

1 **Maternal mortality related to pulmonary embolism in** 2 **the United States, 2003-2020**

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69 IF, LV, LH and SB drafted the manuscript. The rest of the authors critically revised
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77 **Condensation**

78 PE-related maternal mortality rates remained stable during 2003-2020 and was 2
79 deaths per 100,000 live births in 2020, while PE accounted for 6% of all maternal
80 deaths.

81

82 **Short title**

83 Pulmonary embolism-related maternal mortality

84

85 **AJOG at a Glance**

86 A. This study was conducted to describe the changes in PE-related maternal
87 mortality rates in the United States over the past two decades.

88 B. The PE-related maternal mortality rates increased from 0.93 in 2003 to 1.96 in
89 2020; however, when accounting for the implementation of the pregnancy
90 checkbox in the death certificates, the trends in PE-related maternal mortality
91 were largely unchanged from 2003 to 2020. PE accounted for 6% of all
92 maternal deaths.

93 C. Maternal mortality rates due to PE did not decrease during the period 2003-
94 2020, as opposed to mortality rates from PE in the general population.

95

96 Abstract

97 **Background:** Pulmonary embolism is a leading cause of maternal morbidity and
98 mortality in Western countries. In the United States, pulmonary embolism-related
99 mortality rates have plateaued in the general population after an initial decrease the
100 past 20 years.

101 **Objective:** To describe the changes in pulmonary embolism -related maternal
102 mortality rates in the United States over the past two decades.

103 **Study Design:** In this epidemiological study of public vital registration data (death
104 certificates encompassing underlying and contributing causes of death) from the
105 Centers for Disease Control and Prevention Mortality Multiple Cause of Death
106 database (2003-2020) we identified all maternal deaths with a pulmonary embolism
107 code listed in any position of the death certificates. We investigated the changes in
108 annual crude pulmonary embolism -related maternal mortality rates for the years
109 2003 to 2020, considering the effect of the introduction of the pregnancy checkbox in
110 death certificates on the pulmonary embolism -related maternal mortality rates.

111 **Results:** Overall, 735 pulmonary embolism -related maternal deaths out of 12,871
112 total maternal deaths (5.7%) were recorded between 2003 and 2020; the overall
113 pulmonary embolism -related maternal mortality rate was 1.02 (95% confidence
114 interval 0.95-1.10) per 100,000 live births. The pulmonary embolism -related
115 maternal mortality rates increased from 0.93 in 2003 to 1.96 in 2020; however, when
116 accounting for the implementation of the pregnancy checkbox in the death
117 certificates, the trends in pulmonary embolism -related maternal mortality were
118 largely unchanged from 2003 to 2020. The crude pulmonary embolism -related
119 maternal mortality rates differed across maternal age groups (overall 0.61, 1.09, and
120 3.83 maternal deaths per 100,000 live births for ≤ 24 , 25-39, and ≥ 40 years old,

121 respectively) and racial/ethnicity groups (2.89, 0.47, 0.77, and 0.63 maternal deaths
122 per 100,000 live births for black non-Hispanics, other non-Hispanics, white non-
123 Hispanics, and Hispanics, respectively).

124 **Conclusion:** Maternal mortality rates due to pulmonary embolism did not decrease
125 during the period 2003-2020, as opposed to mortality rates from pulmonary embolism
126 in the general population. More research is required to assess whether improvement
127 in venous thromboembolism prevention and pulmonary embolism diagnosis and
128 management strategies might reduce death due to pulmonary embolism in this
129 vulnerable population.

130

131

132 **Keywords:** maternal mortality; pulmonary embolism; pregnancy; epidemiology; CDC
133 multiple causes of death; venous thrombosis

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135

136

137 Introduction

138 Acute venous thromboembolism (VTE), and particularly its potentially fatal
139 manifestation pulmonary embolism (PE), is a leading cause of maternal morbidity
140 and mortality.¹ The risk of VTE during pregnancy is up to 6 times higher than in the
141 non-pregnant female population at reproductive age, with an absolute risk ranging
142 between 2.7 and 12.2 per 10,000 deliveries per year compared to 2 per 10,000
143 persons per year in non-pregnant women.² Estimates regarding maternal PE-related
144 death and its temporal trends are sparse and inconsistent, even in high-income
145 countries.^{2, 3} Reliable information on the occurrence of acute diseases and their
146 associated mortality in vulnerable patient groups, such as in pregnant women, is
147 essential for prospective risk stratification and optimization of management to
148 prevent or treat hemodynamic deterioration during acute PE events.^{3, 4} Therefore,
149 describing the trends in PE-related maternal mortality is of particular importance to
150 better depict the magnitude of this problem, recognize potential gaps in the
151 contemporary clinical evaluation and practice, as well as expand the existing limited
152 knowledge.

