI and parity (model 3.1) yielded higher C-statistics compared with standard risk factors only (model 1.0). The best prediction model performance (model 3.3) included the 6 BPT groups plus all risk factors (C-statistics [95% CIs] for early-onset preeclampsia (0.747 [0.719–0.775]), later-onset preeclampsia (0.731 [0.723–0.740]), and gestational hypertension (0.770 [0.762–0.778]) (all $P < 0.001$). In extended models (Table S3), inclusion of interaction terms for prepregnancy BMI, parity, and racial and ethnic groups had minimal impact on C-statistics (model 3.4). However, the addition of group probabilities for the BPT group assignments to model 3.3 slightly improved the model C-statistics (95% CIs); 0.755 (0.728–0.782) for early-onset preeclampsia, 0.735 (0.727–0.744) for later-onset preeclampsia, and 0.777 (0.769–0.784) for gestational hypertension (model 3.5).

The receiver operating characteristic curves for models 1.0 (standard risk factors only), 3.0 (6 BPT

groups only), and 3.3 (6 BPT groups plus all risk factors) are shown for each HDP outcome, depicting improvement in prediction (Figure S2). Calibration performance was excellent for the models with the BPT groups plus all risk factors (Figure S3), and there was no evidence of poor fit based on Hosmer-Lemeshow ($P = 0.99, 0.99,$ and 0.74 for early-onset preeclampsia, later-onset preeclampsia, and gestational hypertension, respectively). Prediction equations for these models are shown in Data S1 and Table S4.

Risk Stratification for Preeclampsia and Gestational Hypertension: Observed Versus Predicted Percentage

Risk stratification by early pregnancy BPT groups among the overall preeclampsia and gestational hypertension outcomes were evaluated by comparing prediction model estimates of the percentages of HDP and the observed percentages (95% CIs) of HDP among subgroups with 0, only 1, 2, and >2 USPSTF risk factors overall, and stratified by racial and ethnic groups, or various clinical risk factors (Figures 3 and 4 and Tables S5 through S13). The 6 BPT groups showed a gradient of increasing percentages of preeclampsia

Table 2. aORs (95% CIs) for Early Pregnancy BPT Groups Associated With Early-Onset Preeclampsia, Later-Onset Preeclampsia, and Gestational Hypertension Versus No HDP

Variables	aOR (95% CI)		
	Early-onset preeclampsia (<34 wk)	Later-onset preeclampsia (≥34 wk)	Gestational hypertension
Early pregnancy BPT groups			
Elevated stable	12.49 (6.49–24.05)	8.88 (7.35–10.73)	26.31 (20.12–34.40)
Moderate stable	6.37 (3.36–12.06)	5.14 (4.28–6.16)	12.36 (9.49–16.10)
Low increasing	4.04 (2.11–7.71)	3.07 (2.55–3.70)	5.80 (4.44–7.58)
Moderate-fast decline	2.33 (1.16–4.69)	2.81 (2.32–3.42)	5.03 (3.82–6.63)
Low declining	1.87 (0.97–3.59)	1.78 (1.48–2.15)	2.49 (1.90–3.27)
Ultra-low declining	1.0 (Referent)	1.0 (Referent)	1.0 (Referent)
Demographic, clinical risk factors			
Age, y	1.02 (1.01–1.04)	1.02 (1.02–1.03)	1.03 (1.02–1.03)
Parity			
Nulliparous (no prior births)	2.87 (2.38–3.46)	3.46 (3.26–3.68)	2.55 (2.41–2.70)
Parous (≥1 prior births)	1.0 (Referent)	1.0 (Referent)	1.0 (Referent)
Prepregnancy BMI, kg/m ²	1.03 (1.01–1.04)	1.03 (1.02–1.03)	1.04 (1.036–1.044)
Diabetes status			
Pregestational	4.42 (2.85–6.85)	2.70 (2.24–3.25)	1.29 (1.01–1.64)
None	1.0 (Referent)	1.0 (Referent)	1.0 (Referent)
Racial or ethnic group			
Asian	1.56 (1.27–1.93)	1.21 (1.13–1.29)	0.93 (0.87–0.99)
Black	2.17 (1.67–2.81)	1.40 (1.28–1.54)	0.89 (0.81–0.98)
Hispanic	1.48 (1.21–1.82)	1.40 (1.32–1.49)	0.78 (0.73–0.83)
Mixed/Native/unknown	1.15 (0.76–1.72)	1.20 (1.06–1.35)	0.97 (0.86–1.08)
White	1.0 (Referent)	1.0 (Referent)	1.0 (Referent)
Social factors			
Neighborhood deprivation index			
≤−1 (Least deprived)	1.0 (Referent)	1.0 (Referent)	1.0 (Referent)
>−1 and ≤0	1.06 (0.82–1.38)	1.03 (0.95–1.12)	0.95 (0.88–1.03)
>0 and ≤1	1.10 (0.83–1.47)	1.05 (0.96–1.15)	0.92 (0.85–1.01)
>1 (Most deprived)	1.16 (0.83–1.61)	1.10 (1.00–1.22)	0.94 (0.85–1.04)
Government health insurance			
Yes	0.98 (0.72–1.34)	1.20 (1.09–1.31)	1.20 (1.10–1.32)
No	1.0 (Referent)	1.0 (Referent)	1.0 (Referent)
Lifestyle behaviors			
Smoking (cigarette) habit			
Current	0.97 (0.70–1.34)	1.03 (0.93–1.14)	1.10 (1.00–1.21)
Former	0.89 (0.70–1.14)	1.06 (0.99–1.14)	1.12 (1.05–1.20)
Unknown	0.54 (0.13–2.17)	1.14 (0.84–1.55)	1.26 (0.93–1.70)
Never	1.0 (Referent)	1.0 (Referent)	1.0 (Referent)
Rate of gestational weight gain up to 20 wk GA, kg/wk	1.39 (1.03–1.88)	1.17 (1.06–1.29)	1.35 (1.23–1.48)

Model development data set (70%); N=174925 women with 1 singleton gestation with live or still birth among low-to-moderate risk women (2009–2019). Early-onset preeclampsia defined as diagnosis <34 weeks' gestational age; later-onset preeclampsia defined as diagnosis ≥34 weeks' gestational age. All aORs (95% CIs) from multivariable and multinomial logistic regression models based on model development data set. Model sample size is N=173390 because n=1535 women are missing prepregnancy BMI, neighborhood deprivation index, or rate of gestational weight gain up to 20 weeks' GA. aOR indicates adjusted odds ratio; BMI, body mass index; BPT, blood pressure trajectory; GA, gestational age; and HDP, hypertensive disorders of pregnancy.

and gestational hypertension for each risk factor subgroup, although the absolute percentages among the BPT groups increased with the number of moderate

risk factors. The highest risks of preeclampsia and gestational hypertension outcomes were consistently found among the 3 highest BPT groups (elevated

Table 3. Predictive Model Performance for HDP Among Low-to-Moderate Risk Women Using 6 Early Pregnancy BPT Groups, Initial First-Trimester BP, Standard Risk Factors Available in Routine Clinical Care, Lifestyle Behaviors, and Social Factors

Model No.	Predictive models and variables	Model C-statistic (95% CI)		
		Early-onset preeclampsia (<34 wk)	Later-onset preeclampsia (≥34 wk)	Gestational hypertension
1.0.	Standard risk factors: BMI+parity+age+race or ethnicity+diabetes	0.688 (0.659–0.717)	0.695 (0.686–0.704)	0.692 (0.683–0.701)
2.0.	Initial BP only	0.657 (0.626–0.687)	0.631 (0.621–0.641)	0.701 (0.692–0.709)
2.1.	Initial BP+BMI+parity	0.704 (0.675–0.733)	0.708 (0.700–0.717)	0.738 (0.730–0.747)
2.2.	Initial BP+BMI+parity+age+race or ethnicity+diabetes	0.713 (0.685–0.741)	0.714 (0.705–0.722)	0.744 (0.736–0.752)
3.0.	Six BPT groups only	0.711 (0.682–0.739)	0.665 (0.656–0.674)	0.734 (0.726–0.742)
3.1.	Six BPT groups+BMI+parity	0.739 (0.710–0.767)	0.725 (0.717–0.734)	0.764 (0.756–0.772)
3.2.	Six BPT groups+BMI+parity+age+race or ethnicity+diabetes	0.747 (0.720–0.775)	0.730 (0.722–0.739)	0.768 (0.761–0.776)
3.3.	Six BPT groups+BMI+parity+age+race or ethnicity+diabetes+lifestyle behaviors+social factors	0.747 (0.719–0.775)	0.731 (0.723–0.740)	0.770 (0.762–0.778)

Data are given for N=74967 (validation data set). Standard risk factors: prepregnancy BMI (kg/m²), parity (0 vs ≥1), maternal age (years), racial and ethnic groups (Black, Hispanic, Asian, White [referent], and mixed/Native/unknown), and pregestational diabetes. Lifestyle behaviors: smoking during pregnancy and rate of gestational weight gain ≤20 weeks' gestation (kg/wk). Social factors: government health insurance and neighborhood deprivation index. C-statistics for model 1 (standard risk factors), model 2 (initial BP only ≤14 weeks' gestation) or initial BP plus standard risk factors), and model 3 (6 BPT groups only or BPT groups plus standard risk factors, lifestyle behaviors, and social factors). Comparison of C-statistics for model 3.3 vs model 1.0 for early-onset preeclampsia, later-onset preeclampsia, and gestational hypertension (all *P*<0.001). The total number (N) missing covariables for the prediction model (validation data set) is 693. N missing prepregnancy BMI=563, N missing neighborhood deprivation index=130; N missing gestational weight gain <20 weeks' gestation=565. BMI indicates prepregnancy body mass index; BP, blood pressure; BPT, BP trajectory; and HDP, hypertensive disorders of pregnancy.

stable, moderate stable, and low increasing) (Figure 3 and Tables S5 through S13). For example, among women with no risk factors, the predicted risks for preeclampsia ranged from 0.6% to 4.7% from ultra-low–declining to the elevated-stable BPT group, with comparable observed percentages of 0.8% to 4.5% (overall observed risk=1.6%). The observed versus predicted percentages for gestational hypertension ranged from 0.4% to 9.5% and from 0.3% to 8.1%, respectively. For the subgroup with any 2 risk factors, predicted percentages of preeclampsia ranged from 1.9% to 12.8%, whereas observed percentages were 1.4% to 12.2% (ultra-low decreasing to elevated stable), whereas the highest percentages for gestational hypertension were 17.6% and 17.0%, respectively. Furthermore, 921 preeclampsia (74%) and 1014 gestational hypertension (84%) outcomes occurred in the 3 highest BPT groups, which included 58% of this subsample with 2 risk factors. For example, among nulliparas women with obesity (no other risk factors), 86% of preeclampsia cases (n=4277) occurred in the 3 highest BPT groups (Table S9).

For each racial and ethnic group, the predicted and observed risks of preeclampsia and gestational hypertension showed excellent concordance and discrimination for each BPT subgroup and increasing risk with BPT groups. However, overall observed risks of

preeclampsia differed among racial and ethnic groups, with Black race having the highest preeclampsia risk (6.4%), followed in decreasing order by Hispanic ethnicity (5.0%), White race (4.5%), and Asian race (4.2%). The predicted risks of HDP outcomes among parity groups revealed the ability of the 6 BPT groups to accurately predict absolute risk levels comparable to observed outcomes (Table S7), even with the 3 times higher overall absolute risk of preeclampsia for all nulliparas compared with all parous groups. Finally, there was an increasing gradient of predicted and observed preeclampsia and gestational hypertension for the 3 highest BPT groups (Figure 4) across increasing number of moderate risk factors (0 to >2) subgroups, capturing up to 61% to 86% of preeclampsia outcomes and 72% to 89% of gestational hypertension outcomes. The highest 3 BP groups identified 74% of preeclampsia and 82% of gestational hypertension outcomes among 52% of the cohort (Figure 2).

Sensitivity Analyses: BPT Groups With a Restricted Number of BP Measurements

Our main prediction model results included all available BP measurements for each participant. Approximately 78%, 79%, and 84% of women had at least 1 BP measured within 5 to 8, 9 to 12, and

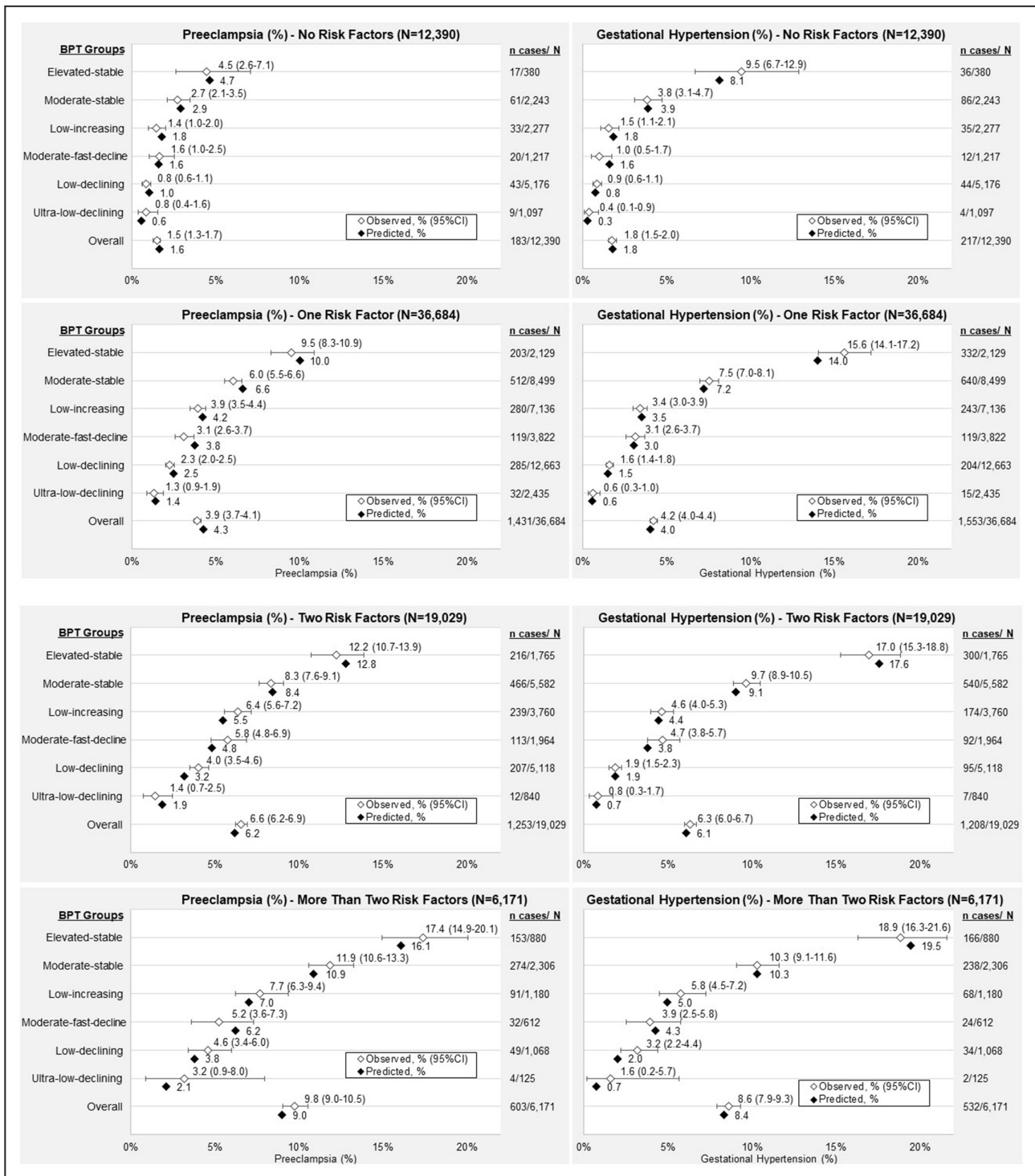


Figure 3. Early pregnancy systolic blood pressure trajectory (BPT) groups stratified by the number of low-to-moderate risk factors based on US Preventive Services Task Force: model average predicted probabilities (percentages) and observed incidence rate of preeclampsia and gestational hypertension (percentages and 95% CIs) for the internal validation sample.

