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Trends and Racial/Ethnic, Socioeconomic, and Geographic Disparities in Maternal Mortality from Indirect Obstetric Causes in the United States, 1999-2017

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ABSTRACT

Background: This study examines trends and inequalities in US maternal mortality from indirect obstetric causes (ICD-10 codes: O98-O99) and specific chronic conditions by maternal race/ethnicity, socioeconomic status, nativity/immigrant status, marital status, place and region of residence, and cause of death.

Methods: National vital statistics data from 1999 to 2017 were used to compute maternal mortality rates by sociodemographic factors. Rate ratios and log-linear regression were used to model mortality trends and differentials.

Results: During 1999-2017, maternal mortality from indirect causes showed an upward trend; the annual rates increased by 11.2% for the overall population, 12.9% for non-Hispanic Whites, and 9.4% for non-Hispanic Blacks. The proportion of all maternal deaths due to indirect causes increased from 12.0% in 1999 to 26.9% in 2017. Maternal mortality from CVD increased sharply over time, from 0.40/100,000 live births in 1999 to 1.82 in 2017. During 2013-2017, compared to non-Hispanic Whites, non-Hispanic Blacks had 83% higher, Hispanics 51% lower, and Asian/Pacific Islanders 55% lower mortality from indirect causes. Non-Hispanic White women with <12 years of education had 4.4 times higher mortality than those with a college degree. Unmarried, US-born, and women living in rural areas and deprived areas had 90%, 80%, 60%, and 97% higher maternal mortality risks than married, immigrant, and women in urban areas and affluent areas, respectively. Maternal mortality from infectious diseases, including HIV, was 4.1 times greater and from respiratory diseases 2.9 greater among non-Hispanic Black women compared to non-Hispanic White women.

Conclusions and Global Health Implications: While maternal mortality from direct obstetric causes has declined during the past two decades, maternal deaths due to indirect causes, particularly from pre-existing medical conditions, including CVD and metabolic disorders, have increased. Understanding complex interactions among social determinants, indirect causes, and proximate/direct causes is important to reducing maternal mortality and improving maternal health.

Key words: • Maternal mortality • Socioeconomic status • Deprivation • Race/ethnicity • Rural-urban • Disparities • Cause of death • Trend

1. Introduction

Although the leading causes of maternal deaths in the United States are hemorrhage, pregnancy-related hypertension, embolism, and obstetric infection, maternal deaths due to indirect obstetric causes, including chronic medical conditions such as cardiovascular disease (CVD), diabetes, respiratory disorders, and mental health conditions, have increased substantially in the past two decades.[1,2] Globally, including the United States, 25-30% of all maternal deaths are attributed to these indirect causes.[3-5] Recent trends and socioeconomic and demographic disparities in US maternal mortality from indirect causes have not been well studied, although the proportionate share of various indirect causes to overall mortality and racial/ethnic patterns have been examined using death certificate-based maternal mortality and Pregnancy Mortality Surveillance System data.[6-9] To our knowledge, none of the US studies have analyzed inequalities in maternal mortality from indirect causes by a wide range of social determinants, including maternal education, marital status, nativity/immigrant status, place of residence, geographic region, and area deprivation. Analyzing disparities according to these social determinants is important in identifying sociodemographic groups and disadvantaged communities that may be at increased risk of maternal morbidity and mortality and which can benefit from targeted social and public heath interventions.

To address the aforementioned gaps in research, we analyzed racial/ethnic, socioeconomic, demographic, rural-urban, and regional variations in US maternal mortality from indirect obstetric causes and specific chronic conditions (ICD-10 codes O98-O99) occurring during or within 42 days after the end of pregnancy.[1,2,10]

2. Methods

We used 1999-2017 data from the National Vital Statistics System, the national mortality database.[1,2,10] Maternal deaths in this study, are defined in accordance with the WHO as those related to or aggravated by pregnancy or pregnancy management and which occur during or within 42 days after the end of pregnancy.[1,2,10] This official definition of maternal mortality differs from the definition of pregnancy-related mortality, which includes deaths during or within 1 year of pregnancy.[8,9]

Rates of maternal mortality from indirect causes were computed annually between 1999 and 2017 for all races, Whites and Blacks. Maternal deaths and rates for Asian and Pacific Islanders (APIs), American Indians and Alaska Natives (AIANs) and Hispanics, maternal education, marital status, nativity/immigrant status, and maternal age were derived using the pooled 5-year mortality and natality data for the period 2013-2017 because of the small numbers of maternal deaths annually and to produce statistically robust estimates for these demographic groups. The numbers of births by these sociodemographic characteristics, obtained from the national natality files, served as the denominators for computing maternal mortality rates.[11]