153 Over the past 20 years, the overall PE-related mortality rate decreased in
154 Europe, whereas it plateaued in the United States (US) after the previous decades-
155 long decline.^{5, 6} In this epidemiological analysis, we sought to evaluate PE-related
156 maternal mortality rates in the US over the past two decades using nationwide vital
157 registration statistics.

158

159 **Materials and Methods**

160 We accessed the Mortality Multiple Cause of Death database (years 2003-2020)
161 provided by the US Centers for Disease Control and Prevention (CDC).⁷ The
162 database provides information on the causes of death of all decedent US residents,
163 as indicated on their death certificates. The database includes demographic
164 (including age, sex, race and ethnicity), as well as geographical (i.e., place of death)
165 and diagnostic data (i.e., indicating whether an autopsy was performed or not). Up to
166 20 causes of death are available for each death record, as reported by physicians
167 (“entity axis” field). Of them, the condition that directly led to death is defined as the
168 underlying cause of death, all other conditions as contributing causes of death. A
169 standardized process of translation of codes, elimination of repetitions, and
170 automatic reassignment converts the causes of death as entered by the physician in
171 the death certificate (“entity axis” in the CDC terminology, as each condition of
172 “entity” is preserved as entered) into a sequence of causes free of contradictions and
173 medically plausible (“record axis” in the CDC terminology, as the sequence and
174 codes are adapted by considering all other conditions in the whole record).⁸ As in
175 previous studies, we used the record axis for this analysis.⁶ Disease classification
176 and ordering details can be found on the CDC website ([cdc.gov](https://www.cdc.gov)).

177 We used the World Health Organization (WHO) definition of maternal death:
178 “the death of a woman while pregnant or within 42 days of termination of pregnancy,
179 irrespective of the duration and the site of the pregnancy, from any cause related to
180 or aggravated by the pregnancy or its management, but not from accidental or
181 incidental causes”.⁹ Accordingly, we primarily identified maternal deaths using the
182 International Classification of Disease, 10th Revision (ICD-10) codes A34, O00-O95,
183 and O98-O99 as underlying cause of death (the full ICD-10 definitions are provided

184 in Supplementary Table 1). We excluded late maternal deaths (death of a woman
185 occurring more than 42 days but less than one year after termination of pregnancy)
186 defined by ICD-10 codes O96 and O97. We used the “WHO application of ICD-10
187 deaths during pregnancy, childbirth and the puerperium” to categorize underlying
188 causes of death in mutually exclusive, totally inclusive groups (Supplementary Table
189 1).⁹

190 Beginning from 2003, a “pregnancy checkbox” has been introduced gradually
191 in US death certificates to reduce the number of maternal deaths missed due to
192 imprecise reporting: its use has been associated with more accurate identification of
193 maternal deaths.¹⁰ This checkbox item specifies whether the decedent was currently
194 in a pregnancy or had a pregnancy in the past year and, in such case, enforced the
195 appropriate use of maternal ICD-10 O-codes. However, the checkbox was not
196 implemented nationwide at the same time, but progressively across States from
197 2003 until 2017, when it was finally adopted in the whole United States. This
198 staggered implementation hinders the evaluation of true temporal maternal mortality
199 trends in this period, since more maternal deaths were captured in each State after
200 the local introduction of the checkbox, thus correcting the maternal mortality rates
201 upwards.¹¹ Indeed, prior reports documented that, when the checkbox was
202 implemented, less clearly defined ICD-10 codes, such as O26.8 (“Other specified
203 pregnancy related conditions”) and O99 (“Other maternal diseases classifiable
204 elsewhere but complicating pregnancy, childbirth and the puerperium”) were used
205 more frequently.¹¹ Therefore, we additionally performed a sensitivity analysis of the
206 temporal trends in PE-related maternal mortality rates, excluding deaths that
207 reported either O26.8 or O99 as an underlying cause of death, which has been
208 shown to mitigate the effect of the pregnancy checkbox implementation and reflects

