

# **Maternal morbidity, infant mortality, and health-care costs attributable to prenatal smoking in the USA during the e-cigarette era: a simulation modelling study**

**Short title:** Prenatal smoking burden in the e-cigarette era

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## **Abstract**

**Background:** Smoking during pregnancy is a preventable cause of maternal morbidity and infant mortality, while nicotine-use patterns are changing with increasing e-cigarette uptake. Long-term estimates of smoking-attributable maternal and infant burden in the e-cigarette era are limited.

**Methods:** We developed a microsimulation model of smoking, e-cigarette use, and pregnancy among US women, incorporating pregnancy-related smoking cessation and postpartum relapse. We calibrated smoking and e-cigarette use trends to the National Health Interview Survey (2014–2024) and Behavioral Risk Factor Surveillance System (2016–2023) and linked projected smoking distributions to national pregnancy outcome risks. We estimated smoking-attributable outcomes, direct medical costs, and maternal quality-adjusted life-year (QALY) losses during 2027–2100 by comparing baseline trends with a no-smoking counterfactual.

**Findings:** Under baseline trends, smoking prevalence among pregnant women declined to 2.9% by 2040 and then stabilised, whereas e-cigarette use increased to 8.5% by 2040 and plateaued. Compared with the no-smoking counterfactual, prenatal smoking was associated with 278 000 ectopic pregnancies, 1.62 million miscarriages, 16 000 placenta previa cases, 61 000 placental abruptions, 414 000 hypertensive disorders of pregnancy, 18 000 eclampsia cases, and 87 000 infant deaths during 2027–2100. Smoking-attributable direct medical costs totalled US\$7.7 billion, and maternal quality-of-life losses totalled 62 000 QALYs.

**Interpretation:** Despite continued declines in prenatal smoking prevalence, smoking during pregnancy is projected to remain a substantial and preventable cause of maternal morbidity, infant mortality, and health-care costs in the USA. This model provides a policy-relevant benchmark for evaluating tobacco-control interventions during pregnancy and postpartum.

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## **Research in context**

### **Evidence before this study**

Smoking during pregnancy increases the risks of miscarriage, ectopic pregnancy, placental complications, hypertensive disorders of pregnancy, and infant death. The most influential US estimates of smoking-attributable maternal and infant burden were produced in an earlier tobacco landscape, before recent declines in prenatal smoking and widespread e-cigarette uptake. Since then, reliable estimates of preventable maternal and infant burden attributable to smoking have been scarce for the 2000s and beyond. Earlier modelling work has largely comprised static attributable-burden estimates, tobacco policy simulation models, and smoking cessation interventions in pregnancy. These studies established that prenatal smoking causes substantial preventable harm, but most treated smoking exposure statically, did not model pregnancy-related cessation or postpartum relapse, did not incorporate e-cigarette use or dual use, and were not designed to project pregnancy-related outcomes in the contemporary nicotine landscape.

## **Added value of this study**

To our knowledge, this is the first US microsimulation model to integrate cigarette smoking, e-cigarette use, and pregnancy-related behavioural dynamics within a single framework to project maternal morbidity, infant mortality, direct medical costs, and maternal quality-adjusted life-year losses. By incorporating pregnancy-related smoking cessation, postpartum relapse, e-cigarette transitions, and calibration to contemporary national smoking and vaping trends, this study updates the evidence base on smoking-attributable pregnancy burden for the e-cigarette era. The no-smoking counterfactual provides a benchmark for estimating the preventable burden that remains despite declining prenatal smoking prevalence.

## **Implications of all the available evidence**

Even as prenatal smoking prevalence declines, smoking during pregnancy is projected to remain a substantial and preventable cause of maternal morbidity, infant mortality, and health-care costs in the USA. Contemporary policy evaluations should account for changing nicotine-use patterns, including e-cigarette uptake and dual use, rather than relying solely on older static smoking-attributable estimates. This framework can support priority-setting and future evaluations of tobacco-control strategies during pregnancy and the postpartum period.

## **Introduction**

Smoking during pregnancy is associated with ectopic pregnancy, miscarriage, placental complications, fetal growth restriction, stillbirth, and infant mortality.<sup>1-3</sup> Although many women try to quit after becoming pregnant, most women who smoke before pregnancy

(77·7%) continue to smoke throughout pregnancy.<sup>4</sup> Despite recent declines in prenatal smoking prevalence, prenatal smoking remains an important preventable cause of maternal and infant harm and health-care costs.<sup>5,6</sup>

At the same time, nicotine use patterns are changing with increasing uptake of e-cigarettes, including among pregnant women.<sup>7</sup> In 2023, 4·8% of pregnant women reported current e-cigarette use.<sup>8</sup> Many adults who smoke report using e-cigarettes in quit attempts, reflecting their use as a perceived harm-reduction or cessation tool.<sup>9</sup> Some pregnant women may also use e-cigarettes in an attempt to reduce harm or stop smoking. However, the health effects of e-cigarette use during pregnancy remain uncertain. A recent systematic review concluded that evidence is mixed and limited in quality, with substantial confounding by prior smoking and dual use; and that firm conclusions on safety cannot be drawn.<sup>10</sup> US preventive guidance concludes that evidence is insufficient to recommend e-cigarettes for smoking cessation, including pregnancy.<sup>11</sup> One randomised trial comparing e-cigarettes with nicotine patches in pregnancy suggested that e-cigarettes might improve smoking abstinence in sensitivity analyses, although the primary abstinence outcome was not statistically significant.<sup>12</sup> Regardless, changing e-cigarette use patterns are reshaping smoking behaviour and may alter downstream maternal and infant health burden.

Given the persistent burden of prenatal smoking and the evolving nicotine landscape, understanding the future maternal and infant consequences of tobacco-use patterns is essential. Yet the long-term population-level projections of maternal and infant outcomes in the USA in the e-cigarette era are limited. Simulation modelling is well suited to this question because the effects of smoking cessation, postpartum relapse,

switching to e-cigarettes, and pregnancy incidence unfold over time through linked pathways that shape maternal and infant outcomes. Without a simulation framework that captures these interdependent dynamics, it is difficult to translate changes in tobacco-use behaviour into projected health burden.

Although previous models have examined smoking in pregnancy, no existing model integrates cigarette and e-cigarette transitions, pregnancy-related smoking cessation and postpartum relapse, and pregnancy-specific maternal morbidity together with infant mortality in the USA.<sup>13</sup> We therefore developed a microsimulation model to project smoking, vaping, and pregnancy-related outcomes under continued baseline trends and to compare these projections with a no-smoking counterfactual, thereby quantifying the preventable burden of prenatal smoking and providing a policy-relevant benchmark for future intervention evaluation.

## **Methods**

We simulated overlapping annual birth cohorts and aggregated results to calendar-year national estimates using US population denominators. We report projected maternal and infant outcomes occurring during 2027–2100, which was the analytic horizon; earlier years were simulated only to initialise cohort smoking histories and calibrate the model to observed smoking and e-cigarette use trends. We modelled pregnancy-related outcomes among individuals with female sex assigned at birth, as recorded in the underlying data sources; hereafter, we refer to this population as women for readability. Reporting followed CHEERS 2022 guidance where applicable to model-based economic analyses.

## Microsimulation Model

Figure 1A shows the smoking, e-cigarette use, and pregnancy (SEP) microsimulation model. Each simulated woman was characterised by smoking status (never, current, or former smoking), e-cigarette use status (never, current, or former use), and pregnancy status (pregnant or not pregnant), yielding 18 possible living state combinations.

Women entered the model in the never-smoking, never-e-cigarette-use, non-pregnant state. In each annual cycle, they could transition between states according to probabilities that varied by age, tobacco-use status, and calendar year. We simulated annual birth cohorts of 10 000 women from 1900 onward and scaled cohort-specific state distributions to US population counts by age and calendar year. Women remained in the microsimulation after pregnancy outcomes and continued to transition among health states in subsequent cycles.