Area-based socioeconomic patterns in maternal mortality were derived by linking the 2008-2012 census-based county-level deprivation index to the race- and county-specific mortality statistics from 2013 to 2017.[12-15] We used previously developed factor-based area deprivation index (ADI), developed by Singh and colleagues, using data from the 2008-2012 American Community Survey.[12-15] The ADI consisted of 21 census-based socioeconomic indicators, which may be viewed as broadly representing educational opportunities, labor force skills, economic, and housing conditions in a given county.[12-15] Selected indicators of education, occupation, wealth, income distribution, unemployment rate, poverty rate, and housing quality were used to construct these indices by factor and principal components analyses.[12-15] The factor loadings (correlations of indicators with the ADI) for the 2008-2012 county index varied from 0.91 for 150% of the poverty rate to 0.23 for home ownership rate.[12,15] To compute maternal mortality rates by deprivation level, we used the weighted population quintile distribution of the deprivation index that classified all 3,141 US counties into 5 groups of approximately equal population size.[12-15] The groups thus created ranged from being the most-deprived (first quintile) to the least-disadvantaged (fifth quintile) population groups.[12-15] To simplify analysis and for statistical robustness, we

combined 2nd, 3rd, and 4th quintiles as the middle deprivation category. Each of the 3,141 counties in the mortality database was assigned one of these 3 deprivation quintiles.

Log-linear regression models were used to estimate annual rates of change in maternal mortality from indirect causes.[13-15] Specifically, the logarithm of mortality rates were modeled as a linear function of time (calendar year), which yielded annual exponential rates of change in mortality rates.[13-15] Disparities in mortality by social factors and deprivation level were described by rate ratios (relative risks=RR) and rate differences (absolute inequalities), which were tested for statistical significance at the 0.05 level.

3. Results

3.1. Trends in Maternal Mortality from Indirect Causes

Maternal mortality from indirect causes showed an upward trend during 1999-2017, with the rate increasing by 11.2% (95% CI=9.0%-13.5%) annually for the overall population, 12.9% (95% CI=10.5%-15.3%) for non-Hispanic Whites, and 9.4% (95% CI=7.2%-11.6%) for non-Hispanic Blacks (Figure 1). During 1999-2017, non-Hispanic Black women had 2-3 times higher mortality from indirect causes than non-Hispanic White women. The proportion of all maternal deaths due to indirect causes rose from 12.0% in 1999 to 26.9% in 2017 (Figure 2). Of 12,135 maternal deaths that occurred during 1999-2017, 3184 deaths were from indirect causes, including 173 deaths from maternal infectious and parasitic diseases, 3011 deaths from all chronic conditions, 993 deaths from CVD, 178 deaths from mental disorders, 191 deaths from respiratory diseases, 48 deaths from digestive diseases, 26 deaths from endocrine/metabolic disorders, and 30 deaths from HIV (Table 1). Maternal mortality from CVD increased sharply over time, from 0.40 per 100,000 live births deaths in 1999 to 1.82 in 2017 (Figure 1). During 1999-2017, the average annual rate of increase in maternal mortality was 8.8% (95% CI=7.0%-10.6%) for CVD, 11.3% (95% CI=8.9%-13.7%) for all chronic conditions combined, and 10.0% (95% CI=7.2%-13.0%) for infectious and parasitic diseases

(Figures 1 and 2). Trends from other causes are not shown because of small numbers of deaths.

3.2. Inequalities in Maternal Mortality from Indirect Causes by Sociodemographic Factors

During 2013-2017, mortality from indirect causes increased consistently with increasing maternal age, with relative risk of mortality being 17.9 times (76.76/4.28) higher for women aged ≥40 years than for those aged <20 (Table 2). Non-Hispanic Blacks had 83% higher (RR=1.83; 95% CI=1.60-2.06) and Hispanics 51% lower (RR=0.49; 95% CI=0.41-0.58) mortality from indirect causes than non-Hispanic Whites. Compared to APIs, non-Hispanic Whites, non-Hispanic Blacks, and AIANs had 2.2 times higher (RR=2.22; 95% CI=1.54-2.89), 4.1 times higher (RR=4.06; 95% CI=2.79-5.33), and 3.1 times higher (RR=3.09; 95% CI=1.48-4.70) mortality from indirect causes, respectively.