13 to 16 weeks of gestation, respectively (Figure S4). When we restricted the number of BP measurements to at most 4, we found that 93.3% of women

were categorized into the same BPT group as when using all available measurements; this decreased to 85.2% for ≤ 3 BP measurements and 71.6% for ≤ 2 BP

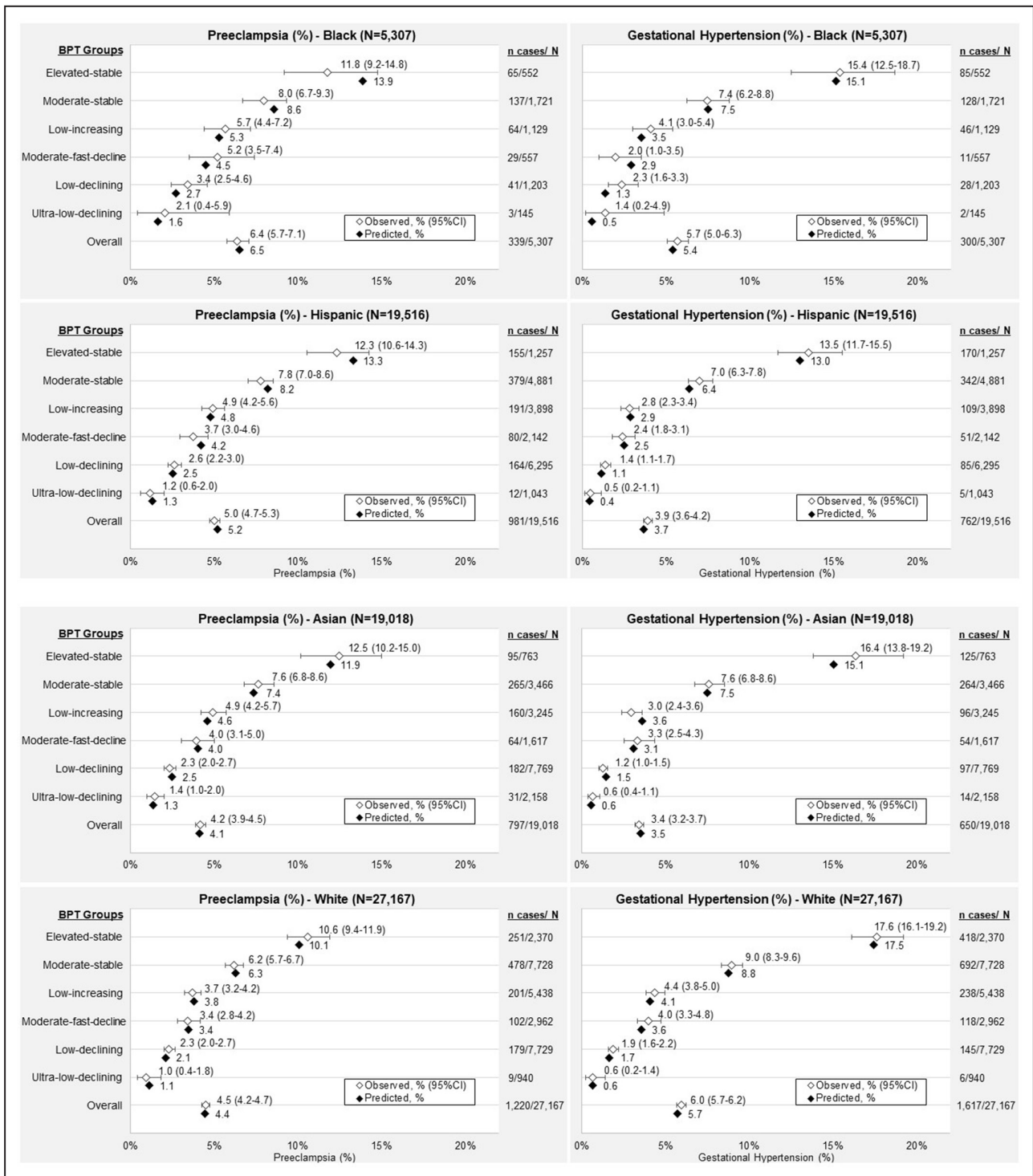


Figure 4. Early pregnancy blood pressure trajectory (BPT) groups stratified by racial and ethnic groups with or without moderate risk factors: model average predicted probabilities (percentages) and observed incidence rate of preeclampsia and gestational hypertension (percentages and 95% CIs) for the internal validation sample.

measurements. The models' predictive performance was similar for ≤ 4 BP measurements (C-statistic [95% CI] for model 3.3: early-onset preeclampsia, 0.742 [0.714–0.770]; later-onset preeclampsia, 0.730

[0.721–0.738]; and gestational hypertension, 0.767 [0.760–0.775]; Table S14). Performance decreased slightly for ≤ 3 and ≤ 2 BP measurements, but prediction was still good, with C-statistics for model 3.3

ranging from 0.727 to 0.768 and from 0.723 to 0.759, respectively (Table S14).

Sensitivity Analyses: BPT Groups Restricted to 16 Weeks' Gestation

The BPT groups restricted up to 16 weeks' gestation for all BP measurements showed similar associations for prediction of the HDP outcomes as well as the C-statistics from models with BPT groups up to 20 weeks' gestation and all risk factors, indicating robust predictive ability of BPT groups within the earlier window (Table S15).

DISCUSSION

Summary of Findings

In this large, diverse, multiracial and ethnic cohort of pregnant patients considered at low-to-moderate risk of HDP, we developed and validated models for early prediction of early- and later-onset preeclampsia and gestational hypertension using readily available routine clinical BP data from the EHR. The 6 BPT groups were associated with a gradient of increasing risk for all 3 HDP groups compared with no HDP. Our prediction models incorporating 6 BPT groups (representing distinct patterns of systolic BP changes from 0–20 weeks' gestation) plus standard risk factors, social factors, and lifestyle behavioral factors for early- and later-onset preeclampsia and gestational hypertension had excellent discrimination (C-statistics ranging from 0.731–0.770). In addition, discrimination was better than models using only an initial BP measurement plus standard risk factors (0.713–0.744) or the standard risk factors only (0.688–0.695). Models incorporating BPT groups discriminated risk of preeclampsia and gestational hypertension among individuals with no moderate risk factors, and among different combinations of moderate risk factors (1, 2, and >2 moderate risk factors), and diabetes as defined by the USPSTF. The absolute observed risk of preeclampsia ranged from 0.5% to >15%, and gestational hypertension ranged from 0.4% to 17.6%, corresponding to increasing BPT groups for all risk factor combinations, and other subgroups (eg, nulliparity, racial and ethnic groups, low income, age, or maternal obesity). These findings provide the first evidence that predictive models incorporating BPT groups discriminate risk among ostensibly low-to-moderate risk populations, revealing a subset of individuals at high risk for preeclampsia or gestational hypertension (ie, >6% to 15% probability) within standard moderate or no risk factor groups. This is especially important for patients with common risk factors, such as nulliparity and obesity, for whom the risk of HDP varied from 1.8% to 13.6% across the 6 BPT

groups, demonstrating the clinical precision of the BPT group risk stratification.

This study advances prediction methods in 2 respects: the models stratify risk of HDP based on initial BP levels as well as changes in the BP patterns over time, and they performed well for prediction of preeclampsia (early and late onset) as well as gestational hypertension, an outcome that previous studies have rarely addressed. Finally, the study addressed the challenge of prediction of HDP within a sample that specifically excluded high-risk clinical conditions, such as prior chronic hypertension, liver, heart, or kidney disease, or a history of preeclampsia with 5- to 10-fold or higher risk of HDP.³⁸ Black and Hispanic groups had slightly higher observed rates of preeclampsia within this low-to-moderate risk sample, but BPT models were similarly effective within each racial and ethnic group. The American College of Obstetrics and Gynecology considers Black race a moderate risk factor because of “environmental, social, and historical inequities shaping health exposures, access to health care, and the unequal distribution of resources, but not biological propensities.”⁶

Comparison to Previous Evidence

Previous strategies have used first-trimester clinical screening criteria plus biophysical and biomarker parameters for a fixed false-positive rate of 10% to accurately identify women who would develop early-onset preeclampsia, but the methods were less successful for later-onset preeclampsia.^{14,18–21,39,40} Other prediction models included clinical risk factors, laboratory tests and the uterine artery index, a single BP measurement before 13 to 18 weeks' gestation,^{19–21,41} and only 2,⁴² or ≥ 1 , BP measurements from >18 to 37 weeks' gestation,^{15,39,40,43–47} delaying prediction until late gestation. For example, models including first-trimester risk factors, mean arterial pressure at 11 to 13 weeks' gestation, uterine artery index, and 2 biomarkers identified 75% of early-onset preeclampsia cases, but only 47% of later-onset preeclampsia.²⁰ The uterine artery pulsatility index is a sensitive marker of placental dysfunction, a hallmark of early-onset preeclampsia,¹⁵ but is less effective to identify later-onset preeclampsia.⁴⁸ Models among “healthy” nulliparas (90% White) women included age, BMI, mean arterial pressure, family history of heart disease, biomarkers, and uterine artery index, yielding an area under the curve of 0.68 to 0.71 for preeclampsia, and modest model prediction (0.68) in validation data sets.^{11,41} For gestational hypertension, first antenatal visit BP and clinical risk factors yielded an area under the curve of 0.68.¹⁵

In summary, previous models for HDP face several limitations. Despite excellent ability to accurately predict early-onset preeclampsia,²⁶ their implementation

is impractical in many settings because of lack of technical expertise and/or the expense of biomarker tests. Second, the methods used to evaluate model prediction have been substandard, with few studies adhering fully to TRIPOD guidelines.¹⁶ Fifty percent or less performed independent validation, and only 12% tested model calibration, which was usually poor.^{15,17,40,49} Many previous studies had sample sizes of <2000 to 3500 patients, low racial and ethnic diversity, and sparse data on gestational hypertension.^{40,42,50} Finally, some models generally can identify clinically high-risk individuals within mixed risk populations, but perform insufficiently for early prediction of later-onset preeclampsia or gestational hypertension among lower- or moderate-risk patients.^{51,52} Finally, the 2021 USPSTF criteria do not incorporate BP levels or changes, and currently classify ~86% of pregnant patients as candidates for LDASA. This global approach to prevention of HDP and preterm birth requires reevaluation of the evidence basis.

Strengths and Limitations

This study's strengths rest on our innovative methods incorporating the longitudinal BPT groups and complete implementation of the TRIPOD guidelines based on the development and internal validation data from predictive models for HDP among ostensibly low-to-moderate risk pregnant individuals. We showed excellent calibration for all models, which discriminated risk for preeclampsia within standard risk factors. This large, community-based sample within a single integrated health care system encompassed broad racial and ethnic diversity. We leveraged 11 years of EHR data to capture routine outpatient longitudinal clinical BP measurements in the first half of gestation (on average, 4 different days of measurements), prepregnancy BMI, clinical risk factors, social determinants of health (neighborhood deprivation index and government health insurance), demographic variables, and lifestyle behavioral factors (smoking and gestational weight gain). We intentionally excluded current and prior medical conditions (ie, cancer and kidney, liver, and cardiovascular disease) and alcohol dependence, used high-quality methods to identify prior chronic or early pregnancy hypertension (<20 weeks), and excluded history of preeclampsia, which confers much higher HDP risk. Our cohort included 478 women with pregestational diabetes without comorbidities to consider them as having "moderate risk" of HDP as relatively healthy women with diabetes. HDP outcomes were identified by *ICD-9/ICD-10* codes within a single integrated health care system and validated by chart review. Our findings are supported by a prior study showing that systolic BP changes across 4 to 16 weeks' gestation differed by risk of HDP more than

diastolic BP changes.⁵³ There were also some limitations. We could not evaluate individual-level social determinants of health (ie, education, economic resources, health care barriers, discrimination, and nativity) that may affect risk differences, identify individuals with prior gestational hypertension, or identify those treated with artificial reproductive technology. The history of preeclampsia may have been underestimated for births before KPNC health plan membership. Our models were not evaluated in an external validation population. Future next steps will be to compare the performance with alternative statistical prediction models that allow for more complex relationships between predictors and the outcomes (eg, neural networks, random forest, and gradient boosting) or functional linear regression models that use smoothed functions directly in the model rather than our 2-stage latent trajectory model approach.

Conclusions and Implications of Findings

Prediction models incorporating longitudinal patterns of BP changes in early pregnancy with standard clinical risk factors more accurately discriminated risk of HDP among individuals currently considered to have low-to-moderate risk pregnancies by USPSTF criteria. The ready availability of clinical BP measurements to evaluate BP patterns through 20 weeks' gestation also increases the feasibility of implementing such models in practice because they do not rely on biomarkers and biophysical parameters. The more individualized approach to early risk assessment incorporating BPT patterns may potentially improve equity in care delivery and better outcomes by identifying women at higher absolute risk for HDP outcomes who may benefit most from targeted interventions and more intensive monitoring.