Smoking initiation and cessation were parameterised using Cancer Intervention and Surveillance Modeling Network (CISNET) smoking inputs.<sup>14</sup> E-cigarette transition probabilities were based on published multistate transition analyses using Population Assessment of Tobacco and Health (PATH) Study data, including age-specific e-cigarette initiation, switching from cigarettes to e-cigarettes, and dual use.<sup>15</sup> For projections during 2027–2100, transition rates were held constant at the most recent available values, allowing prevalence to stabilise over time rather than imposing additional future policy or behavioural changes.

The model was calibrated to reproduce observed age-specific smoking and vaping trends among women of reproductive age and pregnant women using the 2014-2024 National Health Interview Survey (NHIS) and the 2016-2023 Behavioral Risk Factor

Surveillance System (BRFSS) respectively.<sup>8,16</sup> NHIS had insufficient numbers of pregnant respondents for stable prevalence estimates, so BRFSS estimates were used as calibration targets for cigarette and e-cigarette use among pregnant women. BRFSS is widely used for pregnancy-related surveillance because its large, population-based sample permits stable nationally aggregated estimates of smoking and vaping among currently pregnant respondents.

Non-pregnant women aged 15–49 years could transition to the pregnant state. Age-specific pregnancy rates were taken from National Center for Health Statistics estimates for 2010–2019, which combine live births, fetal losses, and induced abortions.<sup>17</sup> These rates were converted to annual conception probabilities so that simulated pregnancy counts matched observed national totals. Pregnancy rates were held constant at 2019 levels throughout the projection horizon to isolate the effects of changing tobacco-use patterns rather than demographic shifts. Pregnancy was represented as lasting one annual cycle, allowing gestation and pregnancy outcomes to occur within a single time step; two pregnancies could not occur within the same cycle, although pregnancies in consecutive cycles were allowed.<sup>18</sup>

We modelled pregnancy-related smoking cessation and postpartum relapse within the annual transition structure. When a current-smoking woman became pregnant, she could either remain in the current-smoking pregnant state or transition directly to the former-smoking pregnant state, representing cessation after pregnancy recognition. This pregnancy-related cessation transition was parameterised using natality data indicating that about 40% of women who reported smoking before pregnancy reported no smoking in the third trimester.<sup>5</sup> Smoking initiation during pregnancy was set to zero,

as it occurs in fewer than 0.5% of pregnancies.<sup>19</sup> After pregnancy, women return to the non-pregnant state except for those with sequential pregnancies; postpartum relapse is modelled by allowing transitions from former-smoking/pregnant to current-smoking/non-pregnant such that 30–50% of those who quit during pregnancy resume smoking within 6–12 months postpartum, consistent with longitudinal studies and meta-analyses.<sup>20</sup>

Existing observational studies report mixed or uncertain effects of pregnancy on vaping uptake or cessation.<sup>10,21</sup> Since evidence remains sparse, we assumed pregnancy does not modify e-cigarette transition probabilities beyond age and smoking status.

### **Pregnancy and Infant Mortality Module**

Pregnancy-related outcomes were estimated in a decision-tree module linked to the microsimulation model's annual age- and smoking-specific pregnancy distributions. The module combined simulated pregnancy counts with US population denominators and outcome probabilities stratified by smoking status and, where data permitted, age and calendar year. After outcome assignment in the module, all individuals remain in the microsimulation and continue to move among health states in subsequent years. This design separates behavioural dynamics (handled in the microsimulation) from clinical outcome assignment (handled in the module), while preserving continuity of individuals across cycles. Because evidence on the causal effects of e-cigarette use on pregnancy outcomes remains insufficient, e-cigarette status did not directly modify outcome risks; its influence was captured indirectly through effects on smoking transitions.

Figure 1B shows the structure of the pregnancy and infant mortality module. The decision tree first assigned early pregnancy outcomes before 20 weeks' gestation. Early

losses were classified as miscarriage, ectopic pregnancy, or induced abortion, with miscarriage and ectopic pregnancy probabilities parameterised using National Survey of Family Growth pregnancy data.<sup>22</sup> Induced abortion was included to ensure complete pregnancy accounting and to remove terminated pregnancies from the risk set for later maternal complications, but it was not treated as a smoking-attributable health outcome; therefore, an overall abortion rate was applied without stratification by smoking status.

Pregnancies continuing to 20 weeks' gestation or later were assigned to no major modelled morbidity or one of four mutually exclusive late maternal complications: placenta previa, placental abruption, hypertensive disorders of pregnancy, or eclampsia. These probabilities were parameterised using National Vital Statistics System natality data.<sup>4</sup> Gestational diabetes was not modelled because evidence for a smoking-attributable effect is inconsistent.<sup>23</sup> Infant mortality was then assigned among live births using smoking- and age-specific probabilities from the National Center for Health Statistics Linked Birth–Infant Death files.<sup>24</sup> Additional details on outcome definitions, risk assumptions, and data sources are provided in the appendix.

### **Health Utilities and Costs**

We adopted a health-care system perspective and included incremental direct medical costs attributable to modelled pregnancy outcomes only. Costs were applied in the year of the event, expressed in 2024 US dollars, and discounted at 3% per year. Routine prenatal care and delivery costs were excluded because they were assumed to occur in both the baseline and no-smoking scenarios and therefore would not affect smoking-attributable incremental costs.

Maternal health effects were expressed as one-year utility decrements associated with each outcome, with uncomplicated pregnancy as the reference state. This utility-decrement framework avoids specifying a population-level baseline utility for uncomplicated pregnancy and ensures that scenario differences reflect avoidable QALY losses attributable to smoking-related complications. No separate utility decrement was applied for smoking status itself, because the health effects of smoking were captured through elevated complication risks in the pregnancy outcomes module. Utility decrements and cost parameters are reported in the appendix.

## Results

The calibrated model reproduced observed smoking and e-cigarette use trends among women of reproductive age and pregnant women (figure 2). Among pregnant women, modelled smoking prevalence declined from 7.0% in 2016 to 4.1% in 2023, whereas e-cigarette use increased from 1.8% in 2016 to 5.3% in 2024.

Under the baseline scenario, smoking prevalence among pregnant women declined to 2.9% by 2040 and remained stable through 2100 (figure 3). E-cigarette use increased to 8.5% by 2040 and stabilised thereafter. Dual use remained below 1% throughout the projection period. In the no-smoking counterfactual, smoking and dual use were set to zero, while e-cigarette use plateaued at 6.7%.

Compared with the no-smoking counterfactual, the baseline scenario resulted in substantial smoking-attributable maternal morbidity and infant mortality during 2027–2100 (table 1). Cumulative smoking-attributable outcomes included 278 000 ectopic pregnancies, 1.62 million miscarriages, 15 700 placenta previa cases, 61 300 placental

abruptions, 414 000 hypertensive disorders of pregnancy, 18 100 eclampsia cases, and 86 600 infant deaths. Smoking-attributable direct medical costs totalled US\$7.7 billion, and maternal quality-of-life losses totalled 61 700 QALYs.

These cumulative estimates corresponded to annual averages of about 3760 ectopic pregnancies, 21 900 miscarriages, 210 placenta previa cases, 830 placental abruptions, 5590 hypertensive disorders of pregnancy, 250 eclampsia cases, 1170 infant deaths, US\$104 million in direct medical costs, and 830 maternal QALYs lost.

## **Discussion**

To our knowledge, this is the first microsimulation model to integrate dynamic cigarette smoking, e-cigarette use, pregnancy-related smoking cessation, and postpartum relapse with pregnancy-specific maternal outcomes and infant mortality. Our projections provide updated estimates of the preventable maternal and infant burden attributable to prenatal smoking in the USA in the e-cigarette era.