Higher educational attainment was associated with lower maternal mortality from indirect causes. Non-Hispanic white women with <12 years of education had 4.4 times higher mortality than their counterparts with a college degree. Unmarried, US-born, and women in rural areas had 90%, 80%, and 60% (RR=1.90, 1.80, 1.60) higher risks of maternal mortality from indirect causes than married, immigrant, and women in urban areas, respectively. Women in the southern region had 3.3 times higher mortality risk from indirect causes than those in the western region of the US.

Maternal mortality related to infectious diseases, including HIV, was 4 times greater among non-Hispanic Black women than non-Hispanic White women (Table 2; data not shown). Compared to non-Hispanic White women, maternal mortality from all chronic conditions combined and from CVD was approximately two times higher among black women but 50% lower among Hispanics. The risk of maternal death due to poor mental health was similar in both non-Hispanic White and Black women but significantly higher compared with that for Hispanic women. Maternal mortality due to respiratory conditions was 2.9 times greater among non-Hispanic Black women than non-Hispanic White women.
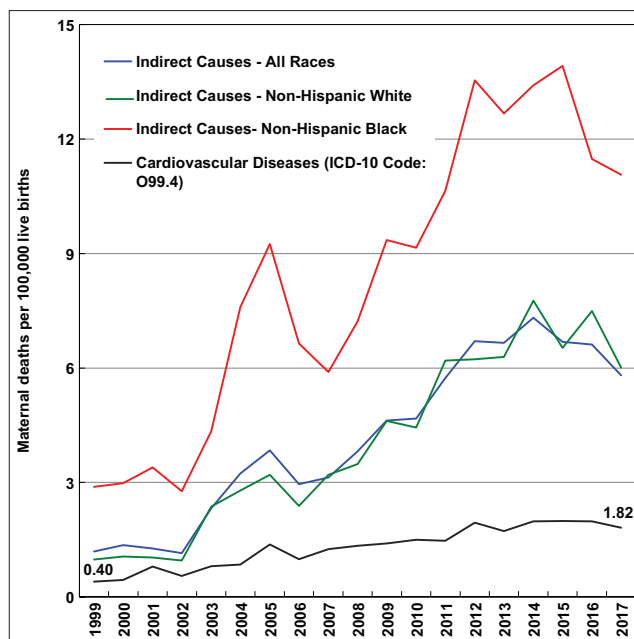
Figure 1: Trends in maternal mortality from indirect obstetric causes (ICD-10 Codes: O98-O99), United States, 1999-2017
Source: Data derived from the National Vital Statistics System.

Table 1: Maternal deaths and mortality rates per 100,000 live births due to specific indirect obstetric causes, (ICD-10 codes: O98-O99), United States, 1999-2017 (number of live births =76,972,334)

Cause of death (ICD-10 codes)	Maternal Deaths	Maternal Mortality Rate
All indirect causes (O98-O99)	3,184	4.14
Maternal infectious and parasitic diseases (O98)	173	0.22
Tuberculosis (O98.0)	9	N/A
Syphilis, Gonorrhea, and other sexually transmitted infections (O98.1-O98.3)	2	N/A
Viral hepatitis (O98.4)	5	N/A
Other viral diseases (O98.5)	12	0.02
Protozoal diseases (O98.6)	0	N/A
HIV (O98.7)	30	0.04
Other maternal infectious and parasitic diseases (O98.8)	115	0.15
Unspecified maternal infectious and parasitic diseases (O98.9)	0	N/A
Chronic diseases (O99)	3,011	3.91
Anemia (O99.0)	22	0.03
Blood & immune disorders (O99.1)	24	0.03
Endocrine and metabolic disorders (O99.2)	26	0.03
Mental disorders and diseases of the nervous system (O99.3)	178	0.23
Cardiovascular diseases (O99.4)	993	1.29
Respiratory diseases (O99.5)	191	0.25
Digestive system diseases (O99.6)	48	0.06
Skin and subcutaneous disorders (O99.7)	5	N/A
Other specified diseases and conditions (O99.8)	1,524	1.98

