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Supplementary appendix

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Online Data Supplement

Table S1. Definition of PE based on ICD-10 codes.

	ICD-10 Code	Description	WHO Mortality Database (2000-2015)	US n/N (%)	Canada n/N (%)	Multiple Cause of Death database (2000-2018)	US n/N (%)
Pulmonary embolism	I26.x	Pulmonary embolism	Underlying cause of death*	143,474/200,610 (71.5%)	11,460/15,798 (72.3%)	Underlying cause of death or contributing condition	567,322/587,875 (96.5%)
	O88.2	Obstetric thromboembolism (code O88 if sub-codes not recorded)	Underlying cause of death	344/200,610 (0.2%)	30/15,798 (0.2%)	Underlying cause of death or contributing condition	679/587,875 (0.1%)
	I82.2, I82.4, I82.6, I82.8, I82.9	Acute embolism and thrombosis of specified or unspecified veins	Underlying cause of death	3,413/200,610 (1.7%)	310/15,798 (2.0%)	Underlying cause of death or contributing condition	23,250/587,875 (4.0%)
Limb vein thrombosis	I80.x	Phlebitis and thrombophlebitis	Underlying cause of death	53,203/200,610 (26.5%)	3,987/15,798 (25.2%)	Underlying cause of death or contributing condition listed along with a pulmonary embolism code	96,886/587,875 (16.5%)
	O870	Superficial thrombophlebitis in the puerperium	Underlying cause of death	1/200,610 (<0.1%)	0	Underlying cause of death or contributing condition listed along with a pulmonary embolism code	0

	O22.2	Superficial thrombophlebitis in pregnancy	Underlying cause of death	3/200,610 (<0.1%)	0	Underlying cause of death or contributing listed along with a pulmonary embolism code	2/587,875 (<0.1%)
	O22.3	Deep vein thrombosis in pregnancy	Underlying cause of death	97/200,610 (<0.1%)	5/15,798 (<0.1%)	Underlying cause of death or contributing condition listed along with a pulmonary embolism code	100/587,875 (<0.1%)
	O87.1	Deep vein thrombosis in the puerperium	Underlying cause of death	4/200,610 (<0.1%)	2/15,798 (<0.1%)	Underlying cause of death or contributing condition listed along with a pulmonary embolism code	4/587,875 (<0.1%)
	O22.9	Venous complication in pregnancy, unspecified	Underlying cause of death	48/200,610 (<0.1%)	3/15,798 (<0.1%)	Underlying cause of death or contributing condition listed along with a pulmonary embolism code	34/587,875 (<0.1)
	O87.9	Venous complication in the puerperium, unspecified	Underlying cause of death	23/200,610 (<0.1%)	1/15,798 (<0.1%)	Underlying cause of death or contributing condition listed along with a pulmonary embolism code	25/587,875 (<0.1)

* Underlying cause of death is defined as "the disease or injury which initiated the train of morbid events leading directly to death, or the circumstances of the accident or violence which produced the fatal injury" in accordance with the rules of the International Classification of Diseases. Source:

https://apps.who.int/healthinfo/statistics/mortality/causeofdeath_query/help/description.html

Table S2. Definition of other conditions in the Multiple Cause of Death Database based on ICD-10 codes or chapters.

Condition	ICD-10 Codes	Definition
Cancer	C.x	Malignant neoplasms
	D00.x to D09.x	Non-benign in situ neoplasms
	D37.x to D45.x	Neoplasms of uncertain behavior, polycythemia vera
	Z85.x	Personal history of malignant neoplasm*
Cardiovascular diseases	I10.x to I15.x	Essential (primary) hypertension; Hypertensive heart disease; Hypertensive chronic kidney disease; Hypertensive heart and chronic kidney disease; Secondary hypertension
	I20.x to I25.x	Ischemic heart diseases
	I27.x	Other pulmonary heart diseases
	I31.x to I33.x	Other diseases of pericardium; Pericarditis in diseases classified elsewhere; Acute and subacute endocarditis
	I4.x	Acute myocarditis; Myocarditis in diseases classified elsewhere; Cardiomyopathy; Cardiomyopathy in diseases classified elsewhere; Atrioventricular and left bundle-branch block; Other conduction disorders; Cardiac arrest; Paroxysmal tachycardia; Atrial fibrillation and flutter; Other cardiac arrhythmias
	I50.x	Heart failure
	I63.x to I67.x	Cerebral infarction; Occlusion and stenosis of precerebral arteries, not resulting in cerebral infarction; Occlusion and stenosis of cerebral arteries, not resulting in cerebral infarction; Other cerebrovascular diseases
	I7.x	Diseases of arteries, arterioles and capillaries
External causes	V.x, W.x, X.x, Y.x	Accidents, falls, drowning, self-harm, assaults, exposure to fire or flames, medical devices with adverse events
Hemorrhage	R04.x	Hemorrhage from respiratory passages
	R58.x	Hemorrhage, not elsewhere classified
	D62.x	Acute posthemorrhagic anemia

	D683	Hemorrhagic disorder due to circulating anticoagulants
	D699	Hemorrhagic condition, unspecified
	K625	Hemorrhage of anus and rectum
	K661	Hemoperitoneum
	K25.x to K28.x	Gastrointestinal ulcer with hemorrhage or hemorrhagic gastritis
	K920.x	Hematemesis
	K921.x	Melena
	K922.x	Gastrointestinal hemorrhage, unspecified
	H113.x	Conjunctival hemorrhage
	H210	Hyphema
	H313	Choroidal hemorrhage and rupture
	H356.x	Retinal hemorrhage
	H431.x	Vitreous hemorrhage
	H450.x	Vitreous hemorrhage in diseases classified elsewhere
	I60.x to I62.x	Subarachnoid or intracerebral bleeding
	I312	Hemopericardium, not elsewhere classified
	J942	Hemothorax
	M250	Hemarthrosis
	N02.x	Hematuria
	N939	Abnormal uterine and vaginal bleeding, unspecified
	N950	Postmenopausal bleeding
	R31.x	Unspecified hematuria
	S06.x	Epidural hemorrhage; Traumatic subdural or subarachnoid hemorrhage
	S271	Traumatic hemothorax
	T792	Traumatic secondary and recurrent hemorrhage
	A.x, B.x	Certain infectious and parasitic diseases

Infectious diseases	R65.x	Symptoms and signs specifically associated with systemic inflammation and infection
Respiratory diseases	J.x	Diseases of the respiratory system

*No PE-related deaths were reported in association with Z-codes.