209 the possible underestimation of maternal mortality rates in the absence of the
210 checkbox.^{11, 12} To prevent misclassification of causes of death as maternal deaths
211 due to errors in the use of the pregnancy checkbox and a subsequent inflation of
212 maternal mortality rates for older women, we excluded deaths of women at aged 55
213 years or older.¹³

214 We defined deaths related to PE as deaths with ICD-10 codes in any place of
215 the death certificate that were specific for PE or DVT, including I26.x and O88.2
216 (PE), as well as I80.x, I82.2, I82.4, I82.9, O22.3, and O87.1 (DVT) in line with
217 previous research.^{5, 14, 15} The ICD-10 codes used to define the different causes of
218 death are presented in **Supplementary Table A1**.

219 In order to calculate race/ethnicity-specific as well as age-specific mortality
220 rates, we used the annual total birth counts for the period 2003-2020 (overall and by
221 maternal race/ethnicity) and the maternal age groups provided by the National Vital
222 Statistics System of the National Center for Health Statistics.¹⁶ Both birth and
223 mortality data were categorized across four racial/ethnicity groups: non-Hispanic
224 black, non-Hispanic other (including American Indian, Alaska Native, Asian and
225 Native Hawaiian or Other Pacific Islander), non-Hispanic white, and Hispanic. Age
226 was categorized in three groups: ≤ 24 years, 25-39 years, and ≥ 40 years.

227 The present study used de-identified data for public use and did not require
228 approval by an institutional review board. Two investigators (ITF, LV) independently
229 performed data extraction and validation, as well as the statistical analysis. This
230 report abides by the Guidelines for Accurate and Transparent Health Estimates
231 Reporting (GATHER) standards.¹⁷

232

233 **Statistical analysis**

234 We investigated the association of mortality related to PE (PE in any place in the
235 death certificate) with mortality related to other causes (in any place in the death
236 certificate) with relative risk regression using a log-link binomial generalized linear
237 model adjusting for age. We calculated crude PE-related maternal mortality rates by
238 dividing the number of PE-related deaths by the total births in any given year (deaths
239 per 100,000 live births). We did not provide age-standardized estimates of PE-
240 related maternal mortality rates because we did not anticipate major differences in
241 the distribution of pregnancies during the 2003-2020 period across the age groups.
242 We estimated the proportionate mortality of PE-related maternal mortality, defined as
243 the proportion of PE-related maternal deaths out of all maternal deaths. Locally
244 estimated scatterplot smoothing with least squares fitting to generate smoothed lines
245 with 95% confidence intervals (CI) were used to depict the trends in crude mortality
246 rates and proportionate mortality over the study period. Differences in contingency
247 tables were explored with the use of the Pearson's Chi-squared test or Fisher's exact
248 test as appropriate. All analyses were stratified by racial/ethnic and age groups.
249 Statistical analysis was performed using R (version 4.1.2).

250

251 Results

252 Overall, 12,871 maternal deaths were recorded in the US from 2003 to 2020 with
253 increasing numbers over time: 496 deaths in 2003 and 863 deaths in 2020 (**Table 1**).
254 This corresponds to an increase in reported all-cause maternal mortality from 12.1
255 maternal deaths per 100,000 live births in 2003 to 23.9 maternal deaths per 100,000
256 live births in 2020. This increase followed the introduction of the pregnancy
257 checkbox.

258 Focusing on the deaths due to PE, 735 PE-related maternal deaths were
259 recorded between 2003 and 2020, corresponding to 5.7% of all maternal deaths
260 recorded in the same period; this figure peaked at 8.2% in 2020. After age
261 adjustment, PE-related maternal deaths were more likely to be associated with non-
262 Hispanic black race and with concomitant cardiovascular causes of death. In
263 contrast, they were less likely to occur in patients with a concomitant respiratory
264 disease (**Figure 1**).

265 The overall maternal mortality rate related to PE between 2003 and 2020 was
266 1.02 (95% CI 0.95-1.10) per 100,000 live births. The trend in PE-related maternal
267 mortality rates remained stable between 2003 and 2015, and increased abruptly
268 thereafter peaking at 1.96 (95% CI 1.7-2.2) maternal deaths per 100,000 live births
269 in 2020 and is depicted in **Figure 2A**. The trend in proportionate PE-related maternal
270 mortality is displayed in **Figure 3A** and shows that the proportion of PE-related death
271 out of all maternal deaths increased in the later years of the period, as the pregnancy
272 checkbox was implemented nationwide.