Source: Derived from the National Mortality and Natality Detail Files, 1999-2017
Maternal mortality rates based on fewer than 10 deaths are not shown because of high variability associated with those rates. N/A = not available
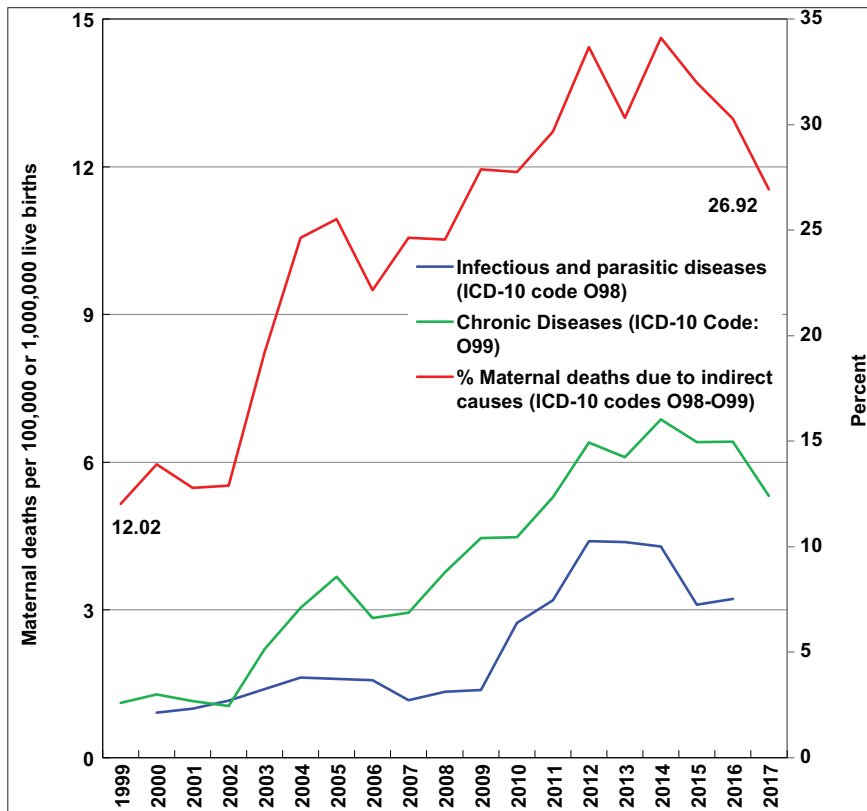
Figure 2: Trends in maternal mortality from infections (ICD-10 code O98) and chronic diseases (ICD-10 code O99), and proportion of all maternal deaths due to indirect obstetric causes (ICD-10 codes: O98-O99), United States, 1999-2017
Source: Data derived from the National Vital Statistics System
Rates of maternal mortality from infections are three-year moving average rates and are per 1,000,000 (million) live births. Rates of maternal mortality from chronic diseases are annual rates and are per 100,000 live births.

3.5. Inequalities in Maternal Mortality from Indirect Causes by Area Deprivation Index

During 2013-2017, women in the middle- and most-deprived area groups had 23% (RR=1.23; 95% CI=1.03-1.43) and 97% (RR=1.97; 95% CI=1.63-2.32) higher risks of maternal mortality from indirect causes than women in the most-affluent area group (Table 3). An approximately two-fold increased risk of maternal mortality from indirect causes was found among Non-Hispanic White and Black women living in the most-deprived areas (Table 3). When disparities across race/ethnicity and deprivation level were considered, maternal mortality rates from indirect causes varied greatly from 3.23 and 5.65 for Hispanics and non-Hispanic

Whites in the most affluent area-group to 14.45 per 100,000 for non-Hispanic Blacks in the most deprived area-group (a 4.5-fold ethnic inequality). Patterns in maternal mortality by deprivation level were similar for all chronic conditions combined and for CVD, with women in the most deprived area-group experiencing about twice the mortality risk of those in the most affluent area-group (Table 3).

4. Discussion

Using national vital statistics mortality data from 1999 to 2017, we found a rising trend in US maternal mortality from indirect causes, including CVD and all chronic conditions combined. The proportion of all maternal deaths due to indirect causes increased from 12.0% in 1999 to 26.9% in 2017, with maternal

Table 2: Maternal mortality rates per 100,000 live births due to indirect obstetric causes (ICD-10 codes: O98-O99) by socio-demographic factors, United States, 2013-2017