Table S3. Total population by country, year, and sex.

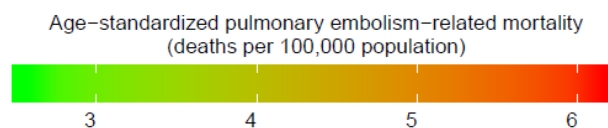
		2000	2001	2002	2003	2004	2005	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
United States	Men	138,761,588	140,249,955	141,624,546	142,928,382	144,227,349	145,568,081	146,962,229	148,389,984	149,828,894	151,244,420	152,610,910	153,923,757	155,189,795	156,408,505	157,581,861	158,712,121	159,798,231	160,840,943
United States	Women	142,949,326	144,358,037	145,654,766	146,887,185	148,127,314	149,425,428	150,796,748	152,218,441	153,657,128	155,063,145	156,400,559	157,660,294	158,854,090	159,992,034	161,091,561	162,166,191	163,217,761	164,243,815
United States	Entire population	281,710,914	284,607,992	287,279,312	289,815,567	292,354,663	294,993,509	297,758,977	300,608,425	303,486,022	306,307,565	309,011,469	311,584,051	314,043,885	316,400,539	318,673,422	320,878,312	323,015,992	325,084,758
Canada	Men	15,152,318	15,299,307	15,449,335	15,605,073	15,769,779	15,945,444	16,133,439	16,332,207	16,537,195	16,741,973	16,941,808	17,134,966	17,322,343	17,505,031	17,685,123	17,864,138	18,042,095	18,218,176
Canada	Women	15,436,061	15,580,765	15,728,925	15,882,973	16,045,711	16,218,869	16,403,555	16,598,588	16,800,443	17,004,120	17,205,758	17,404,190	17,599,688	17,791,504	17,979,215	18,162,530	18,340,847	18,513,915
Canada	Entire population	30,588,379	30,880,072	31,178,260	31,488,046	31,815,490	32,164,313	32,536,994	32,930,795	33,337,638	33,746,093	34,147,566	34,539,156	34,922,031	35,296,535	35,664,338	36,026,668	36,382,942	36,732,091

Population counts used for all calculations of mortality rates by sex and for the entire population. Source: United Nations, Department of Economic and Social Affairs, Population Division. World Population Prospects. <https://population.un.org/wpp/Download>; WPP2019_PopulationByAgeSex_MeWdium.csv (2019).

Accessed 2020-08-12.

Table S4. Trends in PE-related age-standardized mortality rates in the US and Canada from 2000 to 2017: data from the WHO Mortality Database.

		2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
United States	Men	5.9 (5.8-6.1)	5.9 (5.7-6.1)	5.6 (5.5-5.8)	5.8 (5.6-6.0)	5.3 (5.2-5.5)	5.4 (5.3-5.6)	4.3 (4.2-4.5)	4.4 (4.3-4.5)	4.3 (4.2-4.4)	4.1 (4.0-4.3)	4.4 (4.2-4.5)	4.4 (4.3-4.5)	4.4 (4.3-4.5)	4.4 (4.3-4.5)	4.5 (4.4-4.6)	4.7 (4.5-4.8)	4.5 (4.4-4.6)	4.5 (4.4-4.7)
	Women	6.0 (5.9-6.2)	6.1 (6.0-6.3)	6.2 (6.0-6.3)	5.9 (5.8-6.0)	5.5 (5.4-5.7)	5.5 (5.3-5.6)	4.4 (4.3-4.5)	4.5 (4.4-4.6)	4.3 (4.2-4.4)	4.2 (4.1-4.4)	4.2 (4.1-4.3)	4.2 (4.1-4.3)	4.2 (4.1-4.3)	4.2 (4.1-4.3)	4.2 (4.1-4.3)	4.3 (4.1-4.4)	4.1 (4.0-4.3)	4.1 (4.0-4.2)
	Entire population	6.0 (5.9-6.1)	6.1 (5.9-6.2)	6.0 (5.8-6.1)	5.9 (5.8-6.0)	5.5 (5.4-5.6)	5.5 (5.4-5.6)	4.4 (4.3-4.5)	4.5 (4.4-4.6)	4.3 (4.2-4.4)	4.2 (4.1-4.3)	4.3 (4.2-4.4)	4.3 (4.3-4.4)	4.3 (4.2-4.4)	4.3 (4.2-4.4)	4.4 (4.3-4.5)	4.4 (4.4-4.5)	4.3 (4.2-4.4)	4.3 (4.3-4.4)
Canada	Men	4.8 (4.3-5.3)	4.2 (3.8-4.7)	4.2 (3.8-4.7)	4.3 (3.9-4.8)	4.0 (3.6-4.5)	4.1 (3.6-4.5)	2.9 (2.6-3.3)	3.0 (2.6-3.3)	2.9 (2.6-3.3)	3.5 (3.1-3.9)	3.1 (2.8-3.5)	3.1 (2.8-3.4)	2.7 (2.4-3.0)	2.7 (2.4-3.0)	2.7 (2.5-3.0)	2.8 (2.5-3.1)	2.8 (2.5-3.1)	2.6 (2.3-2.9)
	Women	4.6 (4.2-5.0)	4.6 (4.2-5.0)	4.8 (4.4-5.2)	4.6 (4.2-5.0)	4.0 (3.7-4.4)	4.2 (3.9-4.6)	3.0 (2.7-3.3)	3.0 (2.8-3.3)	3.2 (2.9-3.5)	3.0 (2.7-3.3)	2.8 (2.6-3.1)	3.0 (2.7-3.3)	3.0 (2.7-3.2)	2.6 (2.4-2.9)	2.7 (2.4-2.9)	2.8 (2.5-3.1)	2.8 (2.6-3.1)	2.6 (2.4-2.8)
	Entire population	4.7 (4.4-5.0)	4.4 (4.2-4.7)	4.6 (4.3-4.9)	4.5 (4.3-4.8)	4.1 (3.8-4.3)	4.2 (3.9-4.4)	3.0 (2.8-3.2)	3.0 (2.8-3.2)	3.0 (2.8-3.3)	3.2 (3.0-3.4)	3.0 (2.8-3.2)	3.0 (2.8-3.2)	2.9 (2.7-3.1)	2.7 (2.5-2.9)	2.7 (2.5-2.9)	2.8 (2.6-3.0)	2.8 (2.7-3.0)	2.6 (2.4-2.8)