These findings are likely to influence practice standards. Current guidelines recommend that patients with only one moderate risk factor are to be "considered" for treatment with LDASA.⁶ The systolic BPT patterns based on 3 or 4 BP measurements in the first half of pregnancy reclassified a substantial proportion of patients, considered as moderate risk under current guidelines' criteria, as having lower risk for preeclampsia and gestational hypertension. Furthermore, the effectiveness of the early pregnancy BPT patterns to discriminate high-risk individuals within an ostensibly low-to-moderate risk population is a major advancement in precision care without expensive assessments. Finally, these findings apply widely to all health care settings, as well as diverse multiracial and ethnic groups. This evidence demonstrates the inherent value of early pregnancy BP patterns to identify individuals who may experience improved outcomes through higher vigilance and, ultimately, more effective interventions.

ARTICLE INFORMATION

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Affiliations

Division of Research, Kaiser Permanente Northern California, Oakland, CA (E.P.G., B.S., A.S.G., M.N.N.-H., W.T., S.E.A.); Department of Health Systems Science, Kaiser Permanente Bernard J. Tyson School of Medicine, Pasadena, CA (E.P.G., A.S.G.); Department of Obstetrics and Gynecology, Kaiser Permanente, Oakland Medical Center, Oakland, CA (M.G.); The Permanente Medical Group, Kaiser Permanente Northern California, Oakland, CA (N.G.); Departments of Epidemiology, Biostatistics and Medicine, University of California, San Francisco, San Francisco, CA (A.S.G.); Department of Medicine, Stanford University, Palo Alto, CA (A.S.G.); Magee-Womens Research Institute, Department of Obstetrics, Gynecology and Reproductive Sciences, Epidemiology and Clinical and Translational Research, University of Pittsburgh, Pittsburgh, PA (J.M.R.); and Department of Neurology, Kaiser Permanente, Walnut Creek Medical Center, Walnut Creek, CA (M.N.N.-H.).

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Disclosures

None.

Supplemental Material

Data S1

Tables S1–S15

Figures S1–S4

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Supplemental Material

Data S1.

Supplemental Methods

Enhanced Methodology

1. Classification of HDP Outcomes - Preeclampsia and Gestational Hypertension.

To improve and refine the accuracy of the HDP outcome classification, we included additional ICD-9 codes for unspecified hypertension and selected the last diagnosis code closest to the delivery date recorded in the delivery hospitalization discharge summary. When both preeclampsia and gestational hypertension ICD-9/10 codes were found in a record, we classified the outcome as preeclampsia.

Our methodology to improve the accurate classification of gestational hypertension and to define early preeclampsia and late preeclampsia with the following modifications:

- 1) The ICD-codes closest to the delivery hospitalization were selected to classify the specific hypertensive disorder of pregnancy: preeclampsia and gestational hypertension. This process prioritized the discharge summary diagnosis codes in lieu of earlier outpatient visits that are more likely to change later in pregnancy and definitively listed at delivery hospitalization.
- 2) The inclusion of the additional ICD-9 codes, 642.90 through 642.94, for unspecified hypertension complicating pregnancy, which had been previously utilized by mapping only the ICD-10 codes.
- 3) The gestational age of the diagnosis based on the ICD codes was utilized to categorize early preeclampsia and late preeclampsia for the development and validation datasets.

2. Methods to Identify the BPT Trajectory Groups:

We first fit group-based trajectory models to identify distinct early pregnancy BP trajectory groups during the first 20 weeks' gestation using the model development dataset. This statistical approach combines finite mixture modeling and growth curve modeling into a unified model to identify latent classes of individuals with similar patterns of change over time.³¹ Specifically, we fit each trajectory curves with third order polynomial terms to allow for curvature in the patterns of longitudinal BP measurements during the first 20 weeks' gestation; we tested for statistical significance of quadratic and cubic terms to determine the appropriate shape of each trajectory pattern, with model parameters estimated by maximum likelihood, and we used the Bayes Factor to determine the number of latent groups.²⁹ [Reference: Gunderson EP, et al. Early Pregnancy Blood Pressure Patterns Identify Risk of Hypertensive Disorders of Pregnancy Among Racial and Ethnic Groups. *Hypertension*. 2022;79(3):599-613.]

3. Models and Prediction Equations

Table S4 shows the model coefficients for prediction of early-onset preeclampsia, and later-onset preeclampsia and gestational hypertension. The equations for the prediction of each HDP in the models are also shown below.

Prediction Models – Enhanced Supplemental Methods.

General Formula: For a multinomial model with M categories and reference category $m = 1$,
 $\Pr(Y = 1|X = x) = \frac{1}{1 + \sum_{j=2}^M \exp(x\beta_j)}$ and $\Pr(Y = m|X = x) = \frac{\exp(x\beta_m)}{1 + \sum_{j=2}^M \exp(x\beta_j)}$ for $m = 2, \dots, M$.

Example prediction model using multinomial model equations.

Covariates for example woman: Maternal age 25 years, Hispanic, nulliparous, no diabetes, pre-pregnancy BMI = 30 kg/m², blood pressure trajectory group 5 (Moderate-stable), neighborhood deprivation index Q1, no government health insurance, never smoker, rate of gestational weight gain up to 20 weeks gestational age = 0.5 kg per week.

Example Calculations:

$$x\beta_{earlyPE} = -9.4235 + 0.0245(25) + 0.3937 + 1.0544 + 0.0264(30) + 1.8512 + 0.3329(0.5) = -4.5533$$

$$x\beta_{latePE} = -6.7792 + 0.0232(25) + 1.2426 + 1.2426 + 0.0258(30) + 1.6362 + 0.1577(0.5) = -2.1304$$

$$x\beta_{GH} = -7.4698 + 0.0280(25) - 0.2474 + 0.9370 + 0.0391(30) + 2.5145 + 0.2973(0.5) = -2.2441$$

$$1 + \sum_{j=2}^M \exp(x\beta_j) = 1 + \exp(-4.5533) + \exp(-2.1304) + \exp(-2.2441) = 1.2354$$

$$\Pr(Y = \text{early PE}|X = x) = \frac{\exp(x\beta_{earlyPE})}{1 + \sum_{j=2}^M \exp(x\beta_j)} = \frac{\exp(-4.5533)}{1.2354} = 0.0085 = 0.85\%$$

$$\Pr(Y = \text{late PE}|X = x) = \frac{\exp(x\beta_{latePE})}{1 + \sum_{j=2}^M \exp(x\beta_j)} = \frac{\exp(-2.1304)}{1.2354} = 0.0962 = 9.62\%$$

$$\Pr(Y = \text{GH}|X = x) = \frac{\exp(x\beta_{GH})}{1 + \sum_{j=2}^M \exp(x\beta_j)} = \frac{\exp(-2.2441)}{1.2354} = 0.0858 = 8.58\%$$

Table S1. TRIPOD Checklist: Prediction Model Development

Section/Topic	Item	Checklist Item	Page
Title and abstract			
Title	1	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract	2	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	2-3
Introduction			
Background and objectives	3a	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	6-7
	3b	Specify the objectives, including whether the study describes the development or validation of the model or both.	7
Methods			
Source of data	4a	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	8-9
	4b	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	8
Participants	5a	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	8
	5b	Describe eligibility criteria for participants.	8-9
	5c	Give details of treatments received, if relevant.	NA
Outcome	6a	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	10
	6b	Report any actions to blind assessment of the outcome to be predicted.	NA
Predictors	7a	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	9-11
	7b	Report any actions to blind assessment of predictors for the outcome and other predictors.	NA
Sample size	8	Explain how the study size was arrived at.	9
Missing data	9	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	31
Statistical analysis methods	10a	Describe how predictors were handled in the analyses.	11-13
	10b	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	11-13
	10d	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	12
Risk groups	11	Provide details on how risk groups were created, if done.	9-10
Results			
Participants	13a	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	34, 28-29
	13b	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	13, 34
Model development	14a	Specify the number of participants and outcome events in each analysis.	34, 30-31
	14b	If done, report the unadjusted association between each candidate predictor and outcome.	32
Model specification	15a	Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	32
	15b	Explain how to use the prediction model.	21
Model performance	16	Report performance measures (with CIs) for the prediction model.	32
Discussion			
Limitations	18	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	20-21
Interpretation	19b	Give an overall interpretation of the results, considering objectives, limitations, and results from similar studies, and other relevant evidence.	21-22
Implications	20	Discuss the potential clinical use of the model and implications for future research.	4, 21
Other information			
Supplementary information	21	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	Supplmt file
Funding	22	Give the source of funding and the role of the funders for the present study.	22

We recommend using the TRIPOD Checklist in conjunction with the TRIPOD Explanation and Elaboration document.

Table S2. Maternal Characteristics in the Model Development Dataset (N=174,925 and the Internal Independent Validation Dataset (N=74,967) for One Singleton Live or Still Birth per Individual Among Low-to-Moderate Risk Women (2009-2019).

Characteristics	Total Sample N=249,892	Model- Development N=174,925	Model Validation N=74,967	P-value
Mean (SD) or n (%)				
Maternal age, y, mean (SD)	30.9 (5.3)	30.9 (5.3)	31.0 (5.3)	0.12
Age categories, n (%)				0.11
18-25 y	45752 (18)	32163 (18)	13589 (18)	
26-30 y	77836 (31)	54617 (31)	23219 (31)	
31-35 y	83341 (33)	58060 (33)	25281 (34)	
36-40 y	36466 (15)	25541 (15)	10925 (15)	
41-45 y	6497 (3)	4544 (3)	1953 (3)	
Racial and ethnic groups, n (%)				0.40
Asian	63410 (25)	44216 (25)	19194 (26)	
Black	18066 (7)	12708 (7)	5358 (7)	
Hispanic	66003 (26)	46289 (26)	19714 (26)	
White	91329 (37)	63927 (37)	27402 (37)	
Mixed/Native/unknown	11084 (4)	7785 (4)	3299 (4)	
Prenatal parity, n (%)				0.19
Nulliparous (0 prior births)	142872 (57)	99972 (57)	42900 (57)	
Primiparous (1 prior birth)	67194 (27)	47215 (27)	19979 (27)	
Biparous (2 prior births)	27225 (11)	18947 (11)	8278 (11)	
Multiparous (3 or more prior birth)	12601 (5)	8791 (5)	3810 (5)	
Gestational age at first prenatal care visit, (weeks), mean (SD)	8.2 (2.0)	8.2 (2.0)	8.2 (2.0)	0.28
Diabetes, Pregestational, n (%)	1558 (1)	1078 (1)	480 (1)	0.48
Prepregnancy weight, (kg), mean (SD)	68.9 (16.6)	68.9 (16.6)	68.8 (16.5)	0.06
Height, (cm), mean (SD)	162.5 (7.0)	162.5 (7.0)	162.5 (7.0)	0.26
Prepregnancy BMI, kg/m ² , mean (SD)	26.0 (5.8)	26.0 (5.8)	26.0 (5.8)	0.11
Prepregnancy BMI Categories, n (%)				0.24
Underweight (<18.5)	6761 (3)	4666 (3)	2095 (3)	
Normal weight (18.5-24.9)	123198 (50)	86172 (50)	37026 (50)	
Overweight (25-29.9)	67231 (27)	47046 (27)	20185 (27)	
Obesity class I (30-34.9)	30564 (12)	21515 (12)	9049 (12)	
Obesity class II (35-39.9)	12882 (5)	9020 (5)	3862 (5)	
Obesity class III (≥40)	7435 (3)	5248 (3)	2187 (3)	
<u>Social Factors</u>				
Government health insurance, n (%)	18401 (7)	12881 (7)	5520 (7)	1.00
Neighborhood deprivation index, n (%)				0.14
Q1 ≤-1 (least deprived)	28723 (12)	20135 (12)	8588 (11)	
Q2 >-1 and ≤0	125947 (50)	87984 (50)	37963 (51)	
Q3 >0 and ≤1	64742 (26)	45318 (26)	19424 (26)	
Q4 >1 (most deprived)	30076 (12)	21214 (12)	8862 (12)	

Table S2, Continued:

<u>Lifestyle Behaviors</u>				
Smoking status, n (%)				0.60
Current	14087 (6)	9918 (6)	4169 (6)	
Former	30409 (12)	21300 (12)	9109 (12)	
Never	204169 (82)	142836 (82)	61333 (82)	
Unknown	1227 (0)	871 (0)	356 (0)	
Total gestational weight gain, (kg), mean (SD)	13.5 (6.5)	13.5 (6.5)	13.5 (6.4)	0.18
Rate of gestational weight gain \leq 20 weeks GA, (kg per wk), mean (SD)	0.2 (0.2)	0.2 (0.2)	0.2 (0.2)	0.67
<u>Early pregnancy BP trajectory groups, n (%)</u>				
Elevated-stable	17284 (7)	12068 (7)	5216 (7)	
Moderate-stable	63550 (25)	44738 (26)	18812 (25)	
Low-increasing	48066 (19)	33579 (19)	14487 (19)	
Moderate-fast-decline	25288 (10)	17639 (10)	7649 (10)	
Low-declining	80356 (32)	56079 (32)	24277 (32)	
Ultra-low-declining	15348 (6)	10822 (6)	4526 (6)	
No. of BP measurements up to 20 weeks GA, mean (SD)	4.1 (1.7)	4.1 (1.7)	4.1 (1.7)	0.70
Delivery gestational age, (weeks), mean (SD)	39.2 (2.0)	39.2 (2.0)	39.3 (2.0)	0.90

BMI, body mass index; BP, blood pressure; GA, gestational age; SD, standard deviation.

Table S3. Predictive Model Performance for Hypertensive Disorders of Pregnancy Among Low-to-Moderate Risk Women Utilizing Six Early Pregnancy Blood Pressure Trajectory Groups, Standard Risk Factors, Lifestyle Behaviors, and Social Factors (Model 3.3) and With the Addition of Interaction Terms for Pre-pregnancy BMI, Parity, Racial and Ethnic Groups (Model 3.4), or Group Probabilities for BPT Groups (Model 3.5). C-statistics (95%CI) N=74,967 validation dataset.