Baseline projections were consistent with recent surveillance trends. Smoking prevalence among pregnant women declined to less than 3% by 2040 and remained stable thereafter, whereas e-cigarette use increased to 8.5% by 2040 before plateauing.<sup>6,25</sup> These findings suggest that, without additional intervention, a residual proportion of pregnant women will continue to smoke, while nicotine exposure during pregnancy will increasingly involve e-cigarette use rather than cigarette smoking alone.

Prenatal smoking was projected to be associated with approximately 1170 excess infant deaths per year, corresponding to 86 600 smoking-attributable infant deaths by 2100.

This estimate indicates that even low residual smoking prevalence among pregnant

women can have meaningful population-level consequences for infant survival. Earlier population-attributable estimates reported roughly 1000–5000 smoking-attributable infant deaths annually, but those estimates were generated when prenatal smoking prevalence was substantially higher (11-13%).<sup>26,27</sup> Our projections update this evidence by incorporating the declining trajectory of prenatal smoking and the changing nicotine-use landscape.

Eliminating smoking was projected to avert 278 000 ectopic pregnancies, 1.62 million miscarriages, 15 700 placenta previa cases, 61 300 placental abruptions, 414 000 hypertensive disorders of pregnancy, and 18 100 eclampsia cases through 2100. The largest absolute burden was attributable to miscarriage, reflecting both the high baseline frequency of early pregnancy loss and the increased miscarriage risk associated with smoking.<sup>28</sup>

The early increase in hypertensive disorders of pregnancy under the no-smoking counterfactual reflects the model's preservation of smoking history and the well-documented "smoking paradox" in pre-eclampsia, which the model propagates by using empirical smoking-stratified natality risks.<sup>29</sup> The counterfactual does not create a population of lifetime never-smokers; it eliminates current smoking prospectively while preserving prior smoking histories. Women who would otherwise have continued smoking move into the former-smoking category, while observed hypertensive disorder risks remain lower among current smokers than among former or never smokers in the natality data. This structure produces a transient increase early in the projection horizon. Over time, as smoking initiation remains zero and successive cohorts enter pregnancy without prior smoking exposure, the cumulative effect becomes favourable.

This pattern should not be interpreted as evidence that smoking cessation causally increases risk.

Smoking-attributable pregnancy complications imposed substantial costs on the US health-care system. We estimated cumulative direct medical costs of US\$7.71 billion through 2100, corresponding to approximately US\$104 million annually. Previous estimates of smoking-attributable maternal complication costs were higher, partly because they were generated during periods of higher prenatal smoking prevalence and included broader outcomes such as preterm delivery and low birthweight.<sup>30</sup> Our estimate should therefore be interpreted as a conservative lower bound because the model focused on acute pregnancy complications, did not include preterm birth or low birthweight as separate outcomes, and excluded downstream child health-care costs.

Smoking-attributable pregnancy complications were also associated with 61 700 maternal QALYs lost through 2100. These quality-of-life losses reflect acute maternal morbidity from ectopic pregnancy, miscarriage, hypertensive disorders, eclampsia, and bereavement after infant death. Because the model applied one-year maternal utility decrements and did not include infant life-years lost, long-term child morbidity, chronic maternal sequelae, or longer-term psychological effects, the estimated QALY burden is also conservative.

Our findings provide a benchmark against which future tobacco-control interventions during pregnancy and the postpartum period can be evaluated. A previous SimSmoke analysis projected that comprehensive tobacco-control policies could reduce prenatal smoking prevalence and improve maternal and child health outcomes.<sup>13</sup> Our model

extends this work by incorporating individual-level smoking and e-cigarette transitions, pregnancy-related cessation, postpartum relapse, and a broader set of pregnancy-specific outcomes. The baseline and no-smoking scenarios define the approximate upper bound of preventable burden attributable to prenatal smoking; real-world interventions would be expected to achieve smaller gains depending on their reach, effectiveness, and effects on cigarette and e-cigarette use.

The rise of e-cigarette use among pregnant women remains an important source of uncertainty. In the base case, e-cigarette use did not directly modify pregnancy outcome risks because causal evidence on e-cigarette-related maternal and infant outcomes remains insufficient.<sup>10</sup> Instead, e-cigarettes influenced outcomes indirectly through their effects on cigarette smoking transitions. As evidence from cohort studies and trials matures, the SEP model can be updated to incorporate e-cigarette-specific risks and to evaluate interventions that affect smoking, vaping, or dual use. Even under current evidence limitations, the model provides a flexible framework for quantifying how changing nicotine-use patterns may shape future maternal and infant health burden.

### **Limitations**

This study has several limitations. First, the model used annual cycles and represented pregnancy as lasting one model year. This structure prevents two pregnancies from occurring within the same calendar year and could slightly undercount total pregnancies, although closely spaced same-year pregnancies are uncommon.

Pregnancy rates were also held constant after 2019 to isolate the effects of changing tobacco-use patterns. If future fertility trends differ substantially from 2019 levels,

absolute event counts would change, although comparisons between scenarios would probably be less affected.

Second, former smoking was represented as a single state without stratification by time since cessation, which could overstate risks for long-term quitters. We partly addressed this limitation by assigning former-smoking risks differentially across outcomes according to the likely nature and timing of each morbidity. For outcomes plausibly influenced by persistent reproductive damage, such as ectopic pregnancy and miscarriage, former-smoking risks were aligned more closely with current-smoking risks; for acute within-pregnancy placental outcomes, former-smoking risks were aligned with never-smoking risks. The rationale for these assumptions is provided in the appendix.

Third, the model assigned the same age-specific probability of pregnancy regardless of smoking status. Because smoking is associated with reduced fecundability, this assumption could modestly overestimate the absolute number of smoking-attributable complications. We did not apply a smoking-specific fertility penalty to avoid double counting reproductive effects already captured through observed pregnancy rates and downstream early pregnancy losses.

Fourth, the model was focused on perinatal outcomes and acute health-care costs. Maternal deaths from pregnancy complications were not modelled separately, and infants were not followed beyond the first year of life. Consequently, infant QALYs, infant life-years lost, longer-term child morbidity, chronic maternal sequelae, and longer-term psychological effects were not captured. Direct medical costs therefore reflect

incremental acute complication-management costs rather than total lifetime costs attributable to smoking in pregnancy.

Fifth, e-cigarette use was assumed not to directly affect pregnancy outcome risks in the base case because causal evidence remains insufficient. E-cigarettes therefore influenced outcomes only through their effects on cigarette smoking transitions. If future evidence shows independent beneficial or harmful effects of e-cigarette use, vaping, or dual use during pregnancy, projected burdens could change.

Finally, long-term projections depend on assumptions about future smoking, e-cigarette use, fertility, and outcome risks. We calibrated the model to contemporary national data and used a no-smoking counterfactual to estimate preventable burden, but these results should be interpreted as scenario-based projections rather than forecasts of inevitable future outcomes. Additional details on structural assumptions are provided in the appendix.

## **Conclusion**

This study provides a policy-relevant framework for translating tobacco-use patterns during pregnancy into projected maternal morbidity, infant mortality, and health-care costs. Our findings show that, despite declining prevalence, prenatal smoking is projected to remain a substantial and preventable source of harm to maternal and infant health in the USA. By evaluating a no-smoking counterfactual, we quantify the scale of that preventable burden and establish a transparent benchmark for assessing the potential gains from tobacco-control interventions during pregnancy and the postpartum period. Future applications of this model can compare specific policy scenarios as

evidence on smoking, e-cigarette use, and dual use in pregnancy evolves. These estimates can support priority-setting, guide resource allocation, and help decision makers set realistic targets for reducing smoking-related harms in pregnancy. In this way, our study turns tobacco exposure within pregnancy from a recognized public health problem into a measurable target for policy, planning, and prevention.