Data represent annual age-standardized pulmonary embolism-related mortality rates (number of deaths with pulmonary embolism as the underlying cause per 100,000 population) with corresponding 95% confidence intervals. Pulmonary embolism-related mortality rates across age groups are depicted in *Figure 2*.

Table S5. JoinPoint analysis of trends in PE-related age-standardized mortality rates by country and sex (2000-2015).

	<i>Men</i>					
	Period 1		Period 2		Period 3	
<i>Country</i>	<i>Years</i>	<i>Slope (95%CI)</i>	<i>Years</i>	<i>Slope (95%CI)</i>	<i>Years</i>	<i>Slope (95%CI)</i>
United States	2000-2009	-0.04 (-0.05; -0.03)	2009-2015	0.02 (-0.001; 0.04)	-	-
Canada	2000-2015	-0.04 (-0.05; -0.03)	-	-	-	-
	<i>Women</i>					
	Period 1		Period 2		Period 3	
<i>Country</i>	<i>Years</i>	<i>Slope (95%CI)</i>	<i>Years</i>	<i>Slope (95%CI)</i>	<i>Years</i>	<i>Slope (95%CI)</i>
United States	2000-2003	-0.002 (-0.04; 0.04)	2003-2007	-0.08 (-0.12; -0.04)	2007-2015	-0.004 (-0.01; -0.03)
Canada	2000-2003	0.01 (-0.05; 0.07)	2003-2006	-0.13 (-0.22; -0.03)	2006-2015	-0.02 (-0.03; 0.004)
	<i>Total</i>					
	Period 1		Period 2		Period 3	
<i>Country</i>	<i>Years</i>	<i>Slope (95%CI)</i>	<i>Years</i>	<i>Slope (95%CI)</i>	<i>Years</i>	<i>Slope (95%CI)</i>
United States	2000-2003	-0.003 (-0.04; 0.04)	2003-2007	-0.08 (-0.12; -0.04)	2007-2015	0.002 (-0.008; 0.01)
Canada	2000-2003	0.004 (-0.04; 0.05)	2003-2006	-0.12 (-0.22; -0.02)	2006-2015	-0.02 (-0.03; 0.01)

Data represent annual changes in PE-related age-standardized mortality rates (number of deaths with pulmonary embolism as the underlying cause per 100,000 population) for each time period with corresponding 95% confidence intervals.

Table S6. Conditions listed as the *underlying* cause of deaths from records listing PE among the causes of death: data from the Multiple Cause of Death database.

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Count	26,540	27,306	27,556	28,271	27,449	28,241	28,692	28,772	29,746	29,333	30,485	31,584	31,977	32,470	33,438	34,952	35,515	37,333	38,215
Pulmonary embolism, n (%)	8,615 (32·5)	8,866 (32·5)	8,836 (32·1)	8,933 (31·6)	8,363 (30·5)	8,516 (30·2)	7,089 (24·7)	7,336 (25·5)	7,349 (24·7)	7,238 (24·7)	7,534 (24·7)	7,731 (24·5)	7,906 (24·7)	8,153 (25·1)	8,393 (25·1)	8,917 (25·5)	8,768 (24·7)	9,002 (24·1)	9,121 (23·9)
Limb vein thrombosis, n (%)	2,498 (9·4)	2,531 (9·3)	2,545 (9·2)	2,539 (9·0)	2,422 (8·8)	2,379 (8·4)	2,051 (7·1)	2,092 (7·3)	2,061 (6·9)	2,209 (7·5)	2,299 (7·5)	2,329 (7·4)	2,312 (7·2)	2,346 (7·2)	2,337 (7·0)	2,333 (6·7)	2,435 (6·9)	2,425 (6·5)	2,426 (6·3)
Cancer, n (%)	4,972 (18·7)	5,397 (19·8)	5,476 (19·9)	5,745 (20·3)	5,762 (21·0)	6,235 (22·1)	7,019 (24·5)	7,017 (24·4)	7,206 (24·2)	7,263 (24·8)	7,601 (24·9)	8,091 (25·6)	8,207 (25·7)	8,266 (25·5)	8,528 (25·5)	8,827 (25·3)	9,325 (26·3)	9,971 (26·7)	10,316 (27·0)
External causes, n (%)	1,600 (6·0)	1,676 (6·1)	1,534 (5·6)	1,502 (5·3)	1,436 (5·2)	1,419 (5·0)	1,594 (5·6)	1,556 (5·4)	1,492 (5·0)	1,430 (4·9)	1,504 (4·9)	1,507 (4·8)	1,337 (4·2)	1,393 (4·3)	1,439 (4·3)	1,458 (4·2)	1,464 (4·1)	1,571 (4·2)	1,609 (4·2)
Respiratory diseases, n (%)	1,361 (5·1)	1,410 (5·2)	1,430 (5·2)	1,525 (5·4)	1,544 (5·6)	1,692 (6·0)	1,656 (5·8)	1,700 (5·9)	1,953 (6·6)	1,877 (6·4)	1,834 (6·0)	1,961 (6·2)	2,050 (6·4)	2,097 (6·5)	2,147 (6·4)	2,258 (6·5)	2,205 (6·2)	2,397 (6·4)	2,571 (6·7)
Cardiovascular diseases, n (%)	3,581 (13·5)	3,510 (12·9)	3,621 (13·1)	3,720 (13·2)	3,592 (13·1)	3,551 (12·6)	3,762 (13·1)	3,591 (12·5)	3,852 (12·9)	3,568 (12·2)	3,735 (12·3)	3,815 (12·1)	3,907 (12·2)	3,964 (12·2)	4,086 (12·2)	4,266 (12·2)	4,247 (12·0)	4,619 (12·4)	4,613 (12·1)
Infectious diseases, n (%)	309 (1·2)	326 (1·2)	395 (1·4)	382 (1·4)	392 (1·4)	432 (1·5)	542 (1·9)	556 (1·9)	550 (1·8)	617 (2·1)	608 (2·0)	614 (1·9)	634 (2·0)	610 (1·9)	660 (2·0)	741 (2·1)	706 (2·0)	811 (2·2)	767 (2·0)