Model number	Predictive Model Variables	Prediction Model C-statistics (95%CI)		
		Early-onset Preeclampsia (<34 weeks)	Late-onset Preeclampsia (≥34 weeks)	Gestational Hypertension
3.3	Six BPT groups + Standard Risk Factors (BMI + Parity + Age + Race/ethnicity + Diabetes) + Lifestyle Behaviors + Social Factors	0.747 (0.719-0.775)	0.731 (0.723-0.740)	0.770 (0.762-0.778)
3.4	Six BPT groups + Standard Risk Factors (BMI + Parity + Age + Race/ethnicity + Diabetes) + Lifestyle Behaviors + Social Factors + Interaction terms for pre-pregnancy BMI, parity, and racial/ethnic groups	0.748 (0.721-0.776)	0.731 (0.723-0.740)	0.770 (0.762-0.778)
3.5	Six BPT groups + Standard Risk Factors (BMI + Parity + Age + Race/ethnicity + Diabetes) + Lifestyle Behaviors + Social Factors + Group probabilities for BPT groups	0.755 (0.728-0.782)	0.735 (0.727-0.744)	0.777 (0.769-0.784)
<p>Abbreviations: BP, blood pressure; BMI, pre-pregnancy body mass index; BPT, blood pressure trajectory</p> <p>Standard Risk factors: Pre-pregnancy BMI (kg/m²), parity (0 vs ≥1), maternal age (years), racial and ethnic groups [Black, Hispanic, Asian, White (referent), Mixed/Native/unknown], and pregestational diabetes;</p> <p>Lifestyle Behaviors: Smoking during pregnancy, and Rate of gestational weight gain (GWG) ≤ 20 weeks' gestation (kg per week).</p> <p>Social Factors: Government health insurance and Neighborhood deprivation index</p> <p>C-statistics for Model 1: Six BPT + Standard Risk factors, Model 2: Six BPT + Standard Risk Factors + Interaction terms for pre-pregnancy BMI, parity and racial and ethnic groups, Model 3: Six BPT groups + Standard Risk Factors, Lifestyle Behaviors and Social Factors + BPT Group probabilities.</p>				

Table S4. Model coefficients for predicting risk of Early-onset Preeclampsia, Later-onset Preeclampsia, Gestational Hypertension, and No HDP Outcomes for the Model-Development (N=174,925) Dataset; Singleton Gestations, One Live or Still Birth per Individual Among Women at Low-to-Moderate Risk (2009-2019).

Covariate	Early-onset Preeclampsia	Later-onset Preeclampsia	Gestational Hypertension	No HDP (ref)
Intercept	-9.4235	-6.7792	-7.4698	0
Maternal age, years	0.0245	0.0232	0.0280	0
Race and ethnicity,				
Asian	0.4476	0.1906	-0.0710	0
Black	0.7735	0.3397	-0.1155	0
Hispanic	0.3937	0.3372	-0.2474	0
Mixed/Native/unknown	0.1360	0.1795	-0.0350	0
White (referent)	0	0	0	0
Prenatal parity				
Nulliparous	1.0544	1.2426	0.9370	0
Parous (referent)	0	0	0	0
Diabetes, pregestational	1.4863	0.9916	0.2530	0
Pre-pregnancy BMI, kg/m ²	0.0264	0.0258	0.0391	0
Blood Pressure Trajectory Group				
1 Ultra-low-declining (referent)				
2 Low-declining	0.6249	0.5791	0.9134	0
3 Moderate-fast-decline	0.8477	1.0349	1.6163	0
4 Low-increasing	1.3952	1.1222	1.7583	0
5 Moderate-stable	1.8512	1.6362	2.5145	0
6 Elevated-stable	2.5250	2.1835	3.2699	0
<i><u>Social Factors</u></i>				
Neighborhood deprivation index (NDI)				
Q1 (least deprived, referent)	0	0	0	0
Q2	0.0609	0.0292	-0.0468	0
Q3	0.0992	0.0509	-0.0780	0
Q4 (most deprived)	0.1452	0.0989	-0.0608	0
Government health insurance	-0.0165	0.1812	0.1849	0
<i><u>Lifestyle Behaviors</u></i>				
Smoking status, n (%)				
Current	-0.0280	0.0292	0.0922	0
Former	-0.1115	0.0578	0.1138	0
Never (ref)	0	0	0	0
Rate of gestational weight gain up to 20 weeks' gestation (kg per week)	0.3329	0.1577	0.2973	0

HDP, hypertensive disorders of pregnancy; BMI, body mass index; SD, standard deviation. Early-onset Preeclampsia is a diagnosis <34 weeks' gestational age; Later-onset Preeclampsia is a diagnosis ≥34 weeks' gestational age

Table S5. Models for Early Pregnancy Blood Pressure Trajectory Groups Plus Risk Factors Stratified by the Number of Moderate Risk Factors and Diabetes: Average Predicted Probabilities (n, %) and the Observed Incidence Rate (n, % and 95% Confidence Intervals) of Preeclampsia and Gestational Hypertension within the Internal Validation Sample (n=74,274) of Low-to-Moderate Risk Women. USPSTF Moderate Risk Factors = Black race, Obesity, Nulliparity, Age ≥35 years, Low income/Government insurance, or Pregestational Diabetes

BP Trajectory Groups	N (col %) women	Pre- eclampsia n	Average Predicted %	Observed % (95% CI)	Gestational Hypertension n	Average Predicted %	Observed % (95% CI)
No Risk Factors (N=12,390).							
Elevated-stable	380 (3.1)	17	4.7	4.5 (2.6-7.1)	36	8.1	9.5 (6.7-12.9)
Moderate-stable	2,243 (18.1)	61	2.9	2.7 (2.1-3.5)	86	3.9	3.8 (3.1-4.7)
Low-increasing	2,277 (18.4)	33	1.8	1.4 (1.0-2.0)	35	1.8	1.5 (1.1-2.1)
Moderate-fast-decline	1,217 (9.8)	20	1.6	1.6 (1.0-2.5)	12	1.6	1.0 (0.5-1.7)
Low-declining	5,176 (41.8)	43	1.0	0.8 (0.6-1.1)	44	0.8	0.9 (0.6-1.1)
Ultra-low-declining	1,097 (8.9)	9	0.6	0.8 (0.4-1.6)	4	0.3	0.4 (0.1-0.9)
Overall	12,390	183	1.6	1.5 (1.3-1.7)	217	1.8	1.8 (1.5-2.0)
One Risk Factor (N=36,684).							
Elevated-stable	2,129 (5.0)	203	10.0	9.5(8.3-10.9)	332	14.0	15.6(14.1-17.2)
Moderate-stable	8,499 (23.2)	512	6.6	6.0 (5.5-6.6)	640	7.2	7.5 (7.0-8.1)
Low-increasing	7,136 (19.5)	280	4.2	3.9 (3.5-4.4)	243	3.5	3.4 (3.0-3.9)
Moderate-fast-decline	3,822 (10.4)	119	3.8	3.1 (2.6-3.7)	119	3.0	3.1 (2.6-3.7)
Low-declining	12,663 (34.5)	285	2.5	2.3 (2.0-2.5)	204	1.5	1.6 (1.4-1.8)
Ultra-low-declining	2,435 (6.6)	32	1.4	1.3 (0.9-1.9)	15	0.6	0.6 (0.3-1.0)
Overall	36,684	1,431	4.3	3.9 (3.7-4.1)	1553	4.0	4.2 (4.0-4.4)
Two Risk Factors (N=19,029).							
Elevated-stable	1,765 (9.3)	216	12.8	12.2(10.7-13.9)	300	17.6	17.0(15.3-18.8)
Moderate-stable	5,582 (29.3)	466	8.4	8.3 (7.6-9.1)	540	9.1	9.7 (8.9-10.5)
Low-increasing	3,760 (19.8)	239	5.5	6.4 (5.6-7.2)	174	4.4	4.6 (4.0-5.3)
Moderate-fast-decline	1,964 (10.3)	113	4.8	5.8 (4.8-6.9)	92	3.8	4.7 (3.8-5.7)
Low-declining	5,118 (26.9)	207	3.2	4.0 (3.5-4.6)	95	1.9	1.9 (1.5-2.3)
Ultra-low-declining	840 (4.4%)	12	1.9	1.4 (0.7-2.5)	7	0.7	0.8 (0.3-1.7)
Overall	19,029	1,253	6.2	6.6 (6.2-6.9)	1208	6.1	6.3 (6.0-6.7)
More than Two Risk Factors (N=6,171).							
Elevated-stable	880 (14.3)	153	16.1	17.4(14.9-20.1)	166	19.5	18.9(16.3-21.6)
Moderate-stable	2,306 (37.4)	274	10.9	11.9(10.6-13.3)	238	10.3%	10.3 (9.1-11.6)
Low-increasing	1,180 (19.1)	91	7.0	7.7 (6.3-9.4)	68	5.0%	5.8 (4.5-7.2)
Moderate-fast-decline	612 (9.9)	32	6.2	5.2 (3.6-7.3)	24	4.3%	3.9 (2.5-5.8)
Low-declining	1,068 (17.3)	49	3.8	4.6 (3.4-6.0)	34	2.0%	3.2 (2.2-4.4)
Ultra-low-declining	125 (2.0)	4	2.1	3.2 (0.9-8.0)	2	0.7%	1.6 (0.2-5.7)
Overall	6,171	603	9.0	9.8 (9.0-10.5)	532	8.4%	8.6 (7.9-9.3)

Note: n = 693 women excluded from the model due to missing covariates; pre-pregnancy BMI, NDI, or rate of gestational weight gain up to 20 weeks' gestation.

Table S6. Models for Early Pregnancy Blood Pressure Trajectory Groups Plus Risk Factors Stratified by Racial and Ethnic Groups: Average Predicted Probabilities (n, %) and the Observed Incidence Rate (n, % and 95% Confidence Intervals) of Preeclampsia and Gestational Hypertension within the Internal Validation Sample (n=74,274) of Low-to-Moderate Risk Women. USPSTF Moderate Risk Factors = Black race, Obesity, Nulliparity, Age ≥35 years, Low income/Government insurance, or Pregestational Diabetes

BP Trajectory Groups	N (col %) women	Pre- eclampsia n	Average Predicted %	Observed % (95% CI)	Gestational Hypertension n	Average Predicted %	Observed % (95% CI)
Black (N=5,307) with or without moderate risk factors							
Elevated-stable	552 (10.4)	65	13.9	11.8 (9.2-14.8)	85	15.1	15.4(12.5-18.7)
Moderate-stable	1,721 (32.4)	137	8.6	8.0 (6.7-9.3)	128	7.5	7.4 (6.2-8.8)
Low-increasing	1,129 (21.3)	64	5.3	5.7 (4.4-7.2)	46	3.5	4.1 (3.0-5.4)
Moderate-fast-decline	557 (10.5)	29	4.5	5.2 (3.5-7.4)	11	2.9	2.0 (1.0-3.5)
Low-declining	1,203 (22.7)	41	2.7	3.4 (2.5-4.6)	28	1.3	2.3 (1.6-3.3)
Ultra-low-declining	145 (2.7)	3	1.6	2.1 (0.4-5.9)	2	0.5	1.4 (0.2-4.9)
Overall	5,307	339	6.5	6.4 (5.7-7.1)	300	5.4	5.7 (5.0-6.3)
Hispanic (N=19,516) with or without moderate risk factors							
Elevated-stable	1,257 (6.4)	155	13.3	12.3(10.6-14.3)	170	13.0	13.5(11.7-15.5)
Moderate-stable	4,881 (25.0)	379	8.2	7.8 (7.0-8.6)	342	6.4	7.0 (6.3-7.8)
Low-increasing	3,898 (20.0)	191	4.8	4.9 (4.2-5.6)	109	2.9	2.8 (2.3-3.4)
Moderate-fast-decline	2,142 (11.0)	80	4.2	3.7 (3.0-4.6)	51	2.5	2.4 (1.8-3.1)
Low-declining	6,295 (32.3)	164	2.5	2.6 (2.2-3.0)	85	1.1	1.4 (1.1-1.7)
Ultra-low-declining	1,043 (5.3)	12	1.3	1.2 (0.6-2.0)	5	0.4	0.5 (0.2-1.1)
Overall	19,516	981	5.2	5.0 (4.7-5.3)	762	3.7	3.9 (3.6-4.2)
Asian (N=19,018) with or without moderate risk factors							
Elevated-stable	763 (4.0)	95	11.9	12.5(10.2-15.0)	125	15.1	16.4(13.8-19.2)
Moderate-stable	3,466 (18.2)	265	7.4	7.6 (6.8-8.6)	264	7.5	7.6 (6.8-8.6)
Low-increasing	3,245 (17.1)	160	4.6	4.9 (4.2-5.7)	96	3.6	3.0 (2.4-3.6)
Moderate-fast-decline	1,617 (8.5)	64	4.0	4.0 (3.1-5.0)	54	3.1	3.3 (2.5-4.3)
Low-declining	7,769 (40.9)	182	2.5	2.3 (2.0-2.7)	97	1.5	1.2 (1.0-1.5)
Ultra-low-declining	2,158 (11.3)	31	1.3	1.4 (1.0-2.0)	14	0.6	0.6 (0.4-1.1)
Overall	19,018	797	4.1	4.2 (3.9-4.5)	650	3.5	3.4 (3.2-3.7)
White (N=27,167) with or without moderate risk factors							
Elevated-stable	2,370 (8.7)	251	10.1	10.6 (9.4-11.9)	418	17.5	17.6(16.1-19.2)
Moderate-stable	7,728 (28.4)	478	6.3	6.2 (5.7-6.7)	692	8.8	9.0 (8.3-9.6)
Low-increasing	5,438 (20.0)	201	3.8	3.7 (3.2-4.2)	238	4.1	4.4 (3.8-5.0)
Moderate-fast-decline	2,962 (10.9)	102	3.4	3.4 (2.8-4.2)	118	3.6	4.0 (3.3-4.8)
Low-declining	7,729 (28.4)	179	2.1	2.3 (2.0-2.7)	145	1.7	1.9 (1.6-2.2)
Ultra-low-declining	940 (3.5)	9	1.1	1.0 (0.4-1.8)	6	0.6	0.6 (0.2-1.4)
Overall	27,167	1,220	4.4	4.5 (4.2-4.7)	1617	5.7	6.0 (5.7-6.2)

Table S7. Models for Early Pregnancy Blood Pressure Trajectory Groups Plus Risk Factors Stratified by Parity: Average Predicted Probabilities (n, %) and the Observed Incidence Rate (n, % and 95% Confidence Intervals) of Preeclampsia and Gestational Hypertension within the Internal Validation Sample (n=74,274) of Low-to-Moderate Risk Women. USPSTF Moderate Risk Factors = Black race, Obesity, Nulliparity, Age ≥35 years, Low income/Government insurance, or Pregestational Diabetes