273 The use of O26.8 or O99 ICD-10 codes as underlying cause of death in PE-
274 related maternal deaths increased abruptly after 2015 (**Supplementary Figure A2**),
275 following the progressive introduction of the pregnancy checkbox. In the sensitivity
276 analysis accounting for the implementation of the pregnancy checkbox, after the
277 exclusion of deaths with O26.8 and O99 ICD-10 codes as underlying cause of death,
278 the trends in PE-related maternal mortality remained stable from 2003 to 2020
279 (**Figure 2B**). On the other hand, in the sensitivity analysis, the rise in proportionate
280 mortality due to PE in later years is not evident, possibly indicating the effect of the
281 pregnancy checkbox in revealing a higher burden of PE among maternal deaths
282 (**Figure 3B**). Comparing the PE-related maternal deaths in the two periods – the first

283 years of the pregnancy checkbox implementation (2003-2005) versus the period
284 after its universal use across states (2018-2020) – we observed that PE was
285 reported more frequently in the death certificates in the group aged 25-39 years,
286 although autopsy was performed less frequently (**Table 2**). Report of cardiovascular
287 diseases (24% vs 0%), respiratory diseases (5.2% vs 0%) and bleeding (3.6% vs
288 0%) as cause of deaths anywhere in death certificates was more frequent in later
289 than in earlier years of the period considered.

290 The crude PE-related maternal mortality rates differed across maternal age
291 groups (overall 0.61, 1.09, and 3.83 maternal deaths per 100,000 live births for ≤ 24 ,
292 25-39, and ≥ 40 years old, respectively). A steeper increase over time was observed
293 in the age group 25-39 years than in the age group ≤ 24 years (**Figure 3A**), which
294 was not evident in the sensitivity analysis (**Figure 3C**). In contrast, the ≥ 40 years old
295 age group showed fluctuating trends across the time period in both analyses. The
296 crude PE-related maternal mortality rate was 2.89 deaths per 100,000 live births in
297 black non-Hispanics, 0.47 in other non-Hispanics, 0.77 in white non-Hispanics, and
298 0.63 in Hispanic origin. Trends in maternal PE mortality across ethnicities showed a
299 steeper increase among black non-Hispanics than in the other groups (**Figure 3B**
300 and **Figure 3D**).

301

302 Discussion

303 In this epidemiological analysis, the increased specificity of reporting of maternal
304 mortality associated with PE over time in the US database results in an observed
305 increase in maternal mortality rates related to PE from 0.93 per 100,000 live births in
306 the year 2003 to 1.96 per 100,000 live births in 2020 in the US. This is in general
307 accordance with the increase in all-cause maternal mortality rates during the same

308 period as recorded in the literature.¹⁸ However, the increase suggested by death
309 certificates may not represent a true temporal increase in factual PE-related
310 maternal mortality, as it may primarily depend on the way maternal death
311 surveillance was performed and maternal deaths were recorded in death
312 certificates.¹¹ Beginning in 2003, the “pregnancy checkbox” was adopted in the
313 death certificates with the goal of reducing the number of missed maternal deaths.¹⁰
314 The implementation of the checkbox was gradual: by 2018, after all states had
315 adopted it, increased awareness and reduced under-coding were reported.
316 Consequently, the overall maternal mortality rates reported in the US have been
317 increasing since 2003. However, this increase has been observed to have been
318 driven by the potentially inappropriate use of the codes O26.8 and O99¹². In line with
319 these observations, our sensitivity analysis conducted by excluding these codes
320 confirmed that maternal mortality rates remained rather stable in the period
321 considered.