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Count	26,540	27,306	27,556	28,271	27,449	28,241	28,692	28,772	29,746	29,333	30,485	31,584	31,977	32,470	33,438	34,952	35,515	37,333	38,215
Haemorrhage, n (%)	271 (1·0)	234 (0·9)	249 (0·9)	260 (0·9)	274 (1·0)	252 (0·9)	350 (1·2)	352 (1·2)	349 (1·2)	366 (1·2)	358 (1·2)	378 (1·2)	338 (1·1)	364 (1·1)	370 (1·1)	410 (1·2)	409 (1·2)	461 (1·2)	471 (1·2)
Other, n (%)	3,333 (12·6)	3,356 (12·3)	3,470 (12·6)	3,665 (13·0)	3,664 (13·3)	3,765 (13·3)	4,629 (16·1)	4,572 (15·9)	4,934 (16·6)	4,765 (16·2)	5,012 (16·4)	5,158 (16·3)	5,286 (16·5)	5,277 (16·3)	5,478 (16·4)	5,742 (16·4)	5,956 (16·8)	6,076 (16·3)	6,321 (16·5)

The definition of contributing conditions is given in Table S2 of the Supplementary Material.

Table S7. Conditions listed as *contributing* causes of death (any position of the death certificate) from records listing PE among the causes of death: data from the Multiple Cause of Death database.

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Count	26,540	27,306	27,556	28,271	27,449	28,241	28,692	28,772	29,746	29,333	30,485	31,584	31,977	32,470	33,438	34,952	35,515	37,333	38,215
Limb vein thrombosis, n (%)	4,456 (16·8)	4,583 (16·8)	4,636 (16·8)	4,695 (16·6)	4,531 (16·5)	4,629 (16·4)	4,842 (16·9)	4,833 (16·8)	4,991 (16·8)	5,123 (17·5)	5,198 (17·1)	5,370 (17·0)	5,442 (17·0)	5,391 (16·6)	5,580 (16·7)	5,552 (15·9)	5,643 (15·9)	5,691 (15·2)	5,863 (15·3)
Cancer, n (%)	6,279 (23·7)	6,715 (24·6)	6,897 (25·0)	7,039 (24·9)	7,068 (25·7)	7,542 (26·7)	7,678 (26·8)	7,699 (26·8)	7,885 (26·5)	7,934 (27·0)	8,320 (27·3)	8,796 (27·8)	8,943 (28·0)	9,060 (27·9)	9,356 (28·0)	9,706 (27·8)	10,180 (28·7)	11,019 (29·5)	11,395 (29·8)
External causes, n (%)	2,839 (10·7)	2,916 (10·7)	2,790 (10·1)	2,725 (9·6)	2,619 (9·5)	2,543 (9·0)	2,604 (9·1)	2,569 (8·9)	2,493 (8·4)	2,400 (8·2)	2,448 (8·0)	2,520 (8·0)	2,305 (7·2)	2,455 (7·6)	2,507 (7·5)	2,521 (7·2)	2,701 (7·6)	2,807 (7·5)	2,991 (7·8)
Respiratory diseases, n (%)	6,168 (23·2)	6,443 (23·6)	6,663 (24·2)	7,085 (25·1)	7,134 (26·0)	7,446 (26·4)	7,672 (26·7)	7,686 (26·7)	8,376 (28·2)	8,212 (28·0)	8,689 (28·5)	9,371 (29·7)	9,494 (29·7)	9,908 (30·5)	10,256 (30·7)	11,029 (31·6)	11,330 (31·9)	12,306 (33·0)	12,717 (33·3)
Cardiovascular diseases, n (%)	11,824 (44·6)	12,106 (44·3)	12,325 (44·7)	12,656 (44·8)	12,377 (45·1)	12,878 (45·6)	13,168 (45·9)	13,292 (46·2)	13,889 (46·7)	13,641 (46·5)	14,367 (47·1)	15,005 (47·5)	15,625 (48·9)	15,886 (48·9)	16,408 (49·1)	17,394 (49·8)	17,765 (50·0)	18,934 (50·7)	19,653 (51·4)
Infectious diseases, n (%)	1,347 (5·1)	1,346 (4·9)	1,501 (5·4)	1,621 (5·7)	1,683 (6·1)	1,805 (6·4)	1,756 (6·1)	1,880 (6·5)	1,915 (6·4)	2,048 (7·0)	2,082 (6·8)	2,139 (6·8)	2,210 (6·9)	2,305 (7·1)	2,527 (7·6)	2,818 (8·1)	2,950 (8·3)	3,186 (8·5)	3,336 (8·7)
Haemorrhage, n (%)	1,115 (4·2)	1,204 (4·4)	1,203 (4·4)	1,253 (4·4)	1,348 (4·9)	1,305 (4·6)	1,437 (5·0)	1,414 (4·9)	1,463 (4·9)	1,471 (5·0)	1,552 (5·1)	1,649 (5·2)	1,645 (5·1)	1,721 (5·3)	1,833 (5·5)	2,002 (5·7)	2,071 (5·8)	2,230 (6·0)	2,348 (6·1)

The definition of contributing conditions is given in Table S2 of the Supplementary Material.