BP Trajectory Groups	N (col %) women	Pre- eclampsia n	Average Predicted %	Observed % (95% CI)	Gestational Hypertensio n n	Average Predicted %	Observed % (95% CI)
All Parous (N=31,691)							
Elevated-stable	1,790 (5.6)	133	6.4	7.4 (6.3-8.7)	223	10.5	12.5(11.0-14.1)
Moderate-stable	7,223 (22.8)	266	3.7	3.7 (3.3-4.1)	350	4.8	4.8 (4.4-5.4)
Low-increasing	6,050 (19.1)	113	2.2	1.9 (1.5-2.2)	125	2.2	2.1 (1.7-2.5)
Moderate-fast-decline	3,233 (10.2)	62	1.9	1.9 (1.5-2.5)	52	1.9	1.6 (1.2-2.1)
Low-declining	11,195 (35.3)	119	1.2	1.1 (0.9-1.3)	110	0.9	1.0 (0.8-1.2)
Ultra-low-declining	2,200 (6.9)	15	0.6	0.7 (0.4-1.1)	7	0.3	0.3 (0.1-0.7)
Overall	31,691	708	2.3	2.2 (2.1-2.4)	867	2.6	2.7 (2.6-2.9)
Parous with No Risk Factors (N=12,390); All Low Risk							
Elevated-stable	380 (3.1)	17	4.7	4.5 (2.6-7.1)	36	8.1	9.5 (6.7-12.9)
Moderate-stable	2,243 (18.1)	61	2.9	2.7 (2.1-3.5)	86	3.9	3.8 (3.1-4.7)
Low-increasing	2,277 (18.4)	33	1.8	1.4 (1.0-2.0)	35	1.8	1.5 (1.1-2.1)
Moderate-fast-decline	1,217 (9.8)	20	1.6	1.6 (1.0-2.5)	12	1.6	1.0 (0.5-1.7)
Low-declining	5,176 (41.8)	43	1.0	0.8 (0.6-1.1)	44	0.8	0.9 (0.6-1.1)
Ultra-low-declining	1,097 (8.9)	9	0.6	0.8 (0.4-1.6)	4	0.3	0.4 (0.1-0.9)
Overall	12,390	183	1.6	1.5 (1.3-1.7)	217	1.8	1.8 (1.5-2.0)
All Nulliparas (N=42,583)							
Elevated-stable	3,364 (7.9)	456	14.4	13.6(12.4-14.8)	611	18.5	18.2(16.9-19.5)
Moderate-stable	11,407 (26.8)	1,047	9.5	9.2 (8.7-9.7)	1154	9.6	10.1 (9.6-10.7)
Low-increasing	8,303 (19.5)	530	6.0	6.4 (5.9-6.9)	395	4.7	4.8 (4.3-5.2)
Moderate-fast-decline	4,382 (10.3)	222	5.3	5.1 (4.4-5.8)	195	4.0	4.5 (3.9-5.1)
Low-declining	12,830 (30.1)	465	3.4	3.6 (3.3-4.0)	267	1.9	2.1 (1.8-2.3)
Ultra-low-declining	2,297 (5.4)	42	1.9	1.8 (1.3-2.5)	21	0.7	0.9 (0.6-1.4)
Overall	42,583	2,762	6.5	6.5 (6.3-6.7)	2643	6.0	6.2 (6.0-6.4)
Nulliparas with No Risk factors (N=23,803)							
Elevated-stable	1,368 (5.7)	143	12.3	10.5 (8.9-12.2)	236	16.1	17.3(15.3-19.4)
Moderate-stable	5,593 (23.5)	409	8.2	7.3 (6.6-8.0)	490	8.5	8.8 (8.0-9.5)
Low-increasing	4,638 (19.5)	239	5.3	5.2 (4.5-5.8)	184	4.2	4.0 (3.4-4.6)
Moderate-fast-decline	2,490 (10.5)	101	4.7	4.1 (3.3-4.9)	99	3.6	4.0 (3.2-4.8)
Low-declining	8,180 (34.4)	238	3.2	2.9 (2.6-3.3)	155	1.8	1.9 (1.6-2.2)
Ultra-low-declining	1,534 (6.4)	28	1.8	1.8 (1.2-2.6)	14	0.7	0.9 (0.5-1.5)
Overall	23,803	1,158	5.4	4.9 (4.6-5.1)	1178	4.8	4.9 (4.7-5.2)

Table S8. Models for Early Pregnancy Blood Pressure Trajectory Groups Plus Risk Factors Among Nulliparas with No Risk Factors Stratified by All Racial and Ethnic Groups: Average Predicted Probabilities (n, %) and the Observed Incidence Rate (n, % and 95% Confidence Intervals) of Preeclampsia and Gestational Hypertension within the Internal Validation Sample (n=74,274) of Low-to-Moderate Risk Women. USPSTF Moderate Risk Factors = Black race, Obesity, Nulliparity, Age ≥35 years, Low income/Government insurance, or Pregestational Diabetes

BP Trajectory Groups	N (col %) women	Pre- eclampsia n	Average Predicted %	Observed % (95% CI)	Gestational Hypertension n	Average Predicted %	Observed % (95% CI)
Black Nulliparas (N=1,190) No risk factors							
Elevated-stable	85 (7.1)	7	15.6	8.2 (3.4-16.2)	13	14.6	15.3 (8.4-24.7)
Moderate-stable	328 (27.6)	28	10.2	8.5 (5.7-12.1)	30	7.8	9.1 (6.3-12.8)
Low-increasing	272 (22.9)	21	6.4	7.7 (4.8-11.6)	16	3.8	5.9 (3.4-9.4)
Moderate-fast-decline	123 (10.3)	12	5.6	9.8 (5.1-16.4)	3	3.2	2.4 (0.5-7.0)
Low-declining	334 (28.1)	16	3.7	4.8 (2.8-7.7)	9	1.6	2.7 (1.2-5.1)
Ultra-low-declining	48 (4.0)	1	2.1	2.1 (0.1-11.1)	1	0.7	2.1 (0.1-11.1)
Overall	1,190	85	7.1	7.1 (5.7-8.8)	72	4.9	6.1 (4.8-7.6)
Hispanic Nulliparas (N=4,565) No risk factors							
Elevated-stable	222 (4.9)	36	15.2	16.2(11.6-21.7)	25	12.9	11.3 (7.4-16.2)
Moderate-stable	1,076 (23.6)	79	9.9	7.3 (5.9-9.1)	88	6.8	8.2 (6.6-10.0)
Low-increasing	921 (20.2)	63	6.3	6.8 (5.3-8.7)	35	3.4	3.8 (2.7-5.2)
Moderate-fast-decline	534 (11.7)	26	5.7	4.9 (3.2-7.1)	16	2.9	3.0 (1.7-4.8)
Low-declining	1,562 (34.2)	61	3.7	3.9 (3.0-5.0)	22	1.5	1.4 (0.9-2.1)
Ultra-low-declining	250 (5.5)	4	2.1	1.6 (0.4-4.0)	2	0.6	0.8 (0.1-2.9)
Overall	4,565	269	6.4	5.9 (5.2-6.6)	188	3.8	4.1 (3.6-4.7)
Asian Nulliparas (N=7,682) No risk factors							
Elevated-stable	267 (3.5)	28	13.6	10.5 (7.1-14.8)	36	15.8	13.5 (9.6-18.2)
Moderate-stable	1,317 (17.1)	121	8.9	9.2 (7.7-10.9)	100	8.4	7.6 (6.2-9.2)
Low-increasing	1,367 (17.8)	78	5.7	5.7 (4.5-7.1)	40	4.2	2.9 (2.1-4.0)
Moderate-fast-decline	645 (8.4)	29	5.0	4.5 (3.0-6.4)	25	3.6	3.9 (2.5-5.7)
Low-declining	3,222 (41.9)	94	3.3	2.9 (2.4-3.6)	55	1.8	1.7 (1.3-2.2)
Ultra-low-declining	864 (11.2)	17	1.8	2.0 (1.2-3.1)	9	0.7	1.0 (0.5-2.0)
Overall	7,682	367	5.0	4.8 (4.3-5.3)	265	3.9	3.4 (3.1-3.9)
White Nulliparas (N=10,458) No risk factors							
Elevated-stable	822 (7.9)	74	11.0	9.0 (7.1-11.2)	163	17.1	19.8(17.2-22.7)
Moderate-stable	2,958 (28.3)	194	7.2	6.6 (5.7-7.5)	283	9.1	9.6 (8.5-10.7)
Low-increasing	2,124 (20.3)	87	4.7	4.1 (3.3-5.0)	94	4.6	4.4 (3.6-5.4)
Moderate-fast-decline	1,203 (11.5)	42	4.1	3.5 (2.5-4.7)	53	3.9	4.4 (3.3-5.7)
Low-declining	3,012 (28.8)	79	2.7	2.6 (2.1-3.3)	71	2.0	2.4 (1.8-3.0)
Ultra-low-declining	339 (3.2)	6	1.5	1.8 (0.7-3.8)	3	0.8	0.9 (0.2-2.6)
Overall	10,458	482	5.2	4.6 (4.2-5.0)	667	5.9	6.4 (5.9-6.9)

Table S9. Models for Early Pregnancy Blood Pressure Trajectory Groups Plus Risk Factors for Combinations of Any Two Moderate Risk Factors: Average Predicted Probabilities (n, %) and the Observed Incidence Rate (n, % and 95% Confidence Intervals) of Preeclampsia and Gestational Hypertension within the Internal Validation Sample (n=74,274) of Low-to-Moderate Risk Women. USPSTF Moderate Risk Factors = Black race, Obesity, Nulliparity, Age ≥35 years, Low income/Government insurance, or Pregestational Diabetes

BP Trajectory Groups	N (col %) women	Pre- eclampsia n	Average Predicted %	Observed % (95% CI)	Gestational Hypertension n	Average Predicted %	Observed % (95% CI)
Nulliparity and Age ≥35 y (N=5,382)							
Elevated-stable	300 (5.6)	42	14.1	14.0(10.3-18.4)	56	19.7	18.7(14.4-23.5)
Moderate-stable	1,152 (21.4)	99	9.5	8.6 (7.0-10.4)	132	10.7	11.5 (9.7-13.4)
Low-increasing	1,052 (19.5)	85	6.3	8.1 (6.5-9.9)	60	5.4	5.7 (4.4-7.3)
Moderate-fast-decline	565 (10.5)	38	5.5	6.7 (4.8-9.1)	35	4.7	6.2 (4.4-8.5)
Low-declining	1,901 (35.3)	98	3.7	5.2 (4.2-6.2)	44	2.3	2.3 (1.7-3.1)
Ultra-low-declining	412 (7.7)	9	2.1	2.2 (1.0-4.1)	3	0.9	0.7 (0.2-2.1)
Overall	5,382	371	6.1	6.9 (6.2-7.6)	330	5.8	6.1 (5.5-6.8)
Nulliparity and Black (N=1,190)							
Elevated-stable	85 (7.1)	7	15.6	8.2 (3.4-16.2)	13	14.6	15.3 (8.4-24.7)
Moderate-stable	328 (27.6)	28	10.2	8.5 (5.7-12.1)	30	7.8	9.1 (6.3-12.8)
Low-increasing	272 (22.9)	21	6.4	7.7 (4.8-11.6)	16	3.8	5.9 (3.4-9.4)
Moderate-fast-decline	123 (10.3)	12	5.6	9.8 (5.1-16.4)	3	3.2	2.4 (0.5-7.0)
Low-declining	334 (28.1)	16	3.7	4.8 (2.8-7.7)	9	1.6	2.7 (1.2-5.1)
Ultra-low-declining	48 (4.0)	1	2.1	2.1 (0.1-11.1)	1	0.7	2.1 (0.1-11.1)
Overall	1,190	85	7.1	7.1 (5.7-8.8)	72	4.9	6.1 (4.8-7.6)
Nulliparity and Government Health Insurance (N=1,049)							
Elevated-stable	52 (5.0)	8	13.6	15.4 (6.9-28.1)	5	16.3	9.6 (3.2-21.0)
Moderate-stable	209 (19.9)	23	9.1	11.0 (7.1-16.1)	25	8.8	12.0 (7.9-17.1)
Low-increasing	220 (21.0)	12	6.0	5.5 (2.8-9.3)	10	4.5	4.5 (2.2-8.2)
Moderate-fast-decline	123 (11.7)	5	5.3	4.1 (1.3-9.2)	5	3.8	4.1 (1.3-9.2)
Low-declining	382 (36.4)	21	3.6	5.5 (3.4-8.3)	6	1.9	1.6 (0.6-3.4)
Ultra-low-declining	63 (6.0)	0	2.0	0.0 (0.0-5.7)	1	0.8	1.6 (0.0-8.5)
Overall	1,049	69	5.8	6.6 (5.2-8.3)	52	4.7	5.0 (3.7-6.5)
Nulliparity and Obesity (N=4,277)							
Elevated-stable	777 (18.2)	103	14.8	13.3(11.0-15.8)	161	20.8	20.7(17.9-23.7)
Moderate-stable	1,820 (42.6)	197	10.3	10.8 (9.4-12.3)	228	11.5	12.5(11.0-14.1)
Low-increasing	825 (19.3)	68	6.9	8.2 (6.5-10.3)	51	5.8	6.2 (4.6-8.0)
Moderate-fast-decline	375 (8.8)	32	6.1	8.5 (5.9-11.8)	24	5.1	6.4 (4.1-9.4)
Low-declining	456 (10.7)	27	4.1	5.9 (3.9-8.5)	12	2.6	2.6 (1.4-4.6)
Ultra-low-declining	24 (0.6)	0	2.2	0.0 (0.0-14.2)	0	1.0	0.0 (0.0-14.2)
Overall	4,277	427	9.4	10.0 (9.1-10.9)	476	10.5	11.1(10.2-12.1)

Table S9, Continued:

BP Trajectory Groups	N (col %) women	Pre-eclampsia n	Average Predicted %	Observed % (95% CI)	Gestational Hypertension n	Average Predicted %	Observed % (95% CI)
Obesity and Black (N=351)							
Elevated-stable	47 (13.4)	6	7.7	12.8 (4.8-25.7)	4	11.3	8.5 (2.4-20.4)
Moderate-stable	158 (45.0)	11	4.7	7.0 (3.5-12.1)	6	5.6	3.8 (1.4-8.1)
Low-increasing	70 (19.9)	2	2.8	2.9 (0.3-9.9)	0	2.5	0.0 (0.0-5.1)
Moderate-fast-decline	29 (8.3)	0	2.4	0.0 (0.0-11.9)	1	2.1	3.4 (0.1-17.8)
Low-declining	43 (12.3)	1	1.6	2.3 (0.1-12.3)	1	1.0	2.3 (0.1-12.3)
Ultra-low-declining	4 (1.1)	0	0.9	0.0 (0.0-60.2)	0	0.4	0.0 (0.0-60.2)
Overall	351	20	4.1	5.7 (3.5-8.7)	12	4.9	3.4 (1.8-5.9)
Obesity and Government Health Insurance (N=465)							
Elevated-stable	49 (10.5)	2	7.5	4.1 (0.5-14.0)	4	13.0	8.2 (2.3-19.6)
Moderate-stable	186 (40.0)	4	4.3	2.2 (0.6-5.4)	9	6.2	4.8 (2.2-9.0)
Low-increasing	85 (18.3)	1	2.8	1.2 (0.0-6.4)	1	2.9	1.2 (0.0-6.4)
Moderate-fast-decline	50 (10.8)	3	2.4	6.0 (1.3-16.5)	2	2.4	4.0 (0.5-13.7)
Low-declining	91 (19.6)	3	1.6	3.3 (0.7-9.3)	0	1.2	0.0 (0.0-4.0)
Ultra-low-declining	4 (0.9)	0	0.8	0.0 (0.0-60.2)	0	0.5	0.0 (0.0-60.2)
Overall	465	13	3.6	2.8 (1.5-4.7)	16	4.9	3.4 (2.0-5.5)
Obesity and Age ≥35 y (N=1,462)							
Elevated-stable	176 (12.0)	16	7.0	9.1 (5.3-14.3)	24	13.7	13.6 (8.9-19.6)
Moderate-stable	537 (36.7)	25	4.4	4.7 (3.0-6.8)	42	6.7	7.8 (5.7-10.4)
Low-increasing	311 (21.3)	10	2.8	3.2 (1.6-5.8)	11	3.1	3.5 (1.8-6.2)
Moderate-fast-decline	165 (11.3)	4	2.5	2.4 (0.7-6.1)	4	2.7	2.4 (0.7-6.1)
Low-declining	254 (17.4)	4	1.6	1.6 (0.4-4.0)	7	1.3	2.8 (1.1-5.6)
Ultra-low-declining	19 (1.3)	0	0.9	0.0 (0.0-17.6)	1	0.5	5.3 (0.1-26.0)
Overall	1,462	59	3.6	4.0 (3.1-5.2)	89	5.3	6.1 (4.9-7.4)

Table S10. Models for Early Pregnancy Blood Pressure Trajectory Groups Plus Risk Factors Among Women with Obesity and No Risk Factors Stratified by Racial and Ethnic Groups: Average Predicted Probabilities (n, %) and the Observed Incidence Rate (n, % and 95% Confidence Intervals) of Preeclampsia and Gestational Hypertension within the Internal Validation Sample (n=74,274) of Low-to-Moderate Risk Women. USPSTF Moderate Risk Factors = Black race, Obesity, Nulliparity, Age ≥35 years, Low income/Government insurance, or Pregestational Diabetes

BP Trajectory Groups	N (col %) women	Pre- eclampsia n	Average Predicted %	Observed % (95% CI)	Gestational Hypertension n	Average Predicted %	Observed % (95% CI)
Black Race and Obesity (N=351)							
Elevated-stable	47 (13.4)	6	7.7	12.8 (4.8-25.7)	4	11.3	8.5 (2.4-20.4)
Moderate-stable	158 (45.0)	11	4.7	7.0 (3.5-12.1)	6	5.6	3.8 (1.4-8.1)
Low-increasing	70 (19.9)	2	2.8	2.9 (0.3-9.9)	0	2.5	0.0 (0.0-5.1)
Moderate-fast-decline	29 (8.3)	0	2.4	0.0 (0.0-11.9)	1	2.1	3.4 (0.1-17.8)
Low-declining	43 (12.3)	1	1.6	2.3 (0.1-12.3)	1	1.0	2.3 (0.1-12.3)
Ultra-low-declining	4 (1.1)	0	0.9	0.0 (0.0-60.2)	0	0.4	0.0 (0.0-60.2)
Overall	351	20	4.1	5.7 (3.5-8.7)	12	4.9	3.4 (1.8-5.9)
Hispanic and Obesity (N=1,547)							
Elevated-stable	161 (10.4)	13	7.2	8.1 (4.4-13.4)	13	9.5	8.1 (4.4-13.4)
Moderate-stable	499 (32.3)	28	4.4	5.6 (3.8-8.0)	15	4.6	3.0 (1.7-4.9)
Low-increasing	366 (23.7)	8	2.7	2.2 (0.9-4.3)	6	2.2	1.6 (0.6-3.5)
Moderate-fast-decline	167 (10.8)	3	2.4	1.8 (0.4-5.2)	2	1.9	1.2 (0.1-4.3)
Low-declining	342 (22.1)	2	1.5	0.6 (0.1-2.1)	5	0.9	1.5 (0.5-3.4)
Ultra-low-declining	12 (0.8)	0	0.8	0.0 (0.0-26.5)	0	0.3	0.0 (0.0-26.5)
Overall	1,547	54	3.4	3.5 (2.6-4.5)	41	3.4	2.7 (1.9-3.6)
Asian and Obesity (N=393)							
Elevated-stable	46 (11.7)	4	6.0	8.7 (2.4-20.8)	3	10.3	6.5 (1.4-17.9)
Moderate-stable	123 (31.3)	2	3.8	1.6 (0.2-5.8)	7	5.4	5.7 (2.3-11.4)
Low-increasing	88 (22.4)	1	2.3	1.1 (0.0-6.2)	0	2.6	0.0 (0.0-4.1)
Moderate-fast-decline	47 (12.0)	0	2.1	0.0 (0.0-7.5)	0	2.2	0.0 (0.0-7.5)
Low-declining	79 (20.1)	0	1.3	0.0 (0.0-4.6)	0	1.1	0.0 (0.0-4.6)
Ultra-low-declining	10 (2.5)	0	0.8	0.0 (0.0-30.8)	0	0.5	0.0 (0.0-30.8)
Overall	393	7	2.9	1.8 (0.7-3.6)	10	4.0	2.5 (1.2-4.6)
White Race and Obesity (N=1,186)							
Elevated-stable	197 (16.6)	16	5.2	8.1 (4.7-12.9)	35	12.5	17.8(12.7-23.8)
Moderate-stable	444 (37.4)	13	3.1	2.9 (1.6-5.0)	27	6.0	6.1 (4.0-8.7)
Low-increasing	233 (19.6)	3	1.9	1.3 (0.3-3.7)	8	2.9	3.4 (1.5-6.7)
Moderate-fast-decline	120 (10.1)	2	1.7	1.7 (0.2-5.9)	2	2.5	1.7 (0.2-5.9)
Low-declining	183 (15.4)	1	1.1	0.5 (0.0-3.0)	2	1.2	1.1 (0.1-3.9)
Ultra-low-declining	9 (0.8)	0	0.6	0.0 (0.0-33.6)	0	0.5	0.0 (0.0-33.6)
Overall	1,186	35	2.8	3.0 (2.1-4.1)	74	5.3	6.2 (4.9-7.8)

Table S11. Models for Early Pregnancy Blood Pressure Trajectory Groups Plus Risk Factors Among Nulliparas (with or without risk factors) Stratified by Pre-pregnancy BMI Groups: Average Predicted Probabilities (n, %) and the Observed Incidence Rate (n, % and 95% Confidence Intervals) of Preeclampsia and Gestational Hypertension within the Internal Validation Sample (n=74,274) of Low-to-Moderate Risk Women. USPSTF Moderate Risk Factors = Black race, Obesity, Nulliparity, Age ≥35 years, Low income/Government insurance, or Pregestational Diabetes

BP Trajectory Groups	N (col %) women	Pre- eclampsia n	Average Predicted %	Observed % (95% CI)	Gestational Hypertension n	Average Predicted %	Observed % (95% CI)
All Nulliparas with Normal Weight (N=23,042)							
Elevated-stable	947 (4.1)	107	12.4	11.3 (9.4-13.5)	151	15.5	15.9(13.7-18.4)
Moderate-stable	4,546 (19.7)	317	8.3	7.0 (6.2-7.8)	382	8.3	8.4 (7.6-9.2)
Low-increasing	4,382 (19.0)	247	5.4	5.6 (5.0-6.4)	180	4.2	4.1 (3.5-4.7)
Moderate-fast-decline	2,459 (10.7)	106	4.9	4.3 (3.5-5.2)	101	3.7	4.1 (3.4-5.0)
Low-declining	8,947 (38.8)	306	3.3	3.4 (3.1-3.8)	161	1.8	1.8 (1.5-2.1)
Ultra-low-declining	1,761 (7.6)	30	1.9	1.7 (1.2-2.4)	15	0.7	0.9 (0.5-1.4)
Overall	23,042	1,113	5.1	4.8 (4.6-5.1)	990	4.2	4.3 (4.0-4.6)
All Nulliparas with Overweight (N=10,741)							
Elevated-stable	1,035 (9.6)	124	13.8	12.0(10.1-14.1)	181	17.6	17.5(15.2-19.9)
Moderate-stable	3,543 (33.0)	341	9.5	9.6 (8.7-10.6)	364	9.4	10.3 (9.3-11.3)
Low-increasing	2,336 (21.7)	144	6.2	6.2 (5.2-7.2)	114	4.8	4.9 (4.0-5.8)
Moderate-fast-decline	1,146 (10.7)	65	5.6	5.7 (4.4-7.2)	42	4.2	3.7 (2.7-4.9)
Low-declining	2,454 (22.8)	93	3.8	3.8 (3.1-4.6)	61	2.1	2.5 (1.9-3.2)
Ultra-low-declining	227 (2.1)	4	2.2	1.8 (0.5-4.5)	4	0.9	1.8 (0.5-4.5)
Overall	10,741	771	7.3	7.2 (6.7-7.7)	766	6.8	7.1 (6.7-7.6)
All Nulliparas with Obesity (N=7,376)							
Elevated-stable	1,355 (18.4)	224	16.3	16.5(14.6-18.6)	273	21.4	20.1(18.0-22.4)
Moderate-stable	3,158 (42.8)	380	11.3	12.0(10.9-13.2)	396	11.8	12.5(11.4-13.7)
Low-increasing	1,396 (18.9)	123	7.6	8.8 (7.4-10.4)	98	6.0	7.0 (5.7-8.5)
Moderate-fast-decline	644 (8.7)	47	6.8	7.3 (5.4-9.6)	43	5.2	6.7 (4.9-8.9)
Low-declining	784 (10.6)	46	4.4	5.9 (4.3-7.7)	30	2.7	3.8 (2.6-5.4)
Ultra-low-declining	39 (0.5)	0	2.4	0.0 (0.0-9.0)	1	1.1	2.6 (0.1-13.5)
Overall	7,376	820	10.3	11.1(10.4-11.9)	841	10.9	11.4(10.7-12.1)

Table S12. Models for Early Pregnancy Blood Pressure Trajectory Groups Plus Risk Factors Among Pre-pregnancy Body Mass Index Categories: Average Predicted Probabilities (n, %) and the Observed Incidence Rate (n, % and 95% Confidence Intervals) of Preeclampsia and Gestational Hypertension within the Internal Validation Sample (n=74,274) of Low-to-Moderate Risk Women. USPSTF Moderate Risk Factors = Black race, Obesity, Nulliparity, Age ≥35 years, Low income/Government insurance, or Pregestational Diabetes

BP Trajectory Groups	N (col %) women	Pre- eclampsia n	Average Predicted %	Observed % (95% CI)	Gestational Hypertension n	Average Predicted %	Observed % (95% CI)
All Underweight (N=2,092)							
Elevated-stable	30 (0.1)	1	10.2	3.3 (0.1-17.2)	6	12.1	20.0 (7.7-38.6)
Moderate-stable	221 (0.8)	10	5.9	4.5 (2.2-8.2)	16	5.9	7.2 (4.2-11.5)
Low-increasing	265 (1.0)	18	3.8	6.8 (4.1-10.5)	6	2.8	2.3 (0.8-4.9)
Moderate-fast-decline	182 (0.7)	5	3.5	2.7 (0.9-6.3)	9	2.5	4.9 (2.3-9.2)
Low-declining	964 (3.6)	21	2.3	2.2 (1.4-3.3)	18	1.2	1.9 (1.1-2.9)
Ultra-low-declining	430 (1.6)	9	1.2	2.1 (1.0-3.9)	1	0.5	0.2 (0.0-1.3)
Overall	2,092	64	2.9	3.1 (2.4-3.9)	56	2.0	2.7 (2.0-3.5)
All Normal weight (N=36,978)							
Elevated-stable	1,272 (4.7)	128	10.5	10.1 (8.5-11.8)	186	13.5	14.6(12.7-16.7)
Moderate-stable	6,545 (24.2)	372	6.7	5.7 (5.1-6.3)	458	7.0	7.0 (6.4-7.6)
Low-increasing	6,720 (24.8)	279	4.2	4.2 (3.7-4.7)	219	3.4	3.3 (2.8-3.7)
Moderate-fast-decline	3,822 (14.1)	122	3.7	3.2 (2.7-3.8)	121	2.9	3.2 (2.6-3.8)
Low-declining	15,273 (56.4)	358	2.4	2.3 (2.1-2.6)	215	1.4	1.4 (1.2-1.6)
Ultra-low-declining	3,346 (12.4)	43	1.3	1.3 (0.9-1.7)	18	0.5	0.5 (0.3-0.8)
Overall	36,978	1,302	3.8	3.5 (3.3-3.7)	1,217	3.2	3.3 (3.1-3.5)
All Overweight (N=20,148)							
Elevated-stable	1,527 (5.6)	150	11.2	9.8 (8.4-11.4)	242	14.9	15.8(14.1-17.8)
Moderate-stable	5,900 (21.8)	420	7.1	7.1 (6.5-7.8)	483	7.4	8.2 (7.5-8.9)
Low-increasing	4,386 (16.2)	180	4.3	4.1 (3.5-4.7)	159	3.6	3.6 (3.1-4.2)
Moderate-fast-decline	2,162 (8.0)	87	3.9	4.0 (3.2-4.9)	58	3.1	2.7 (2.0-3.5)
Low-declining	5,580 (20.6)	139	2.4	2.5 (2.1-2.9)	94	1.4	1.7 (1.4-2.1)
Ultra-low-declining	593 (2.2)	5	1.3	0.8 (0.3-2.0)	7	0.6	1.2 (0.5-2.4)
Overall	20,148	981	5.0	4.9 (4.6-5.2)	1,043	4.8	5.2 (4.9-5.5)
All Obesity (N=15,056)							
Elevated-stable	2,325 (8.6)	310	12.5	13.3 (12.0-14.8)	400	17.5	17.2(15.7-18.8)
Moderate-stable	5,964 (22.0)	511	8.1	8.6 (7.9-9.3)	547	9.0	9.2 (8.5-9.9)
Low-increasing	2,982 (11.0)	166	5.0	5.6 (4.8-6.5)	136	4.3	4.6 (3.8-5.4)
Moderate-fast-decline	1,449 (5.3)	70	4.4	4.8 (3.8-6.1)	59	3.6	4.1 (3.1-5.2)
Low-declining	2,208 (8.2)	66	2.6	3.0 (2.3-3.8)	50	1.7	2.3 (1.7-3.0)
Ultra-low-declining	128 (0.5)	0	1.3	0.0 (0.0-2.8)	2	0.6	1.6 (0.2-5.5)
Overall	15,056	1,123	6.9	7.5 (7.0-7.9)	1,194	7.7	7.9 (7.5-8.4)