### **Contributors**

JT conceived and designed the study and obtained funding. JT developed the original microsimulation framework, which AD adapted, extended, and implemented for the present analysis. AD curated the input data, programmed and calibrated the model, conducted the formal analysis, generated all figures and tables, and wrote the first draft of the manuscript. SS and CC contributed to data acquisition, parameter inputs, and components of the statistical analysis. MJ contributed to interpretation of the findings and provided external review of the results and manuscript. JT supervised the project and provided administrative, technical, and material support. All authors contributed to interpretation of the findings, critically revised the manuscript for important intellectual content, and approved the final version. AD and JT directly accessed and verified the underlying data and model outputs reported in the manuscript. AD and JT act as guarantors and take responsibility for the integrity of the data and the accuracy of the analysis. All authors had full access to the study results and contributed to the decision to submit the manuscript for publication.

### **Declaration of interests**

All authors declare no competing interests.

## **Data sharing**

All input datasets used in this study are publicly available from the National Health Interview Survey, Behavioral Risk Factor Surveillance System, National Vital Statistics System Natality files, National Center for Health Statistics Linked Birth–Infant Death files, National Survey of Family Growth, and other publicly available sources described in the appendix. No new individual participant data were collected for this study. With publication, model code, parameter tables, calibration targets, analysis scripts, and aggregate model outputs needed to reproduce the main results will be made available at <https://github.com/jamietam/sep-microsim.git>. Data will be shared without investigator approval and without a data access agreement, subject to the terms of use of the original public data sources. The appendix provides additional model structure, assumptions, parameter sources, and supplementary results.

## **Role of the funding source**

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## **Ethics approval**

This study used deidentified, publicly available secondary data and did not involve new data collection from human participants. Ethics approval was not required.

## **Use of AI-assisted technologies**

During manuscript preparation, ChatGPT (OpenAI; GPT-5.5 Thinking, accessed May 2026) was used to support language editing, formatting consistency, and manuscript polishing. Prompts asked the tool to revise author-provided manuscript text for clarity, grammar, consistency with Lancet Public Health style, and adherence to reporting requirements. The tool was not used to generate scientific findings, conduct analyses, interpret results, or draw conclusions. All AI-assisted text was reviewed, edited, and verified by the authors, who take full responsibility for the accuracy, originality, and integrity of the manuscript.

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## Tables

**Table 1. Projected smoking-attributable maternal and infant outcomes, direct medical costs, and maternal QALY losses, USA, 2027–2100**

Outcome	Cumulative Through Year				Annual Average
	2040	2060	2080	2100	
<b>Ectopic pregnancy</b>	13 100	95 300	188 000	278 000	3760
<b>Miscarriage</b>	68 300	533 000	1 080 000	1 620 000	21 900
<b>Placenta previa</b>	2770	7160	11 500	15 700	210
<b>Placental abruption</b>	12 000	29 000	45 400	61 300	830
<b>Hypertensive disorders of pregnancy</b>	-9060	114 000	266 000	414 000	5590
<b>Eclampsia</b>	-158	4860	11 600	18 100	250
<b>Infant deaths</b>	8610	33 400	60 400	86 600	1170
<b>Direct medical costs, US\$ millions</b>	1140	4450	6570	7710	104
<b>Maternal QALY losses</b>	6350	33 600	51 900	61 700	830

**Notes:** Values represent baseline minus no-smoking counterfactual estimates and are rounded to three significant figures. Positive values indicate adverse outcomes, direct medical costs, or maternal QALY losses that would be averted if smoking were eliminated; negative values indicate outcomes projected to increase under the no-smoking counterfactual. Annual averages were calculated as cumulative values through 2100 divided by 74 calendar years, corresponding to 2027–2100 inclusive. Costs are reported in millions of 2024 US dollars. QALY=quality-adjusted life-year.

## Figure legends

### **Figure 1: Smoking, e-cigarette use, and pregnancy model structure**

A, State-transition diagram of the smoking, e-cigarette use, and pregnancy (SEP) microsimulation model. The schematic shows possible transitions between smoking status, e-cigarette use status, and pregnancy status within one annual cycle. N=never smoking; C=current smoking; F=former smoking; O=never e-cigarette use; E=current e-cigarette use; Q=former e-cigarette use; P=pregnant; U=not pregnant. For clarity, not all self-transitions are shown; in each state, the probabilities of all outgoing transitions and remaining in the same state sum to 1. B, Pregnancy and infant mortality module linked to the microsimulation model. The example decision tree shows maternal morbidity and infant mortality outcomes for pregnant women who currently smoke and have never used e-cigarettes. Corresponding outcome trees are linked to other tobacco-use states.

### **Figure 2: Model calibration to observed smoking and e-cigarette use prevalence, 2016–2024**

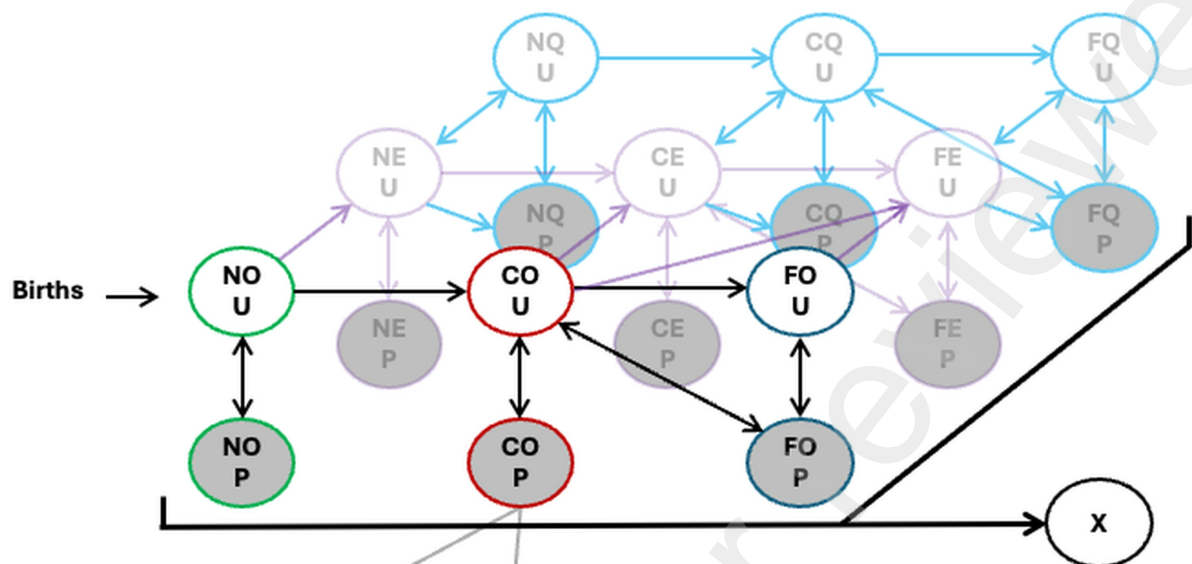
Observed survey estimates and model-predicted prevalence of smoking status and e-cigarette use among women of reproductive age and pregnant women. Points show survey estimates with 95% CIs; lines show model predictions. Calibration targets were derived from the National Health Interview Survey for women of reproductive age and the Behavioral Risk Factor Surveillance System for pregnant women.