Table S8. Underlying cause-specific age-standardized mortality rates from records listing PE among the causes of death: data from the Multiple

Cause of Death database.

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Pulmonary embolism or limb vein thrombosis	5.65 (5.54-5.76)	5.69 (5.58-5.80)	5.56 (5.46-5.67)	5.50 (5.40-5.60)	5.10 (5.01-5.20)	5.10 (5.00-5.20)	4.13 (4.04-4.22)	4.18 (4.10-4.27)	4.07 (3.99-4.15)	3.98 (3.89-4.06)	4.08 (4.00-4.16)	4.08 (4.00-4.16)	4.08 (4.00-4.16)	4.10 (4.02-4.18)	4.13 (4.05-4.21)	4.23 (4.15-4.31)	4.12 (4.04-4.19)	4.13 (4.06-4.21)	4.11 (4.03-4.19)
Cancer	2.57 (2.50-2.65)	2.76 (2.68-2.83)	2.75 (2.68-2.82)	2.85 (2.78-2.93)	2.81 (2.74-2.89)	3.00 (2.93-3.08)	3.30 (3.22-3.38)	3.25 (3.17-3.32)	3.27 (3.19-3.35)	3.20 (3.13-3.28)	3.28 (3.21-3.36)	3.41 (3.34-3.49)	3.39 (3.31-3.46)	3.34 (3.26-3.41)	3.34 (3.27-3.42)	3.40 (3.33-3.47)	3.49 (3.42-3.57)	3.66 (3.59-3.73)	3.70 (3.63-3.77)
External causes	0.82 (0.78-0.86)	0.84 (0.80-0.88)	0.75 (0.71-0.78)	0.72 (0.68-0.76)	0.67 (0.64-0.71)	0.66 (0.63-0.70)	0.72 (0.69-0.76)	0.68 (0.65-0.72)	0.64 (0.61-0.68)	0.61 (0.58-0.64)	0.63 (0.60-0.67)	0.61 (0.58-0.64)	0.53 (0.50-0.56)	0.54 (0.51-0.57)	0.55 (0.52-0.58)	0.55 (0.52-0.58)	0.54 (0.51-0.56)	0.57 (0.54-0.60)	0.57 (0.54-0.60)
Respiratory diseases	0.73 (0.69-0.77)	0.74 (0.70-0.78)	0.75 (0.71-0.79)	0.78 (0.74-0.82)	0.78 (0.74-0.82)	0.85 (0.81-0.89)	0.82 (0.78-0.86)	0.82 (0.78-0.86)	0.92 (0.88-0.97)	0.86 (0.82-0.90)	0.83 (0.79-0.87)	0.87 (0.83-0.91)	0.88 (0.84-0.92)	0.88 (0.85-0.92)	0.88 (0.84-0.92)	0.91 (0.87-0.95)	0.86 (0.83-0.90)	0.92 (0.88-0.96)	0.96 (0.92-1.00)
Cardiovascular diseases	1.92 (1.86-1.99)	1.84 (1.78-1.90)	1.86 (1.80-1.93)	1.89 (1.83-1.95)	1.81 (1.75-1.87)	1.76 (1.71-1.82)	1.82 (1.76-1.88)	1.70 (1.64-1.75)	1.79 (1.73-1.84)	1.62 (1.57-1.67)	1.66 (1.61-1.71)	1.65 (1.60-1.71)	1.65 (1.60-1.70)	1.63 (1.58-1.69)	1.65 (1.59-1.70)	1.70 (1.65-1.75)	1.63 (1.58-1.68)	1.74 (1.69-1.79)	1.70 (1.65-1.75)

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Infectious diseases	0·15 (0·14- 0·17)	0·16 (0·14- 0·17)	0·19 (0·17- 0·21)	0·18 (0·16- 0·20)	0·19 (0·17- 0·21)	0·21 (0·19- 0·23)	0·25 (0·23- 0·28)	0·25 (0·23- 0·27)	0·24 (0·22- 0·26)	0·27 (0·25- 0·30)	0·26 (0·24- 0·29)	0·26 (0·24- 0·28)	0·26 (0·24- 0·28)	0·24 (0·22- 0·26)	0·26 (0·24- 0·28)	0·29 (0·27- 0·31)	0·27 (0·25- 0·29)	0·30 (0·28- 0·32)	0·28 (0·26- 0·30)
Haemorrhage	0·14 (0·12- 0·16)	0·12 (0·11- 0·14)	0·13 (0·11- 0·15)	0·13 (0·11- 0·15)	0·13 (0·12- 0·15)	0·13 (0·11- 0·14)	0·17 (0·15- 0·18)	0·17 (0·15- 0·18)	0·16 (0·14- 0·18)	0·16 (0·15- 0·18)	0·16 (0·14- 0·17)	0·16 (0·15- 0·18)	0·14 (0·13- 0·16)	0·15 (0·14- 0·17)	0·15 (0·14- 0·17)	0·16 (0·15- 0·18)	0·16 (0·14- 0·17)	0·17 (0·16- 0·19)	0·17 (0·16- 0·19)