Table S13. Models for Early Pregnancy Blood Pressure Trajectory Groups Plus Risk Factors Among Women with Diabetes with or without Other Risk Factors: Average Predicted Probabilities (n, %) and the Observed Incidence Rate (n, % and 95% Confidence Intervals) of Preeclampsia and Gestational Hypertension within the Internal Validation Sample (n=74,274) of Low-to-Moderate Risk Women. USPSTF Moderate Risk Factors = Black race, Obesity, Nulliparity, Age ≥35 years, Low income/Government insurance, or Pregestational Diabetes

BP Trajectory Groups	N (col %) women	Pre- eclampsia n	Average Predicted %	Observed % (95% CI)	Gestational Hypertension n	Average Predicted %	Observed % (95% CI)
Pregestational Diabetes with or without Risk Factors (N=478)							
Elevated-stable	65 (13.6)	13	25.8	20.0(11.1-31.8)	13	16.5	20.0(11.1-31.8)
Moderate-stable	179 (37.4)	28	18.9	15.6(10.7-21.8)	14	9.3	7.8 (4.3-12.8)
Low-increasing	89 (18.6)	12	12.8	13.5 (7.2-22.4)	8	4.7	9.0 (4.0-16.9)
Moderate-fast-decline	68 (14.2)	7	10.1	10.3 (4.2-20.1)	4	3.9	5.9 (1.6-14.4)
Low-declining	61 (12.8)	7	7.0	11.5 (4.7-22.2)	5	1.9	8.2 (2.7-18.1)
Ultra-low-declining	16 (3.3)	0	3.2	0.0 (0.0-20.6)	0	0.6	0.0 (0.0-20.6)
Overall	478	67	15.4	14.0(11.0-17.5)	44	7.4	9.2 (6.8-12.2)

Table S14. Sensitivity Analysis of Model Predictive Performance for Hypertensive Disorders of Pregnancy Utilizing Six Early Pregnancy Systolic Blood Pressure Trajectories Based on ≤ 4 , ≤ 3 , and ≤ 2 Blood Pressure Measurements. C-statistics and 95% Confidence Intervals (95% CIs); N=74,967 Validation Dataset of Low-to-Moderate Risk Women.

Maximum Number of BPs used to determine BPT group	Model number	Prediction Model C-statistics (95%CI)		
		Early-onset Preeclampsia (<34 weeks)	Late-onset Preeclampsia (≥ 34 weeks)	Gestational Hypertension
All available (main results)	3.0	0.711 (0.682-0.739)	0.665 (0.656-0.674)	0.734 (0.726-0.742)
	3.1	0.739 (0.710-0.767)	0.725 (0.717-0.734)	0.764 (0.756-0.772)
	3.2	0.747 (0.720-0.775)	0.730 (0.722-0.739)	0.768 (0.761-0.776)
	3.3	0.747 (0.719-0.775)	0.731 (0.723-0.740)	0.770 (0.762-0.778)
4	3.0	0.702 (0.674-0.730)	0.662 (0.653-0.671)	0.730 (0.722-0.738)
	3.1	0.732 (0.704-0.760)	0.724 (0.715-0.732)	0.761 (0.754-0.769)
	3.2	0.743 (0.715-0.770)	0.729 (0.720-0.737)	0.766 (0.758-0.774)
	3.3	0.742 (0.714-0.770)	0.730 (0.721-0.738)	0.767 (0.760-0.775)
3	3.0	0.693 (0.664-0.722)	0.657 (0.647-0.666)	0.730 (0.722-0.738)
	3.1	0.726 (0.697-0.755)	0.720 (0.712-0.729)	0.762 (0.754-0.769)
	3.2	0.734 (0.705-0.763)	0.726 (0.717-0.734)	0.766 (0.759-0.774)
	3.3	0.734 (0.705-0.763)	0.727 (0.718-0.735)	0.768 (0.760-0.776)
2	3.0	0.682 (0.654-0.710)	0.650 (0.641-0.660)	0.718 (0.710-0.726)
	3.1	0.719 (0.690-0.748)	0.717 (0.708-0.725)	0.752 (0.744-0.760)
	3.2	0.727 (0.698-0.756)	0.722 (0.713-0.730)	0.757 (0.749-0.765)
	3.3	0.726 (0.697-0.755)	0.723 (0.714-0.732)	0.759 (0.751-0.767)

Abbreviations: BP, blood pressure; BMI, pre-pregnancy body mass index; BPT, blood pressure trajectory
Standard Risk factors: pre-pregnancy BMI (kg/m²), parity (0 vs ≥ 1), maternal age (years), racial and ethnic groups [Black, Hispanic, Asian, White (referent), Mixed/Native/unknown], and pregestational diabetes;
Lifestyle Behaviors: Smoking during pregnancy, and Rate of gestational weight gain (GWG) ≤ 20 weeks' gestation (kg per week).
Social Factors: Government health insurance and Neighborhood deprivation index.
C-statistics for Model 3: Six BPT groups Only, or BPT groups plus Standard Risk Factors, Lifestyle Behaviors and Social Factors.

The total number (N) missing covariables for the prediction model (validation dataset) is 693.

Table S15. Sensitivity Analysis - Model Predictive Performance for Hypertensive Disorders of Pregnancy Utilizing Six Early Pregnancy Systolic Blood Pressure Trajectory Groups Limited to Blood Pressures measured up to 16 Weeks' Gestation (BPTL groups) and Risk Factors Available in Routine Prenatal Care (Clinical, Behavioral, and Social) Among Low-to-Moderate Risk Pregnant Women. C-statistics and (95% Confidence Intervals); N=74,913 validation dataset.

Model number	Predictive Model Variables	Prediction Model C-statistics (95%CI)		
		Early-onset Preeclampsia (<34 weeks)	Late-onset Preeclampsia (≥34 weeks)	Gestational Hypertension
1.0.	Standard Risk Factors:(BMI + Parity + Age + Race/ethnicity + Diabetes)	0.688 (0.659-0.717)	0.695 (0.686-0.704)	0.692 (0.683-0.701)
2.0.	Initial BP Only	0.657 (0.626-0.687)	0.631 (0.621-0.641)	0.701 (0.692-0.709)
2.1.	Initial BP + BMI + Parity	0.704 (0.675-0.733)	0.708 (0.700-0.717)	0.738 (0.730-0.746)
2.2.	Initial BP + BMI + Parity + Age + Race/ethnicity + Diabetes	0.713 (0.685-0.741)	0.714 (0.705-0.722)	0.744 (0.736-0.752)
3.0.	Six BPTL groups Only	0.705 (0.677-0.733)	0.656 (0.647-0.665)	0.723 (0.715-0.731)
3.1.	Six BPTL groups + BMI + Parity	0.737 (0.708-0.766)	0.720 (0.712-0.729)	0.757 (0.749-0.764)
3.2.	Six BPTL groups + Standard Risk Factors (BMI + Parity + Age + Race/ethnicity + Diabetes)	0.748 (0.721-0.775)	0.725 (0.716-0.733)	0.761 (0.753-0.769)
3.3.	Six BPTL groups + Standard Risk factors (BMI + Parity + Age + Race/ethnicity + Diabetes) + Lifestyle Behaviors + Social Factors	0.748 (0.721-0.775)	0.726 (0.718-0.735)	0.763 (0.755-0.771)

Abbreviations: BP, blood pressure; BMI, pre-pregnancy body mass index; BPTL, blood pressure trajectory groups limited to BP measurements from 0 to 16 weeks' gestation.

Standard Risk factors: pre-pregnancy BMI (kg/m²), parity (0 vs ≥1), maternal age (y), and racial and ethnic groups [Black, Hispanic, Asian, Mixed/Native/unknown, White (referent)], and pregestational Diabetes;

Lifestyle Behaviors: Smoking during pregnancy, and Rate of gestational weight gain (GWG) ≤ 20 weeks (kg per week)

Social Factors: Government insurance and Neighborhood deprivation index.

C-statistics for Model 1: Standard Risk factors, **Model 2:** Initial BP Only (≤14 weeks' gestation), or Initial BP plus Standard Risk Factors, and **Model 3:** Six BPTL groups Only, or BPTL groups plus Standard Risk Factors, and BPTL groups, Standard Risk Factors plus Lifestyle Behaviors and Social Factors. (Models Missing n = 54 women with no BP measurements ≤16 weeks' gestation).

Figure S1. Sample Selection Flow Chart

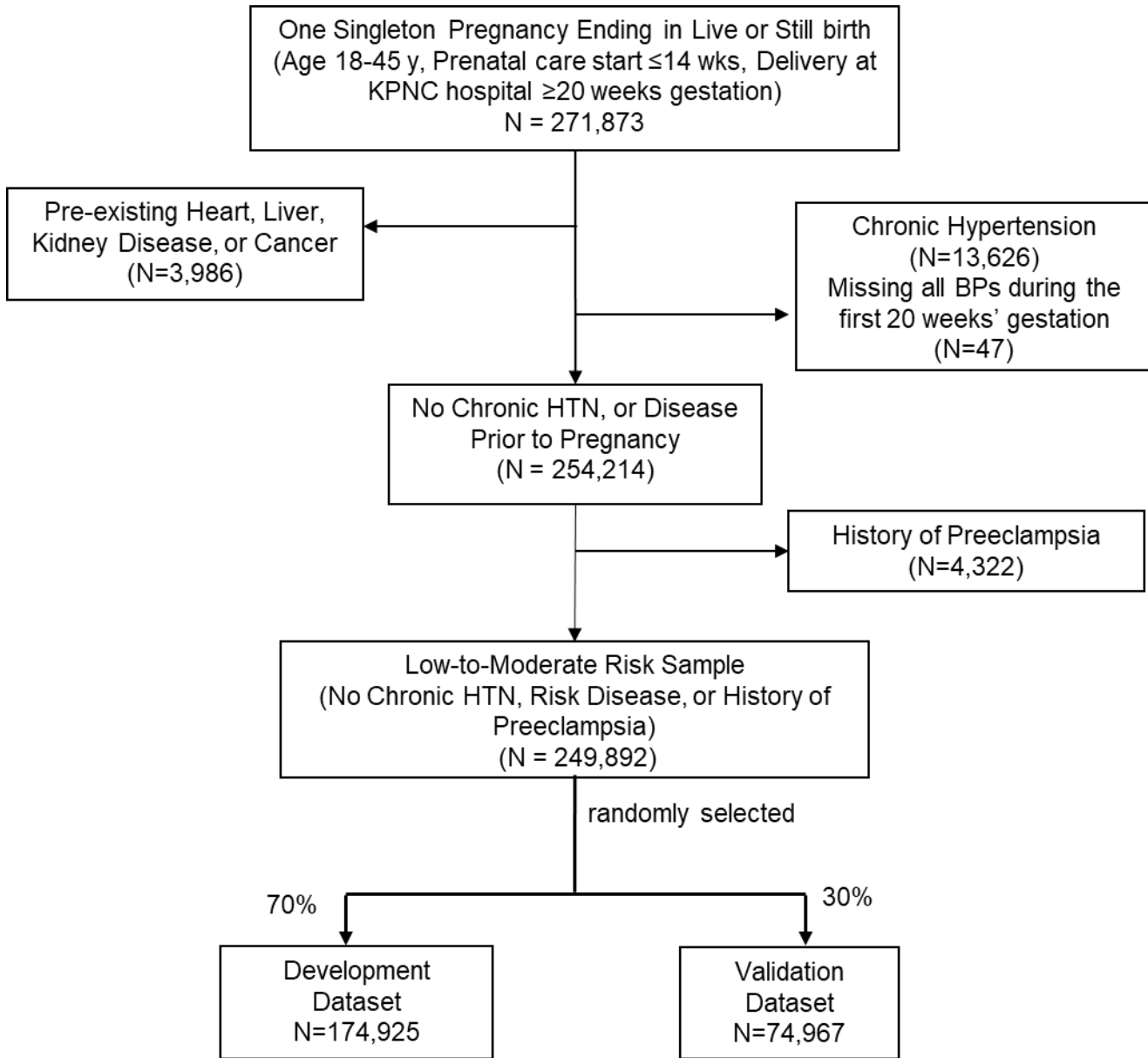
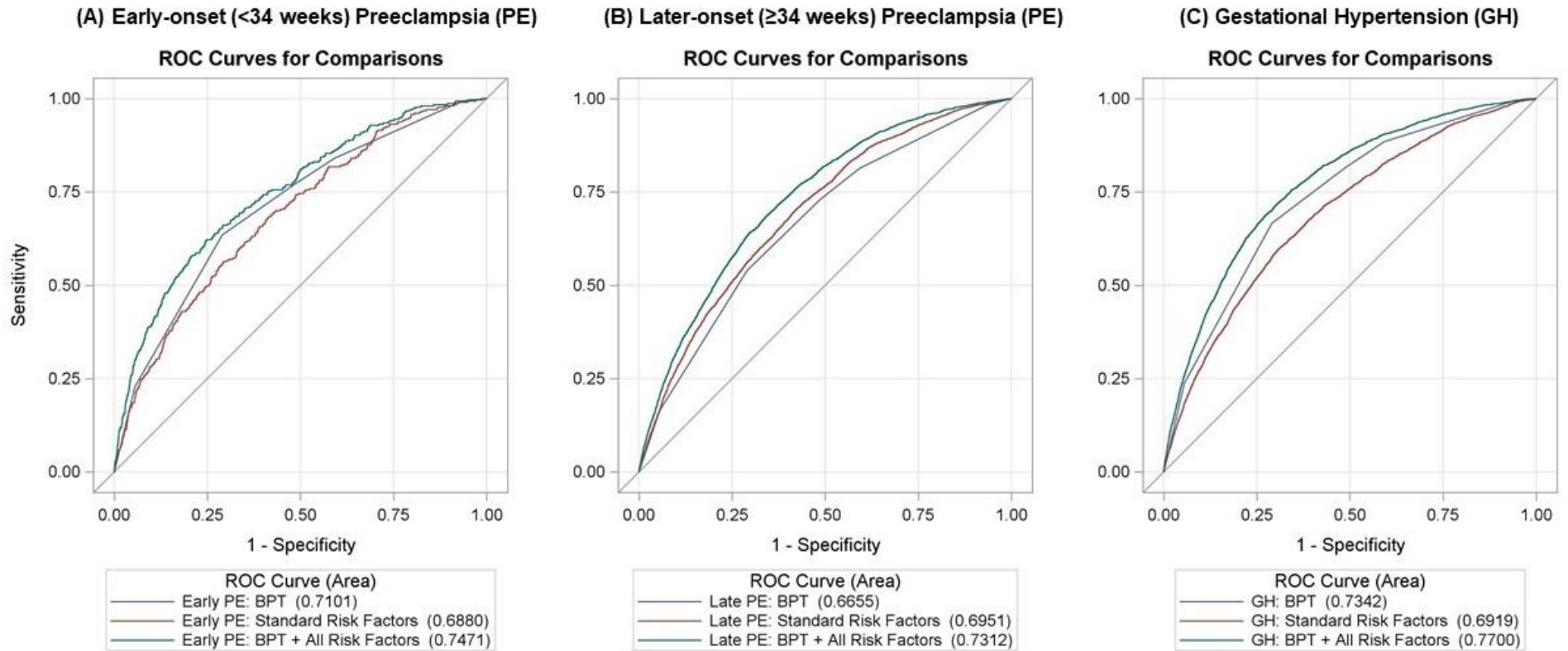


Figure S2: Receiver Operating Characteristic (ROC) Curves for the Predictive Models: (A) Early-onset preeclampsia (<34 weeks gestational age), (B) Later-onset preeclampsia (\geq 34 weeks gestational age), and (C) Gestational Hypertension.