Demographic variable	All races maternal deaths	All races number of live births	All races maternal mortality rate	NH White maternal deaths	NH White number of live Births	NH White maternal mortality rate	NH Black maternal deaths	NH Black number of live births	NH Black maternal mortality rate	Hispanic maternal deaths	Hispanic number of live births	Hispanic maternal mortality rate
Maternal age												
<20	50	1,168,621	4.28	22	456,900	4.82	13	260,307	4.99	11	408,367	2.69
20-24	146	4,198,579	3.48	76	1,978,431	3.84	41	864,004	4.75	25	1,160,512	2.15
25-29	206	5,691,179	3.62	107	3,158,790	3.39	66	826,627	7.98	21	1,262,475	1.66
30-34	229	5,415,637	4.23	118	3,198,425	3.69	65	599,400	10.84	29	1,028,383	2.82
35-39	211	2,622,901	8.04	119	1,441,324	8.26	55	303,462	18.12	30	554,553	5.41
40+	463	603,212	76.76	277	299,454	92.50	127	79,115	160.53	38	142,067	26.75
All ages	1,305	19,700,129	6.62	719	10,533,324	6.83	367	2,932,915	12.51	154	4,556,357	3.38
Maternal education[1]												
<12 years	175	2,183,696	8.01	79	604,099	13.08	41	322,009	12.73	51	1,134,894	4.49
12 years	420	4,310,035	9.74	230	1,993,110	11.54	126	857,512	14.69	43	1,233,191	3.49
13-15 years	279	4,369,295	6.39	146	3,079,823	4.74	89	948,012	9.39	31	1,068,122	2.90
16+ years	195	4,802,830	4.06	121	4,101,778	2.95	46	461,563	9.97	11	534,346	2.06
RR (low/high education)	1.97 (1.57-2.38)			4.43 (3.18-5.69)			1.28 (0.74-1.81)			2.18 (0.76-3.60)		
Marital status[2]												
Married	493	11,496,272	4.29	305	7,368,124	4.14	85	858,295	9.90	72	2,045,025	3.52
Unmarried	628	7,716,306	8.14	294	3,027,397	9.71	230	2,043,382	11.26	75	2,286,040	3.28
RR (unmarried/married)	1.90 (1.67-2.12)			2.35 (1.97-2.72)			1.14 (0.85-1.42)			0.93 (0.63-1.23)		
Nativity/immigrant status[2]												
US-born	970	15,240,735	6.36	575	9,930,504	5.79	300	2,499,661	12.00	66	2,328,713	2.83
Foreign-born	157	4,443,057	3.53	26	708,301	3.67	19	452,563	4.20	81	2,222,324	3.64
RR (foreign-born/US-born)	0.56 (0.46-0.65)			0.63 (0.38-0.88)			0.35 (0.19-0.51)			1.29 (0.87-1.70)		
Place of residence												
Metro (urban)	1,043	17026691	6.13	531	8434231	6.30	329	2758825	11.93	135	4744212	2.85
Non-Metro (rural)	262	2673438	9.80	188	1879286	10.00	38	287276	13.23	19	364094	5.22
RR (non-metro/metro)	1.60 (1.38-1.82)			1.59 (1.32-1.85)			1.11 (0.74-1.48)			1.83 (0.95-2.71)		
Geographic region												
Northeast	194	3,135,978	6.19	90	1,784,944	5.04	58	423,627	13.69	30	610809	4.91
Midwest	287	4,142,090	6.93	197	2,897,115	6.80	63	586,531	10.74	15	425090	3.53
South	691	7,635,103	9.05	348	3,807,352	9.14	239	1,680,107	14.23	83	1756884	4.72

(Contd...)

Table 2: (Continued)

Demographic variable	All races maternal deaths	All races number of live births	All races maternal mortality rate	NH White maternal deaths	NH White number of live Births	NH White maternal mortality rate	NH Black maternal deaths	NH Black number of live births	NH Black maternal mortality rate	Hispanic maternal deaths	Hispanic number of live births	Hispanic maternal mortality rate
West	133	4,786,958	2.78	84	2,043,913	4.11	<10	242,650	2.88	26	1763574	1.47
RR (South/West)	3.26 (2.65-3.86)			2.22 (1.69-2.75)			4.93 (1.23-8.65)			3.20 (1.80-4.63)		
Cause of death												
Infections (O98)	78	19,700,129	0.40	29	10,533,324	0.28	34	2,932,915	1.16	<10	4,556,357	0.20
HIV	24	19,700,129	0.12	N/A			19	2,932,915	0.65	N/A		
Chronic diseases (O99)	1,227	19,700,129	6.23	690	10,533,324	6.55	333	2,932,915	11.35	145	4,556,357	3.18
Mental disorders (O99.3)	86	19,700,129	0.44	60	10,533,324	0.57	17	2,932,915	0.58	<10	4,556,357	0.18
CVD (O99.4)	374	19,700,129	1.90	189	10,533,324	1.79	120	2,932,915	4.09	41	4,556,357	0.90
Respiratory diseases (O99.5)	62	19,700,129	0.31	28	10,533,324	0.27	23	2,932,915	0.78	10	4,556,357	0.22