322 Our findings suggest that PE remains a significant driver of maternal mortality,
323 contributing to 8.2% of all maternal deaths in the year 2020. In an analysis of
324 German nationwide inpatient data, the PE-related maternal mortality rate was
325 estimated at 0.8 per 100,000 live births.³ Although the German study used only
326 inpatient data, out-of-hospital deaths are unlikely to be the sole reason of the low
327 reported rate, since the present analysis indicates that ~90% of PE-associated
328 maternal deaths in the US occurred in the hospital. Therefore, the considerable
329 difference between the US and the German mortality rate suggests that a similar
330 underreporting of maternal deaths may occur in other Western countries as in the
331 US before the implementation of the pregnancy checkbox. Since the universal
332 implementation of the pregnancy checkbox in 2018, the PE-related maternal

333 mortality rate in the US almost doubled. Accordingly, and while taking into account
334 that the temporal trends in maternal mortality were stable in our analysis, we may
335 consider the true PE-related maternal mortality rates to be best represented by the
336 years 2018-2020 (nationwide implementation of the checkbox), when they
337 approached 2 deaths per 100,000 live births. We have previously published mortality
338 data from the general population in US and Canada denoting stable or decreasing
339 PE-related mortality trends.⁶ Given that PE is a preventable cause of death, and that
340 pregnancy and especially the early postpartum period is a known significant risk
341 factor for PE, we would expect that PE-related mortality rates would be decreasing in
342 this vulnerable population. However, we did not observe such a decrease.

343 In concordance with our findings, a retrospective analysis of the US
344 Nationwide Inpatient Sample (NIS) by Elgendy et al. indicated that the rates of acute
345 PE per 100,000 pregnancy-related hospitalizations did not change significantly from
346 2007 to 2015 (18.01 in 2007 vs 19.36 in 2015).¹⁹ However, cardiovascular risk
347 factors, such as obesity²⁰, new-onset hypertension²¹, and smoking remain
348 considerable in younger women, which could also contribute to explain the higher
349 prevalence of cardiovascular causes of death in the later period.²²
350 Thromboprophylaxis could be another potential driver of the trends observed.²³ Data
351 from MBRRACE in the United Kingdom indicate that maternal deaths from VTE have
352 decreased after the introduction of thromboprophylaxis guidelines, suggesting an
353 increased use of thromboprophylaxis; trends of thromboprophylaxis use among
354 pregnant women are lacking in the US.

355 Taken together, these factors could partly explain the unchanged rates of
356 hospitalizations as reported by Elgendy et al., but also the stable mortality rates of
357 our study. The risk for PE during a pregnancy-associated hospitalization increased

358 particularly in women aged >40 years, similar to our study. The risk was also greater
359 in pregnant women of black race, as in the present analysis, possibly reflecting
360 social factors and healthcare inequalities.^{6, 24} A trend analysis using NIS data from
361 2000 to 2018 indicated that the PE rates averagely increased 4.9% per year for
362 cesarean delivery hospitalizations and 8.7% per year for vaginal delivery
363 hospitalizations.²⁵ A similar trend was not observed in our analysis.

364

365 **Strengths and Limitations**

366 A limitation of our analysis is that there was no knowledge of whether the
367 pregnancy checkbox was used (or even existed) in each individual death certificate,
368 and therefore we were not able to analyze separately deaths without the use of the
369 pregnancy checkbox to identify more accurate temporal trends in the report of PE-
370 related maternal mortality. However, we believe that the sensitivity analysis
371 excluding the clearly defined codes O26.8 and O99 provides an insight into the true
372 temporal trends of PE-related maternal mortality, as per previous analyses.¹² We
373 cannot exclude that some PE deaths were misclassified as maternal deaths due to
374 the misuse of the pregnancy checkbox, but we partially addressed this limitation by
375 excluding from the analysis women 55 years or older at the time of death. Lastly, the
376 CDC Mortality Multiple Cause of Death database provides 4-digit ICD-10 codes as
377 causes of death; this prevented us from differentiating between mortality rates
378 occurring during pregnancy, delivery or puerperium, which would have required the
379 more detailed 7-digit ICD-10 codes. Also, we had no reliable information on the
380 prevalence of risk factors such as obesity, smoking, and hypertension, which are not
381 provided in death certificates.

382 **Conclusions**

383 In conclusion, this analysis found that the PE-related maternal mortality rate
384 was 2 deaths per 100,000 live births in 2020 and PE accounted for 6% of all maternal
385 deaths in the entire period. Maternal mortality rates related to PE remained stable
386 during the period 2003-2020. The risk for PE-related maternal mortality was highest
387 in women aged >40 years and women of black race. More research is required to
388 assess whether public health strategies to promote awareness improvements in VTE
389 prevention, or advances in the diagnosis and management of PE would reduce the
390 risk of death from PE in this vulnerable population.