Specific Models:

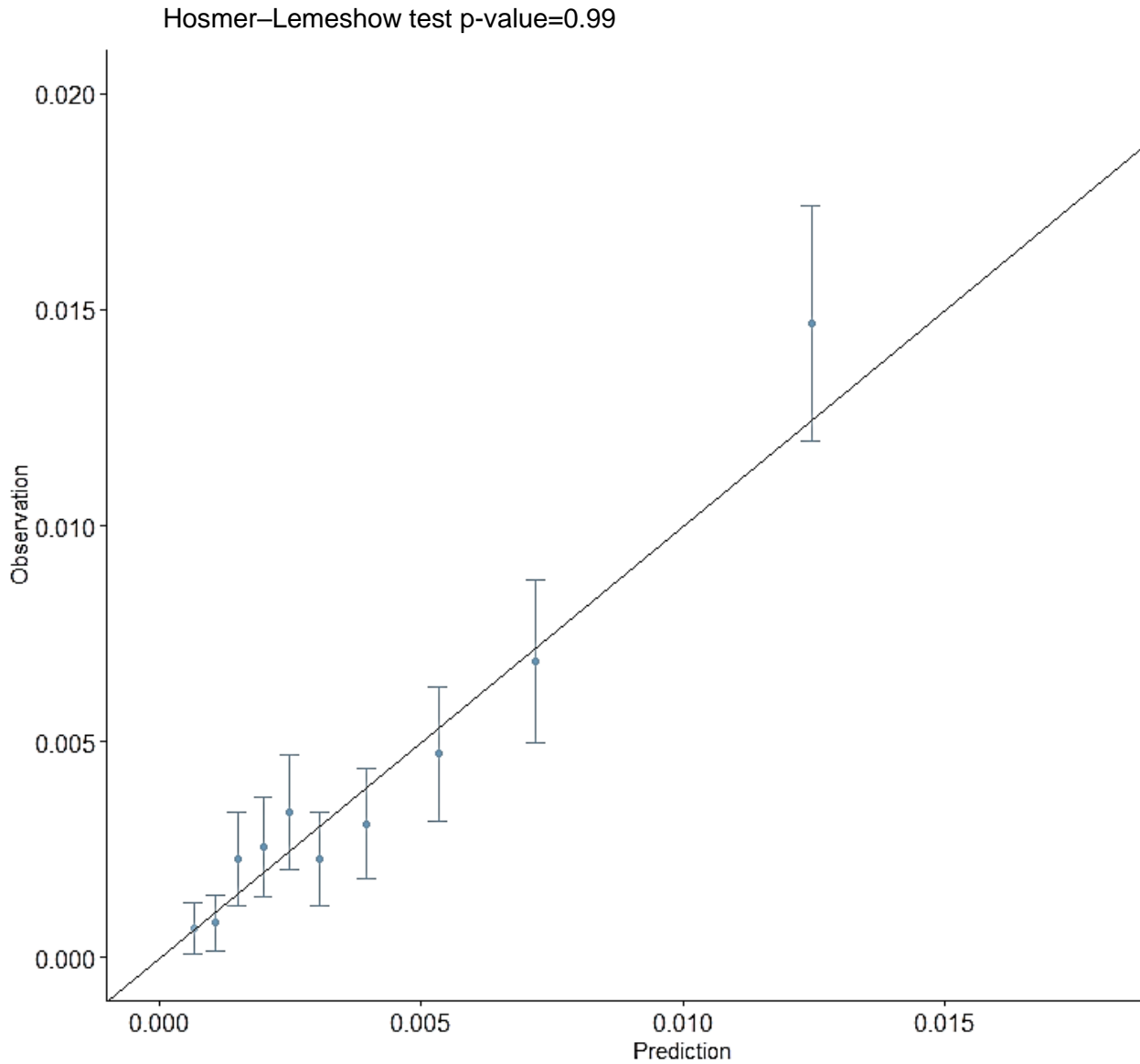
BPT Model (purple): Blood pressure trajectory groups.

Standard Risk Factors (red): BMI + Parity + Age + Race/ethnicity + Diabetes.

BPT + All Risk Factors Model (green): BMI + Parity + Age + Race/ethnicity + Diabetes + Lifestyle Behaviors + Social Factors

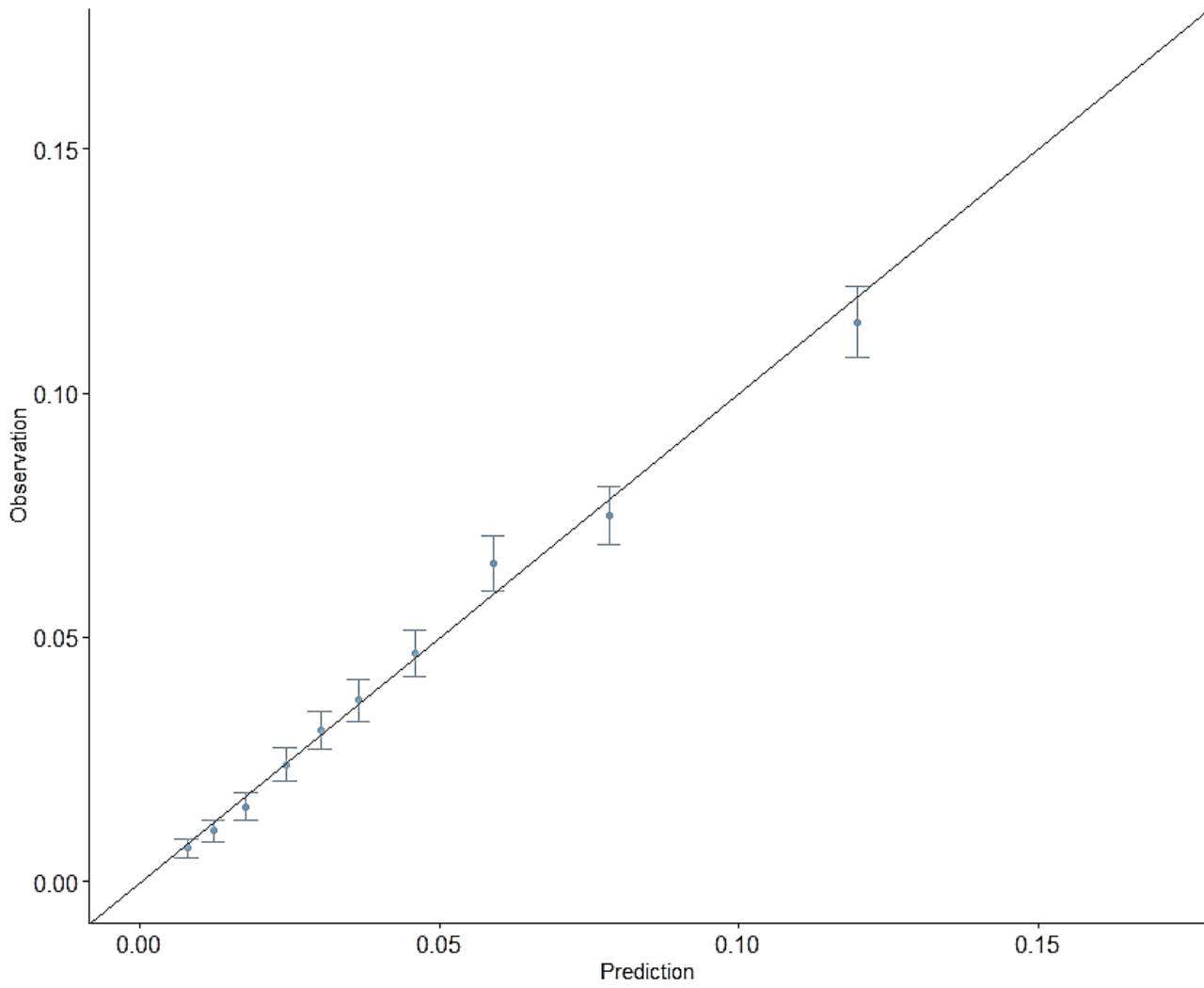
Figure S3. Decile Calibration Plots for Observation versus Prediction Models: (A) Early-onset preeclampsia <34 weeks gestational age; (B) Later-onset preeclampsia ≥34 weeks gestational age; and (C) Gestational hypertension. Models include Early Pregnancy Systolic Blood Pressure Trajectory (BPT) Groups and All Risk Factors.

(A) Early-onset preeclampsia (BPT groups + All Risk Factors Model)



(B) Later-onset preeclampsia (BPT groups + All Risk Factors Model)

Hosmer-Lemeshow test p-value=0.99



C) Gestational hypertension (BPT groups + All Risk Factors).

Hosmer-Lemeshow test p-value=0.74

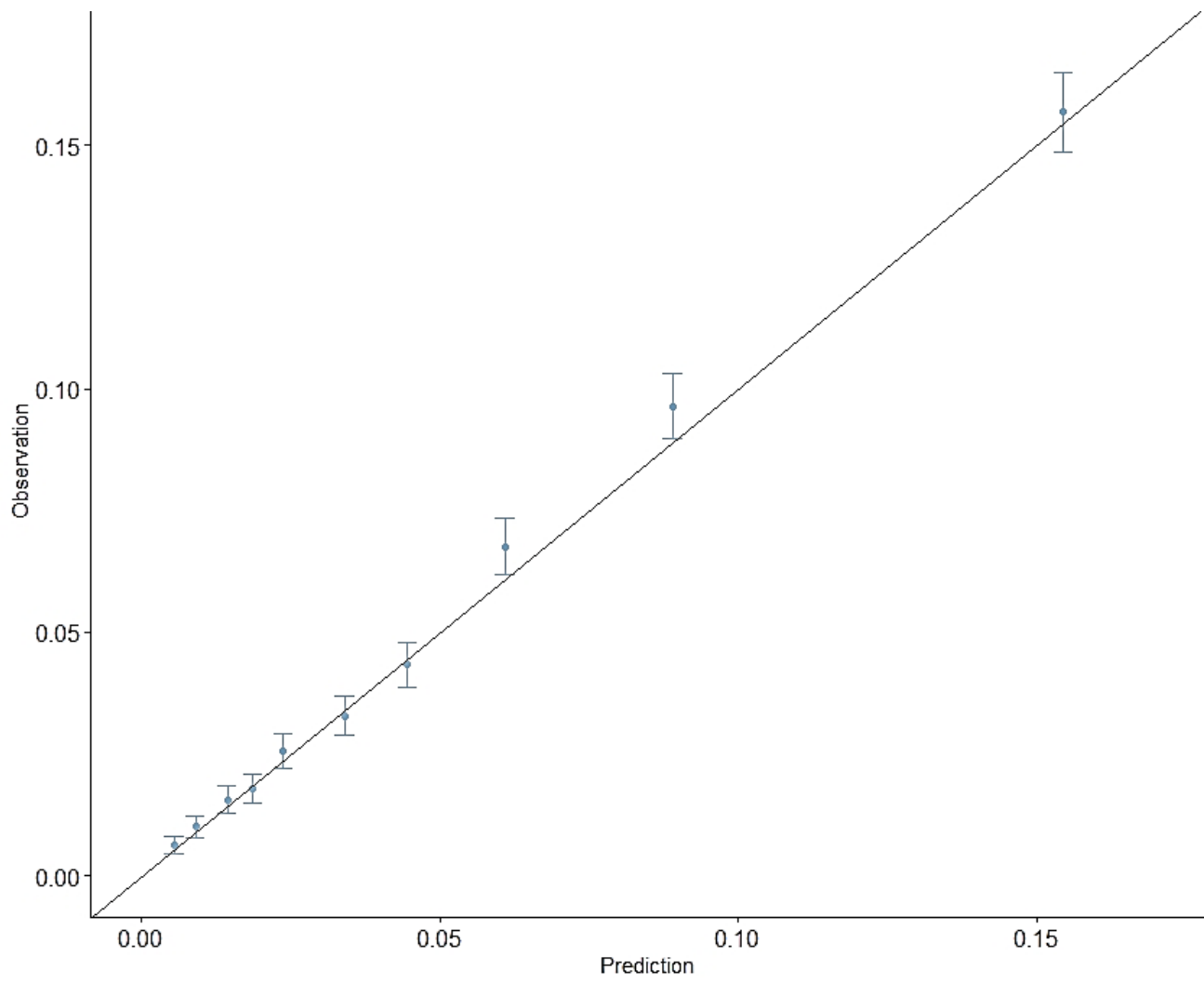


Figure S4. Distribution of Blood Pressure Measurements by Gestational Age; Percentage of Women with Two Blood Pressure (BP) Measurements, One Blood Pressure Measurement, or Any (One or More) Blood Pressure Measurements within Specific Gestational Age Intervals from 0-20 weeks of gestation.