Source: Derived from the National Mortality and Natality Detail Files, 2013-2017. NH = Non-Hispanic; RR = relative risk or rate ratio. SE (Mortality Rate) = Rate/SQRT(Deaths). The 5-year pooled mortality statistics for APIs: 44 deaths and a rate of 3.08 (95% CI=2.17-6.75) per 100,000 live births; for AIANs: 21 deaths and a rate of 9.52 (95% CI=5.45-13.59). Foreign-born or immigrants are defined as those born outside the 50 states and the District of Columbia in both natality and mortality files. Data were derived for mothers aged 20-49 years. †Data were derived for mothers aged 15-49 years. For non-Hispanic Blacks in the West region, the maternal mortality rate is based on <10 deaths and should be interpreted with caution because of high variability associated with the rate. N/A = not available because deaths <10

mortality from CVD increasing almost 5-fold during this time period. Our study shows marked disparities in maternal mortality from indirect causes by a wide array of social determinants, including maternal education, marital status, immigrant status, place of residence, geographic region, and area deprivation, which, although shown previously for overall maternal mortality and pregnancy-related mortality[8,9,16], had not been documented for mortality from indirect causes to the best of our knowledge. Analysis of a broad range of disparities is important in showing the potential for reductions in US maternal mortality that can be achieved by implementing effective policies and interventions among high-risk groups and communities.

Efforts to reduce maternal mortality in the United States should be focused on indirect obstetric causes, in addition to addressing direct complications of pregnancy and childbirth.[3,5,8,9] While maternal mortality from direct obstetric causes such as hemorrhage, pregnancy-related hypertension, and embolism has declined during the past two decades, maternal deaths due to indirect causes, particularly from pre-existing medical conditions, including CVD and metabolic disorders have risen.[1-4,8,9] Given the increasing relative importance of indirect maternal causes of death, increased attention should be given to the healthcare needs of pregnant women with pre-existing conditions and high-risk pregnancies.[5,17] Tackling the rising prevalence of obesity, diabetes, chronic hypertension, kidney diseases, and cardiovascular conditions among women of reproductive age should become a priority.[3,5]

Trends and social inequalities in mortality from indirect causes reported here are generally consistent with those observed for maternal mortality overall (direct + indirect causes), pregnancy-related mortality, various risk factors, chronic medical conditions, and maternal complications including pre-pregnancy obesity, maternal diabetes, chronic hypertension, poor mental health, and cardiovascular conditions among women of reproductive age.[8,9,16,18,19] For example, consistent with patterns in maternal mortality from indirect causes in our study, a recent study of the 2012-2014 US birth cohorts found that the risk of pre-pregnancy obesity was significantly higher among non-Hispanic Blacks, AIANs, non-Hispanic Whites, unmarried, US-born, women aged ≥35, women with

Table 3: Maternal deaths and mortality rates per 100,000 live births due to indirect obstetric causes (ICD-10 codes: O98-O99) by Area Deprivation Index, United States, 2013-2017 (number of live births =19,699,940)

Area deprivation Index	Maternal Deaths	Number of Live Births	Maternal Mortality Rate	Maternal Mortality RR	95% CI
All indirect causes (ICD codes: O98-O99)					
All races					
1st quintile (low SES)	389	3,982,978	9.77	1.97	1.63-2.32
2nd-4th quintile (middle SES)	730	11,959,599	6.10	1.23	1.03-1.43
3rd quintile (high SES)	186	3,757,363	4.95	1.00	Reference
Non-Hispanic White					
1st quintile (low SES)	215	1,966,293	10.93	1.93	1.50-2.37
2nd-4th quintile (middle SES)	385	6,572,306	5.86	1.04	0.82-1.25
3rd quintile (high SES)	119	2,105,188	5.65	1.00	Reference
Non-Hispanic Black					
1st quintile (low SES)	115	796,033	14.45	1.82	1.10-2.54
2nd-4th quintile (middle SES)	221	1,771,290	12.48	1.57	0.98-2.16
3rd quintile (high SES)	31	389,812	7.95	1.00	Reference
Hispanic					
1st quintile (low SES)	40	1,024,822	3.90	1.21	0.60-1.82
2nd-4th quintile (middle SES)	90	2,789,575	3.23	1.00	0.55-1.45
3rd quintile (high SES)	24	741,950	3.23	1.00	Reference
All chronic diseases (ICD code: O99)					
All races					
1st quintile (low SES)	362	3,982,978	9.09	1.91	1.57-2.25
2nd-4th quintile (middle SES)	686	11,959,599	5.74	1.21	1.01-1.40
3rd quintile (high SES)	179	3,757,363	4.76	1.00	Reference
Non-Hispanic White					
1st quintile (low SES)	202	1,966,293	10.27	1.83	1.41-2.25
2nd-4th quintile (middle SES)	370	6,572,306	5.63	1.00	0.80-1.21
3rd quintile (high SES)	118	2,105,188	5.61	1.00	Reference
Non-Hispanic Black					
1st quintile (low SES)	106	796,033	13.32	2.00	1.14-2.85
2nd-4th quintile (middle SES)	201	1,771,290	11.35	1.70	1.01-2.40
3rd quintile (high SES)	26	389,812	6.67	1.00	Reference
Hispanic					
1st quintile (low SES)	38	1,024,822	3.71	1.15	0.56-1.74
2nd-4th quintile (middle SES)	83	2,789,575	2.98	0.92	0.50-1.34
3rd quintile (high SES)	24	741,950	3.23	1.00	Reference