391

392

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395

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Tables

Table 1. Characteristics and causes of maternal deaths 2003-2020 in the presence versus absence of pulmonary embolism (PE).

Characteristic	Overall N = 12,871¹	Maternal deaths with PE N = 735¹	Maternal deaths without PE N = 12,136¹	p- value
<i>Age group</i>				<0.001
≤24	2,290 (18)	134 (18)	2,156 (18)	
25-39	7,727 (60)	520 (71)	7,207 (59)	
≥40	2,854 (22)	81 (11)	2,773 (23)	
<i>Race</i>				<0.001
Black	4,380 (34)	303 (41)	4,077 (34)	
Hispanic	2,061 (16)	107 (15)	1,954 (16)	
Other	733 (5.7)	28 (3.8)	705 (5.8)	

Characteristic	Overall N = 12,871¹	Maternal deaths with PE N = 735¹	Maternal deaths without PE N = 12,136¹	p- value
White	5,697 (44)	297 (40)	5,400 (44)	
<i>Autopsy performed</i>	5,931 (46)	451 (61)	5,480 (45)	<0.001
<i>Marital status</i>				0.3
Divorced	1,203 (9.3)	55 (7.5)	1,148 (9.5)	
Married	5,797 (45)	342 (47)	5,455 (45)	
Single	5,593 (43)	326 (44)	5,267 (43)	
Unknown	127 (1.0)	6 (0.8)	121 (1.0)	
Widowed	151 (1.2)	6 (0.8)	145 (1.2)	
<i>Place of death</i>				
Decedent's home	1,768 (14)	66 (9.0)	1,702 (14)	

Characteristic	Overall N = 12,871¹	Maternal deaths with PE N = 735¹	Maternal deaths without PE N = 12,136¹	p- value
Hospice facility	178 (1.4)	2 (0.3)	176 (1.5)	
Hospital, Clinic or Medical Center - Dead on Arrival	157 (1.2)	15 (2.0)	142 (1.2)	
Hospital, clinic or Medical Center - Inpatient	7,829 (61)	371 (50)	7,458 (61)	
Hospital, Clinic or Medical Center - Outpatient or admitted to Emergency Room	2,420 (19)	268 (36)	2,152 (18)	
Nursing home/long term care	133 (1.0)	0 (0)	133 (1.1)	
Other	315 (2.4)	11 (1.5)	304 (2.5)	
Unknown	71 (0.6)	2 (0.3)	69 (0.6)	
<i>Other causes of death</i>				
Cardiovascular diseases	569 (4.4)	46 (6.3)	523 (4.3)	0.013

Characteristic	Overall N = 12,871¹	Maternal deaths with PE N = 735¹	Maternal deaths without PE N = 12,136¹	p- value
Respiratory diseases	364 (2.8)	10 (1.4)	354 (2.9)	0.013
Cancer	163 (1.3)	4 (0.5)	159 (1.3)	0.071
Bleeding	159 (1.2)	8 (1.1)	151 (1.2)	0.7
Autoimmune disease	40 (0.3)	1 (0.1)	39 (0.3)	0.7
Obesity	127 (1.0)	18 (2.4)	109 (0.9)	0.2
COVID-19	103 (0.8)	3 (0.4)	100 (0.8)	<0.001
<i>Causes of death related to pregnancy, childbirth and the puerperium</i>				
Pregnancy with abortive outcome	512 (4.0)	5 (0.7)	507 (4.2)	
Hypertensive disorders in pregnancy, childbirth and the puerperium	938 (7.3)	7 (1.0)	931 (7.7)	
Obstetric hemorrhage	744 (5.8)	19 (2.6)	725 (6.0)	

Characteristic	Overall N = 12,871¹	Maternal deaths with PE N = 735¹	Maternal deaths without PE N = 12,136¹	p- value
Pregnancy-related infection	281 (2.2)	1 (0.1)	280 (2.3)	
Other obstetric complications*	2,586 (20)	535 (73)	2,051 (17)	
Unanticipated complications of management	34 (0.3)	2 (0.3)	32 (0.3)	
Non-obstetric complications	4,312 (34)	68 (9.3)	4,244 (35)	
Unknown/undetermined	460 (3.6)	2 (0.3)	458 (3.8)	
Contributory cause	3,004 (23)	96 (13)	2,908 (24)	

¹ n (%)

*includes the O88.2 ICD code

Table 2. Characteristics in maternal deaths related to pulmonary embolism in the two periods 2003-2005 and 2018-2020.