### **Figure 3: Observed and projected tobacco-use prevalence among pregnant women, 2016–2100**

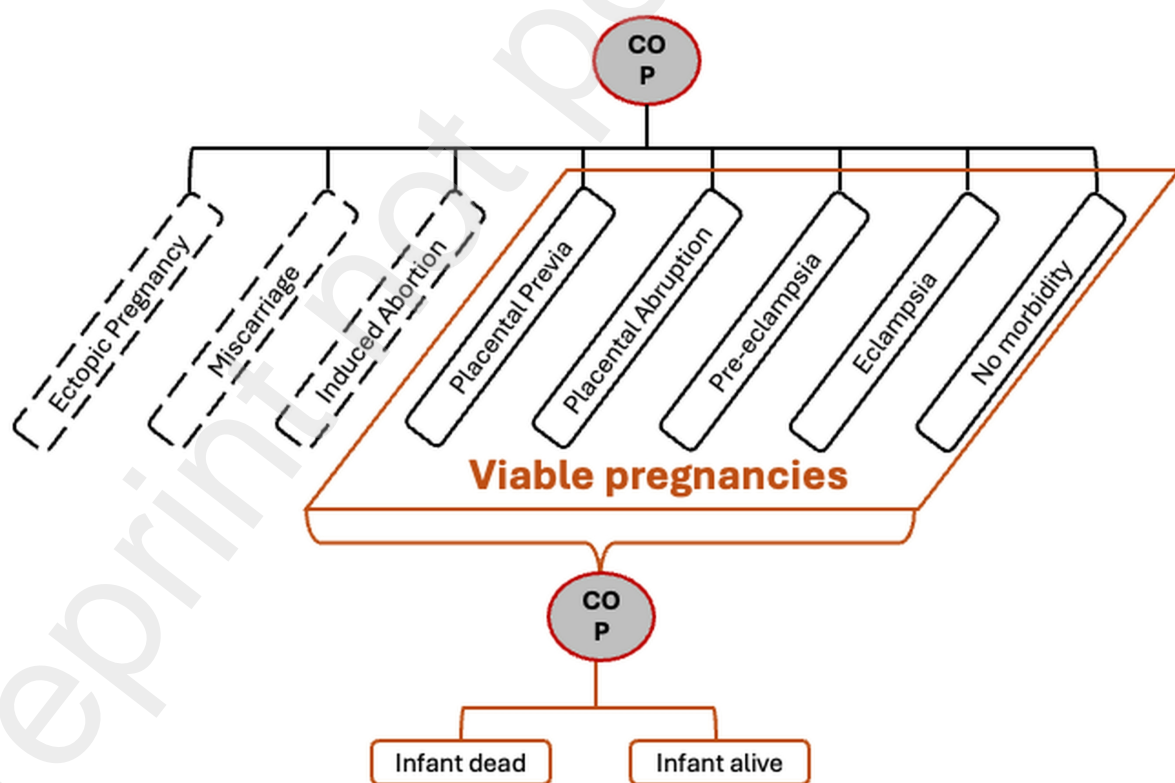
Observed survey estimates and model projections of current smoking, e-cigarette use,

and dual use among pregnant women under baseline trends and the no-smoking counterfactual. Points show Behavioral Risk Factor Surveillance System estimates with 95% CIs; lines show model projections. In the no-smoking counterfactual, smoking and dual use were eliminated prospectively, while e-cigarette transitions were otherwise allowed to continue.

## A. Microsimulation model



## B. Pregnancy & Infant mortality module

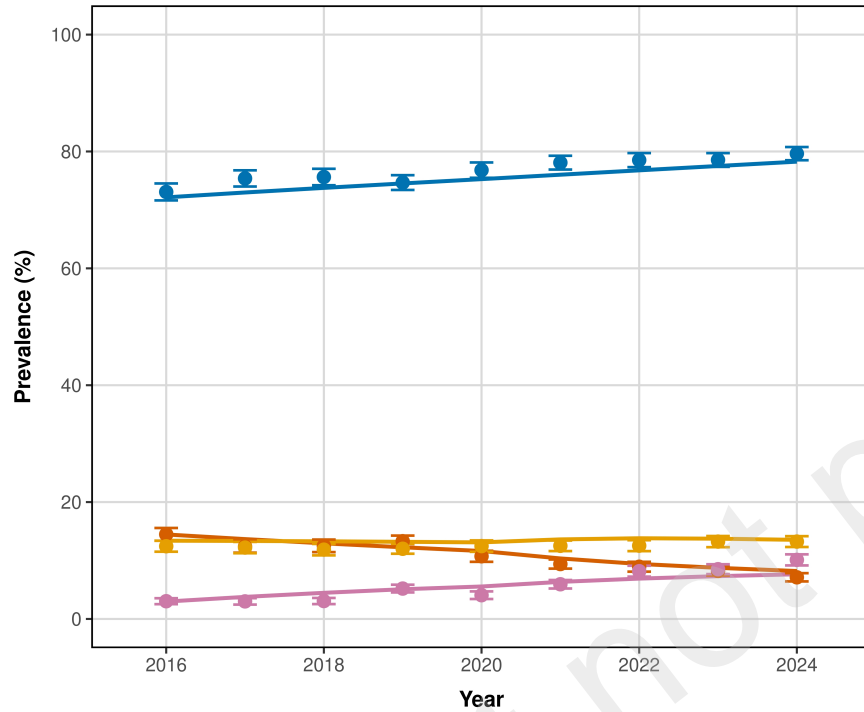


# Model calibration: tobacco-use prevalence, 2016–2024

Points: Survey data with 95% CI | Lines: Model predictions

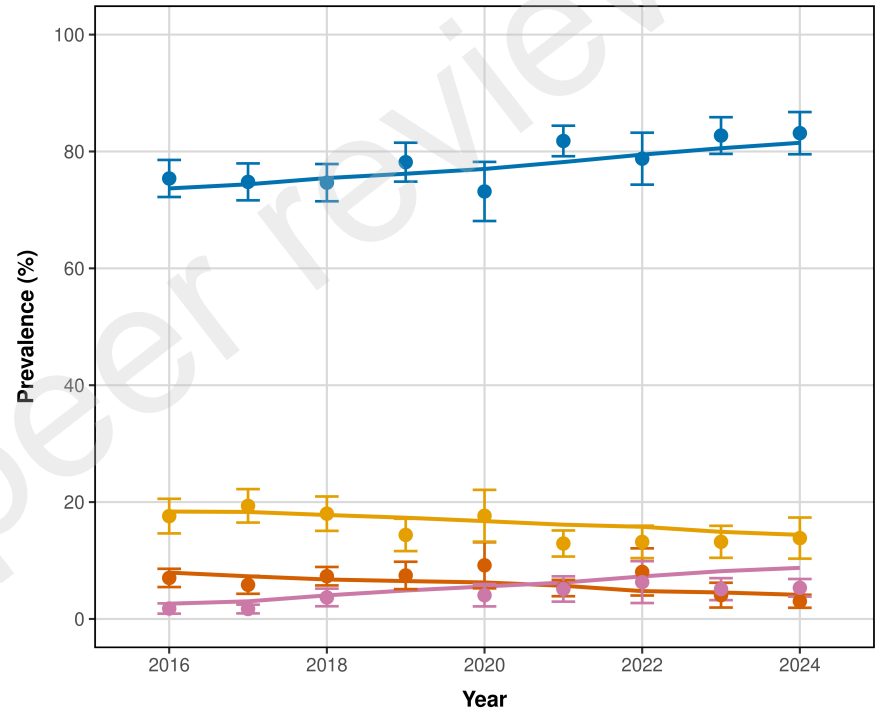
## A. Women of reproductive age (NHIS)