(Contd...)

Table 3: *(Continued)*

Area deprivation Index	Maternal Deaths	Number of Live Births	Maternal Mortality Rate	Maternal Mortality RR	95% CI
Cardiovascular diseases (ICD code: O99.4)					
All races					
I[st] quintile (low SES)	108	3,982,978	2.71	2.17	1.57-2.38
2nd-4th quintile (middle SES)	219	11,959,599	1.83	1.46	1.57-2.38
3rd quintile (high SES)	47	3,757,363	1.25	1.00	Reference
Non-Hispanic White					
I[st] quintile (low SES)	51	1,966,293	2.59	1.76	0.98-2.55
2nd-4th quintile (middle SES)	107	6,572,306	1.63	1.11	0.67-1.55
3rd quintile (high SES)	31	2,105,188	1.47	1.00	Reference
Non-Hispanic Black					
I[st] quintile (low SES)	38	796,033	4.77	2.06	0.56-3.57
2nd-4th quintile (middle SES)	73	1,771,290	4.12	1.78	0.55-3.02
3rd quintile (high SES)	<10	389,812	2.31	1.00	Reference

Source: Derived from the National Mortality and Natality Detail Files and American Community Survey, 2013-2017.

RR = relative risk or rate ratio. SE (Mortality Rate) ≈ Rate/SQRT(Deaths). Cardiovascular disease mortality rates for Hispanics are not shown because of small numbers of deaths. Maternal mortality rates based on fewer than 10 deaths are not shown because of high variability associated with those rates

less education, and rural residents.[20] Mothers with less than a high school or with a high school diploma had more than twice the risk of pre-pregnancy obesity than those with a college degree, and US-born women had 59% higher risk than immigrant women[20] – estimates similar to those reported in our study on maternal mortality from indirect causes.

Another recent US study showed marked disparities in maternal hypertension (consisting of both chronic hypertension and pregnancy-related hypertension) by various social determinants.[19] AIANs, non-Hispanic Blacks, and Pacific Islanders had higher risks of maternal hypertension and chronic hypertension, whereas Asians, Hispanics, and non-Hispanic Whites had lower risks of maternal hypertension, including chronic hypertension.[19] Increasing maternal age, lower education, US-born status, rural residence, pre-pregnancy obesity, excess weight gain during pregnancy, and gestational diabetes were all associated with increased risks of maternal hypertension.[19] In addition, smoking before and during pregnancy was associated with significantly increased risk of chronic hypertension.[19]

Data on women of reproductive age (18-49 years) from the 2010-2014 US National Health Interview Survey indicate markedly higher prevalence of CVD, hypertension, diabetes, kidney disease, asthma, and serious psychological distress among non-Hispanic Black and AIAN women, women at older ages, those at lower education and income levels, unmarried (divorced/separated/never married) women, US-born women, current smokers, and women with obesity.[18,19] Ethnic-minority and socially-disadvantaged groups in the US differ greatly from the majority, affluent groups in their social, physical, and living environments that might influence pre-existing chronic and medical conditions and related risks such as pre-pregnancy obesity, smoking, gestational diabetes, pregnancy-related hypertension, and weight gain during pregnancy.[19] They have limited access to neighborhood amenities such as sidewalks, parks/playgrounds, green spaces, public transportation, and heathy, affordable foods that promote physical activity, healthy lifestyle, and healthy living.[19,21] Many of the risk factors identified above are modifiable, and maternal deaths from most of the indirect causes are largely preventable. Several community-

based federal programs have been successful in reducing rates of obesity, physical inactivity, smoking, and chronic hypertension and promoting healthy eating and weight management.[19-21]