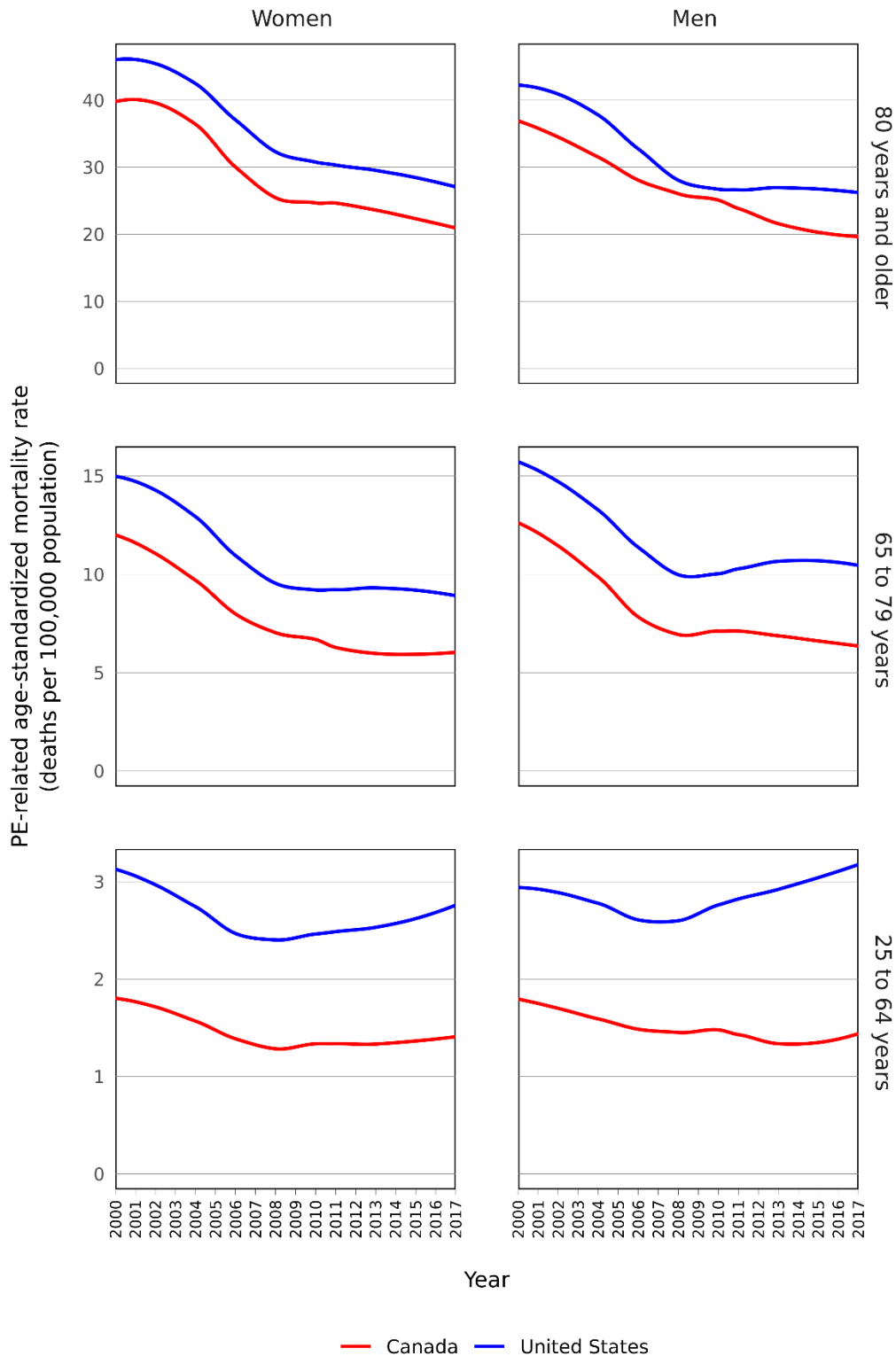
Numbers are expressed as underlying cause-specific deaths per 100,000 population-years (95% confidence interval). The definition of contributing conditions is given in Table S2 of the Supplementary Material.

Table S9. Contributing cause-specific age-standardized mortality rates from records listing PE among the causes of death: data from the Multiple Cause of Death database.