Age 18–49



## B. Pregnant women (BRFSS)

Age 18–49



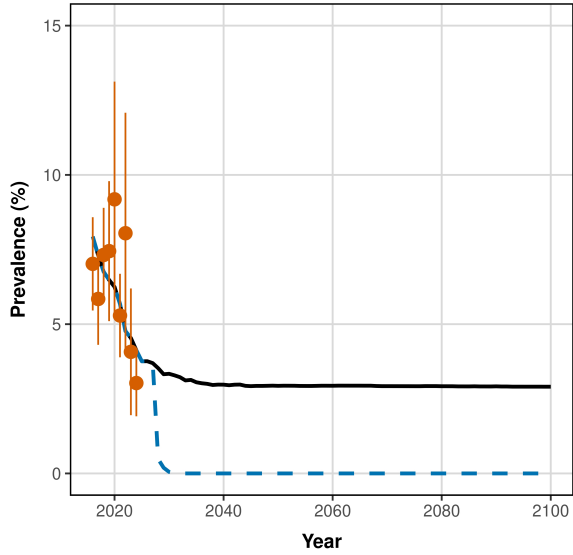
Status — Current smoking — E-cigarette use — Former smoking — Never smoking

# Observed and projected tobacco-use prevalence among pregnant women, 2016–2100

Baseline vs No Smoking Scenario | Age 18–49

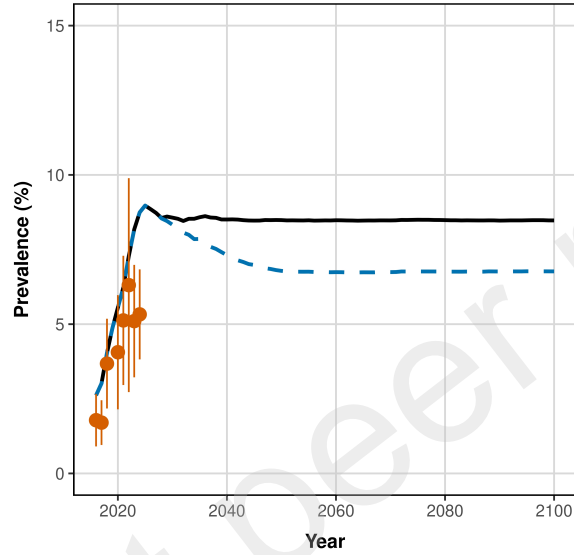
### A. Current Smoking

Pregnant women, age 18–49



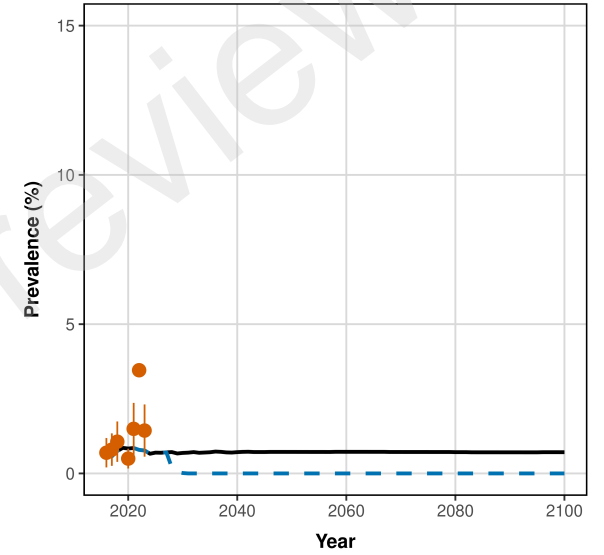
### B. E-cigarette Use

Pregnant women, age 18–49



### C. Dual Use (Smoking + E-cigarette)

Pregnant women, age 18–49



Scenario — Baseline — No Smoking ● BRFSS Data

Preprint not Peer-Reviewed

# Model calibration: tobacco-use prevalence, 2016–2024

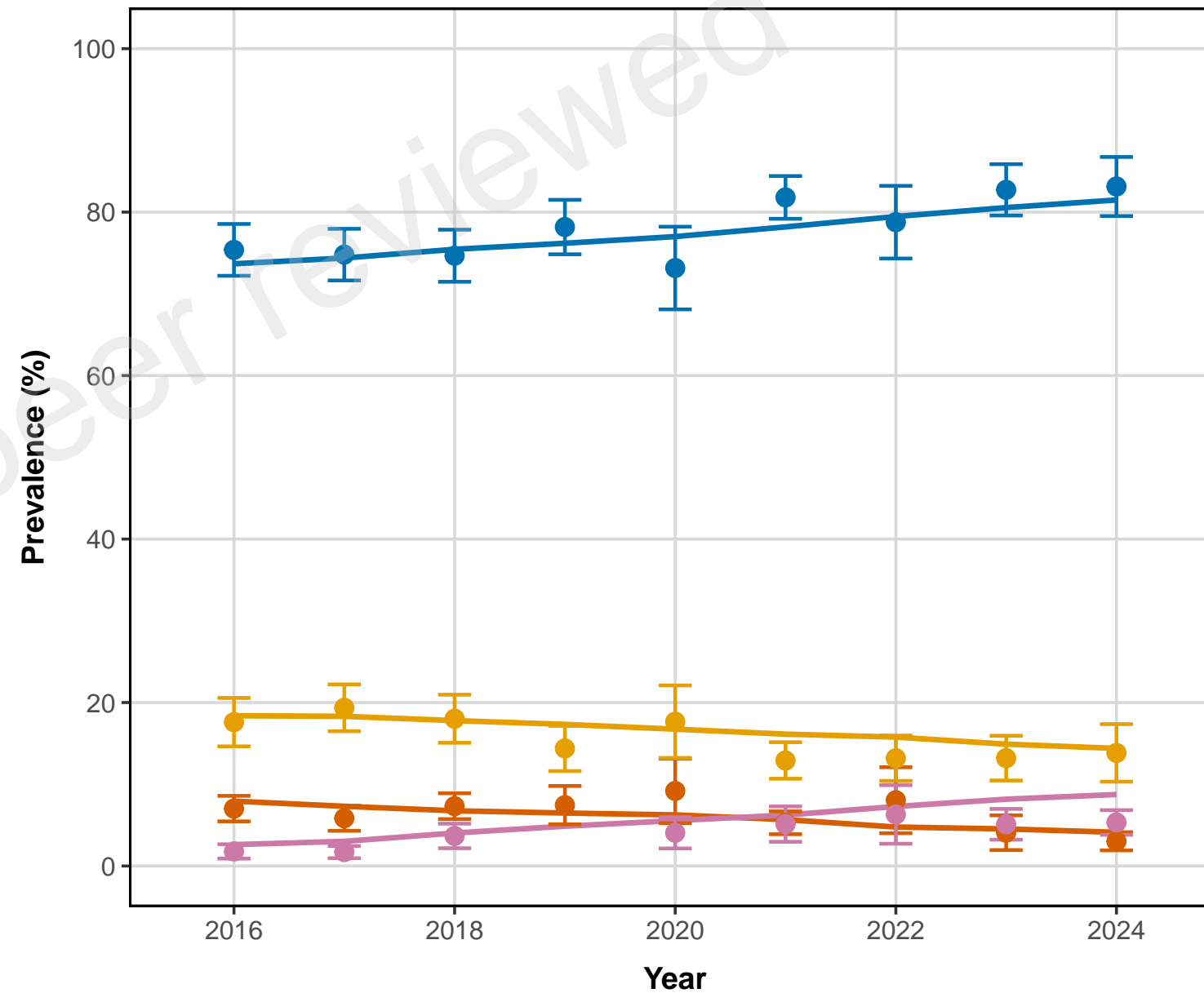
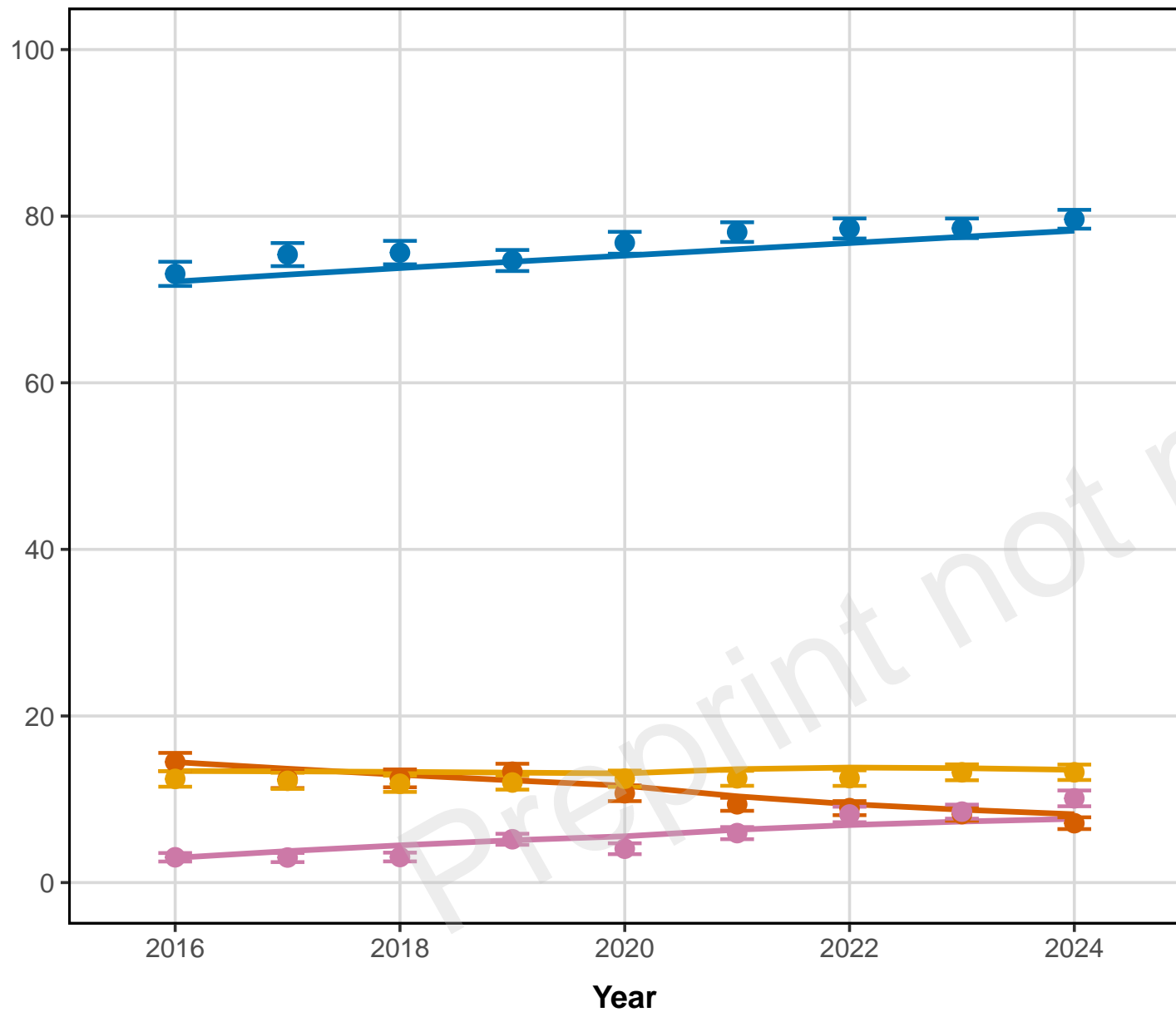
Points: Survey data with 95% CI | Lines: Model predictions