Characteristic	2003-2005, N = 116 [†]	2018-2020, N = 193 [†]	p-value
<i>Age group</i>			<i>0.013</i>
≤24	28 (24)	22 (11)	
25-39	78 (67)	151 (78)	
≥40	10 (8.6)	20 (10)	
<i>Race/Hispanic origin</i>			<i>0.3</i>
Black	57 (49)	79 (41)	
Hispanic	18 (16)	25 (13)	
Other	4 (3.4)	8 (4.1)	
White	37 (32)	81 (42)	
<i>Autopsy performed</i>	<i>84 (72)</i>	<i>99 (51)</i>	<i><0.001</i>
<i>Other causes of death</i>			
Cardiovascular diseases	0 (0)	46 (24)	<0.001
Respiratory diseases	0 (0)	10 (5.2)	0.015
Cancer	1 (0.9)	3 (1.6)	>0.9
Bleeding	0 (0)	7 (3.6)	0.048

Characteristic	2003-2005, N	2018-2020, N	p-value
	= 116 ¹	= 193 ¹	
Autoimmune disease	0 (0)	1 (0.5)	>0.9
Obesity	2 (1.7)	14 (7.3)	0.034
<i>Causes of death related to pregnancy, childbirth and the puerperium</i>			
			<0.001
Pregnancy with abortive outcome	2 (1.7)	1 (0.5)	
Hypertensive disorders in pregnancy, childbirth and the puerperium	1 (0.9)	2 (1.0)	
Obstetric hemorrhage	2 (1.7)	3 (1.6)	
Pregnancy-related infection	0 (0)	0 (0)	
Other obstetric complications	101 (87)	85 (44)	
Unanticipated complications of management	2 (1.7)	0 (0)	
Non-obstetric complications	1 (0.9)	59 (31)	
Unknown/undetermined	2 (1.7)	0 (0)	
Contributory cause	5 (4.3)	43 (22)	

¹n (%)

Figure legends

Figure 1. Title: Forest plot of the association of covariates with the maternal deaths related to PE. **Legend:** The figure depicts the association of age, race/Hispanic origin and other causes of death to the maternal deaths related to PE. All risk ratios have been adjusted for age.

PE: pulmonary embolism.

Figure 2. Title: Trends in maternal mortality rates related to pulmonary embolism during the period from 2003 to 2020. **Legend:** The figure depicts the rates in the overall population (A), and in the sensitivity analysis excluding O26.8 (“Other specified pregnancy related conditions”) and O99 (“Other maternal diseases classifiable elsewhere but complicating pregnancy, childbirth and the puerperium”) ICD-10 codes as underlying causes of death, which mitigates the effect of the pregnancy checkbox implementation (B). The points in red represent the observed crude rates at each year, while the solid line is the result of statistical smoothing along with 95% confidence interval (shaded surface).

PE: pulmonary embolism.

Figure 3. Title: Trends in pulmonary embolism related proportionate maternal mortality during the 2003-2020 period. **Legend:** The figure depicts the proportionate mortality due to PE among all maternal deaths in the overall population (A), and in the sensitivity analysis excluding O26.8 (“Other specified pregnancy related conditions”) and O99 (“Other maternal diseases classifiable elsewhere but complicating pregnancy, childbirth and the puerperium”) ICD-10 codes as underlying causes of death, which mitigates the effect of the pregnancy checkbox implementation and shows the possible underestimation of maternal deaths in the absence of the checkbox (B). The points in red represent the observed proportionate mortality at each year, while the line is the result of statistical smoothing along with 95% confidence interval (shaded surface).

Figure 4. Title: Trends in maternal mortality rates related to pulmonary embolism during the period from 2003 to 2020 in different subgroups. **Legend:** According to age groups (A) and race/Hispanic origin (B). Sensitivity analysis excluding O26.8 and O99 as underlying causes of death, according to age groups (C) and race/Hispanic origin (D). Crude rates are depicted without statistical smoothing. PE: pulmonary embolism.