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Cancer	3.27 (3.19- 3.35)	3.45 (3.36- 3.53)	3.48 (3.40- 3.56)	3.51 (3.42- 3.59)	3.47 (3.39- 3.55)	3.65 (3.56- 3.73)	3.62 (3.54- 3.71)	3.57 (3.49- 3.65)	3.59 (3.51- 3.67)	3.51 (3.44- 3.59)	3.61 (3.53- 3.69)	3.72 (3.64- 3.80)	3.71 (3.63- 3.78)	3.67 (3.59- 3.75)	3.69 (3.61- 3.76)	3.75 (3.68- 3.83)	3.83 (3.75- 3.91)	4.06 (3.98- 4.14)	4.10 (4.02- 4.18)
External causes	1.46 (1.41- 1.52)	1.46 (1.41- 1.52)	1.36 (1.31- 1.41)	1.32 (1.27- 1.37)	1.23 (1.19- 1.28)	1.20 (1.15- 1.25)	1.19 (1.14- 1.23)	1.14 (1.10- 1.19)	1.09 (1.05- 1.14)	1.03 (0.99- 1.07)	1.04 (1.00- 1.08)	1.03 (0.99- 1.07)	0.93 (0.89- 0.97)	0.97 (0.93- 1.01)	0.97 (0.93- 1.01)	0.96 (0.92- 1.00)	1.00 (0.96- 1.04)	1.02 (0.99- 1.06)	1.07 (1.03- 1.11)
Respiratory diseases	3.28 (3.20- 3.36)	3.36 (3.28- 3.44)	3.41 (3.33- 3.50)	3.57 (3.49- 3.66)	3.57 (3.49- 3.66)	3.68 (3.60- 3.77)	3.70 (3.62- 3.79)	3.63 (3.55- 3.72)	3.89 (3.80- 3.97)	3.70 (3.62- 3.79)	3.86 (3.78- 3.94)	4.05 (3.97- 4.14)	4.01 (3.93- 4.10)	4.10 (4.02- 4.18)	4.13 (4.05- 4.21)	4.35 (4.27- 4.43)	4.35 (4.27- 4.44)	4.62 (4.54- 4.70)	4.66 (4.58- 4.75)
Cardiovascular diseases	6.27 (6.16- 6.39)	6.27 (6.16- 6.39)	6.29 (6.18- 6.40)	6.35 (6.23- 6.46)	6.13 (6.02- 6.24)	6.30 (6.19- 6.41)	6.28 (6.17- 6.39)	6.21 (6.10- 6.32)	6.36 (6.26- 6.47)	6.11 (6.00- 6.21)	6.32 (6.21- 6.42)	6.43 (6.32- 6.53)	6.53 (6.43- 6.64)	6.49 (6.38- 6.59)	6.56 (6.46- 6.66)	6.82 (6.71- 6.92)	6.77 (6.67- 6.88)	7.08 (6.98- 7.19)	7.19 (7.09- 7.29)
Infectious diseases	0.68 (0.65- 0.72)	0.68 (0.64- 0.71)	0.74 (0.70- 0.78)	0.78 (0.75- 0.82)	0.81 (0.77- 0.85)	0.86 (0.82- 0.90)	0.82 (0.78- 0.86)	0.86 (0.82- 0.90)	0.85 (0.82- 0.89)	0.90 (0.86- 0.94)	0.90 (0.86- 0.94)	0.90 (0.86- 0.94)	0.90 (0.87- 0.94)	0.93 (0.89- 0.97)	0.99 (0.95- 1.03)	1.08 (1.04- 1.13)	1.10 (1.06- 1.14)	1.17 (1.13- 1.21)	1.20 (1.15- 1.24)
Haemorrhage	0.58 (0.55- 0.62)	0.62 (0.59- 0.66)	0.61 (0.58- 0.65)	0.63 (0.59- 0.66)	0.66 (0.63- 0.70)	0.64 (0.61- 0.68)	0.69 (0.65- 0.72)	0.66 (0.63- 0.70)	0.67 (0.64- 0.71)	0.66 (0.63- 0.70)	0.68 (0.65- 0.72)	0.71 (0.68- 0.75)	0.70 (0.66- 0.73)	0.71 (0.67- 0.74)	0.74 (0.71- 0.78)	0.79 (0.75- 0.82)	0.80 (0.76- 0.83)	0.84 (0.81- 0.88)	0.86 (0.83- 0.90)

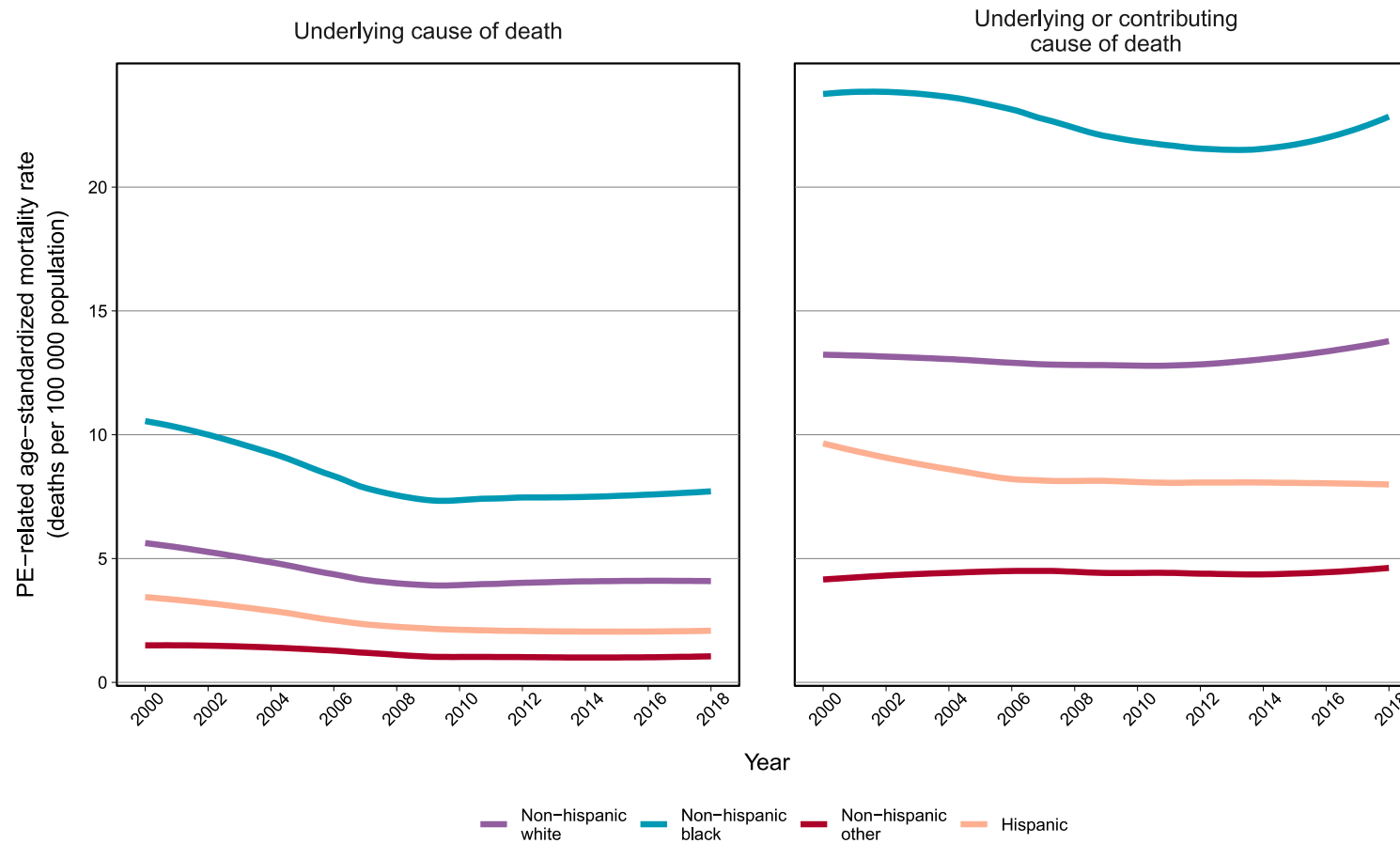
	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Total	13·65	13·78	13·66	13·78	13·22	13·45	13·33	13·10	13·29	12·76	13·06	13·20	13·09	13·00	13·11	13·45	13·31	13·74	13·78
	(13·49-	(13·62-	(13·49-	(13·62-	(13·06-	(13·29-	(13·17-	(12·95-	(13·14-	(12·61-	(12·91-	(13·05-	(12·95-	(12·86-	(12·96-	(13·30-	(13·17-	(13·60-	(13·64-
	13·82)	13·95)	13·82)	13·95)	13·38)	13·61)	13·49)	13·26)	13·45)	12·91)	13·21)	13·35)	13·24)	13·15)	13·25)	13·59)	13·45)	13·88)	13·92)