4.1. Limitations

This study has limitations. Underreporting of mortality statistics for Hispanics, APIs, and AIANs on the death certificate may lead to an underestimation of maternal mortality rates for these racial/ethnic groups.[1,10] Inconsistencies in the reporting of race/ethnicity, educational attainment, marital status, nativity status, and maternal age in numerator (deaths) and denominator (births) databases may lead to misestimation of maternal mortality rates.[1,10,11] Because of the small numbers of deaths, our analysis does not show the full extent of racial/ethnic disparities in maternal mortality from indirect causes as overall maternal mortality rates among API and Hispanic subgroups have been shown to vary greatly, with Filipinos and Puerto Ricans, for example, at substantially higher risks of maternal mortality than Chinese, Asian Indians, and Central/South Americans.[16]

Another limitation refers to the fact that data used in this study come from two different unlinked data sources: national mortality and national natality databases. The natality database was only used to derive the total number of births overall and by social determinants, which were used as denominators to compute maternal mortality rates. This differs from the CDC's Pregnancy Mortality Surveillance System that links pregnancy-related deaths up to one year to corresponding cohorts of live births and fetal deaths, which allows one to analyze severe maternal morbidity (SMM) outcomes such as hypertensive disorders in pregnancy, eclampsia, obstetric infections, hemorrhage, embolism, uterine rupture, and other pregnancy complications and their impacts on maternal mortality.[8,9] Because of the unlinked nature of our data sources, we were unable to carry out detailed individual-level analyses of maternal mortality that are typical of SMM studies. Lastly, the differential adoption of a pregnancy checkbox item on the death certificate by many states may have been a factor influencing

the recent trend (or apparent increase or misclassification) in maternal deaths and mortality from indirect causes.[1,9,10,16,22,23]

5. Conclusions and Global Health Implications

While US maternal mortality from direct obstetric causes has declined during the past two decades, maternal deaths due to indirect causes, particularly from pre-existing medical conditions, including CVD, have increased.[1,9,10,16] As is the case with overall maternal mortality[16], socially and economically-disadvantaged demographic groups and communities experience 2-to-6 times higher risk of maternal mortality from indirect causes. There is a growing understanding that the contribution of indirect causes is misclassified and underestimated.[5,17] Pre-pregnancy obesity, for example, increases the risk of both direct and indirect causes of maternal mortality, including chronic and gestational diabetes, pregnancy-related hypertension, pre-eclampsia and eclampsia, spontaneous abortion, hemorrhage, and uterine rupture.[17,19] Yet, obesity is only considered an indirect or contributing condition rather than an underlying cause of maternal death.[17] Monitoring social inequalities is important in that they represent the impact of underlying social determinants on both indirect and direct causes of maternal mortality.[4,24] Understanding the complex interactions among social determinants, indirect causes, and more proximal direct causes of maternal deaths is important to reducing maternal mortality and improving maternal health.[5,17]

Compliance with Ethical Standards

Key Messages

► During 1999-2017, maternal mortality rates due to indirect obstetric causes and pre-existing chronic conditions increased annually by 11.2% for the overall population, 12.9% for non-Hispanic Whites, and 9.4% for non-Hispanic Blacks.

► The proportion of all maternal deaths due to indirect causes increased from 12.0% in 1999 to 26.9% in 2017. Maternal mortality from CVD increased 4.6-fold during 1999-2017.

► Social determinants were strongly linked to maternal mortality from indirect causes. Non-Hispanic White women without a high school diploma had 4.4 times higher mortality than their counterparts with a college degree. Unmarried, US-born, and women living in rural and deprived areas had 1.6-2.0 times higher risk of maternal mortality than married, immigrant, and women in urban and affluent areas, respectively.

► Maternal mortality from infectious diseases, including HIV, was 4.1 times greater, from CVD 2.3 times greater, and from respiratory diseases 2.9 greater among non-Hispanic Black women compared to non-Hispanic White women.

► Understanding complex interactions among social determinants, indirect causes (pre-existing medical conditions (e.g., CVD, diabetes, respiratory disorders, and mental disease), and proximate direct causes (e.g., hemorrhage, pregnancy-related hypertension, and embolism) is important to reducing maternal mortality and improving maternal health.

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