## A. Women of reproductive age (NHIS)

Age 18–49

## B. Pregnant women (BRFSS)

Age 18–49



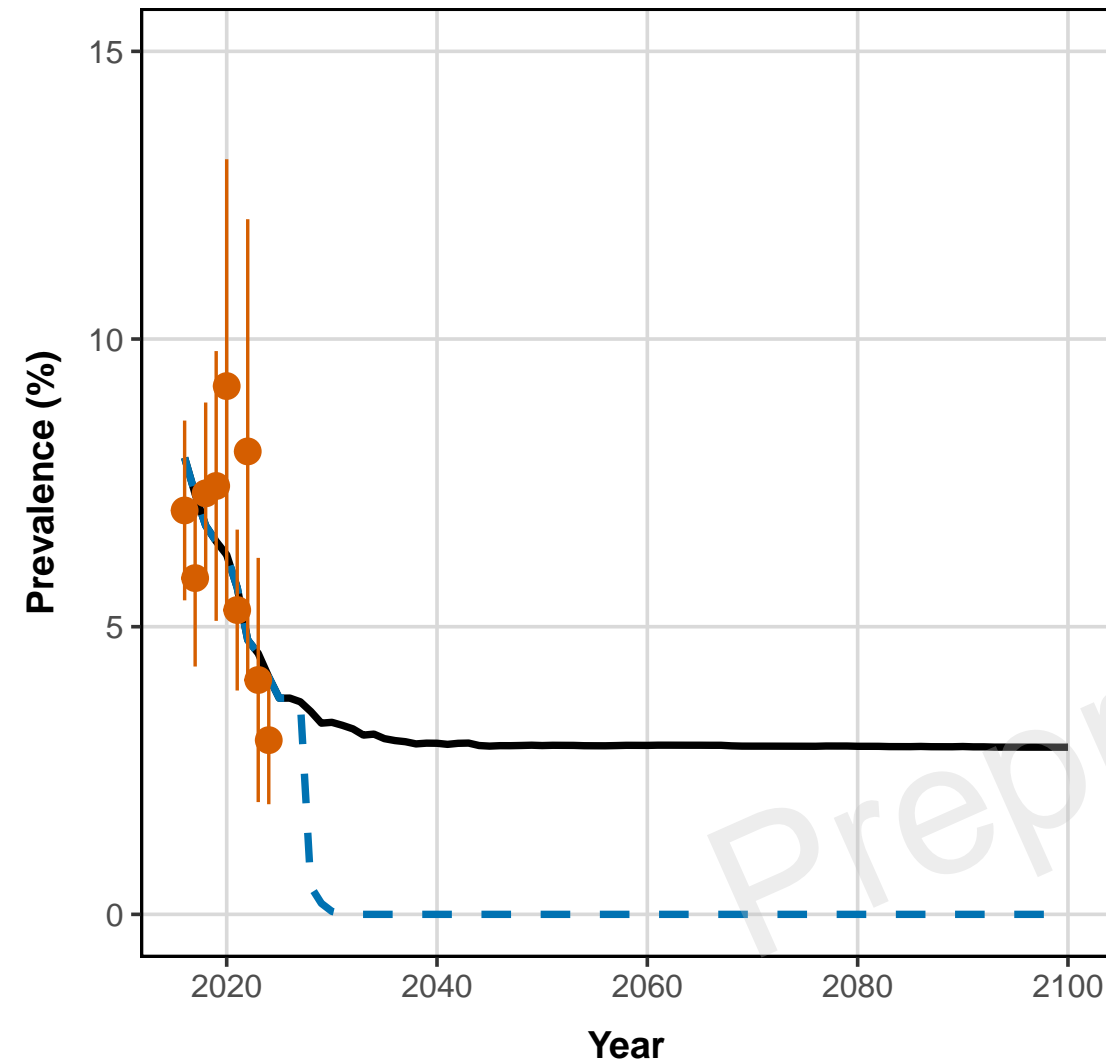
**Status** — Current smoking — E-cigarette use — Former smoking — Never smoking

# Observed and projected tobacco-use prevalence among pregnant women, 2016–2100

Baseline vs No Smoking Scenario | Age 18–49

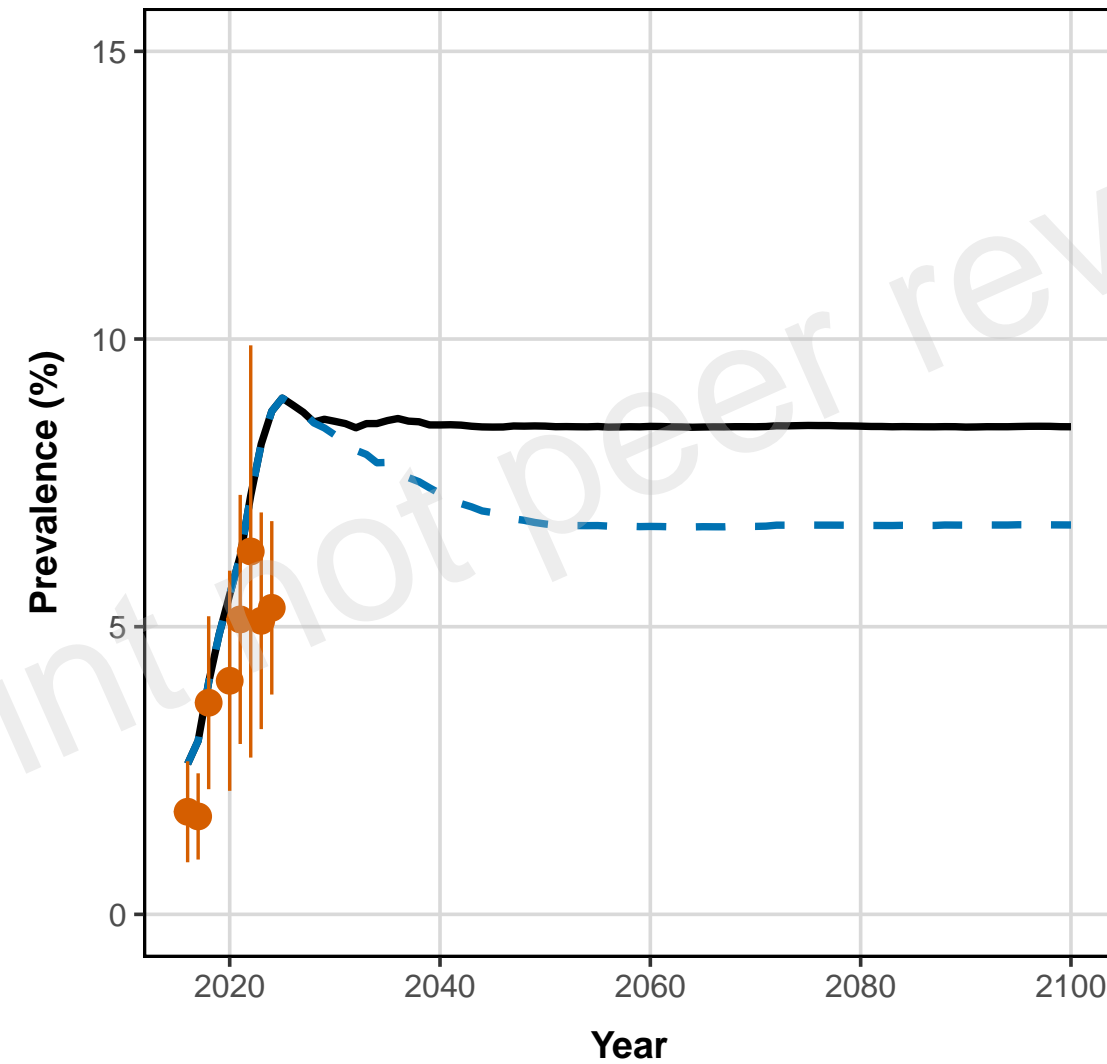
## A. Current Smoking

Pregnant women, age 18–49



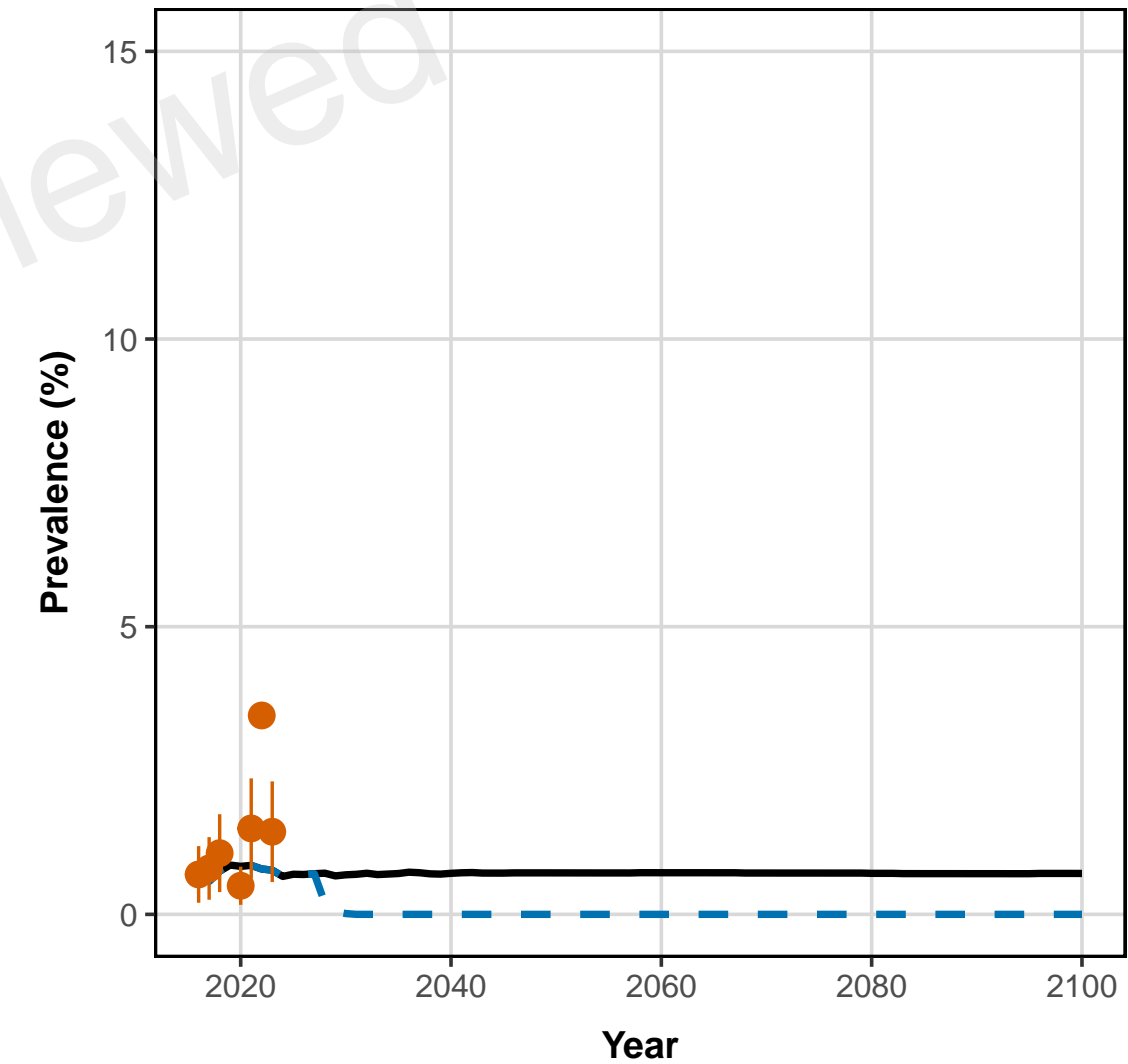
## B. E-cigarette Use

Pregnant women, age 18–49



## C. Dual Use (Smoking + E-cigarette)

Pregnant women, age 18–49



Scenario — Baseline — No Smoking ● BRFSS Data

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