Figure S1. Trends in PE-related age-standardized mortality in the US and Canada from 2000 to 2015.



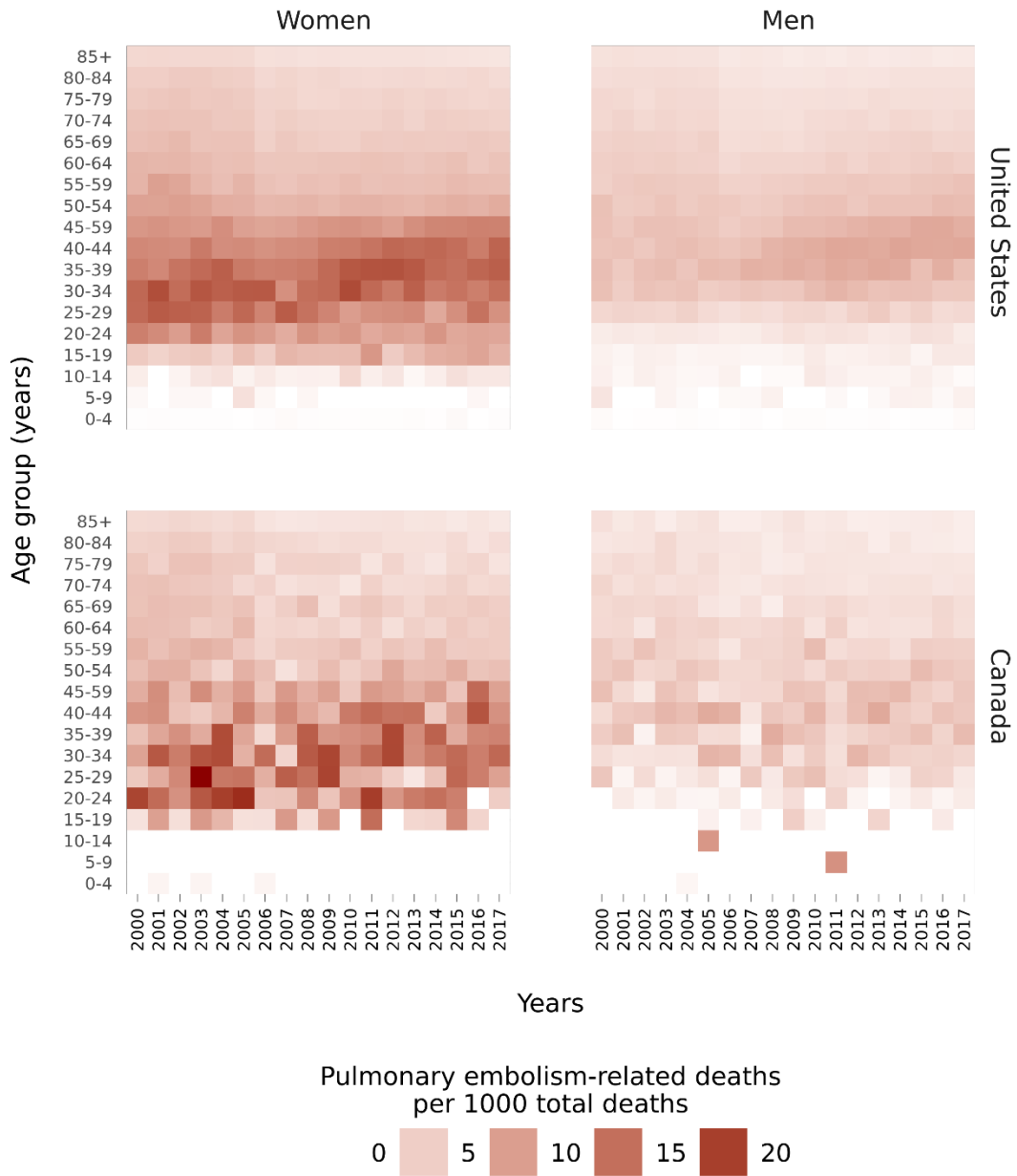
Data from the WHO Mortality Database. Locally weighted scatterplot smoother (LOESS) lines were used to depict the annual age-standardized pulmonary embolism-related mortality rate (number of deaths with pulmonary embolism as the underlying cause per 100,000 population).

Figure S2. Trends in PE-related age-standardised mortality for ethnicity and sex in the United States from 2000 to 2018.



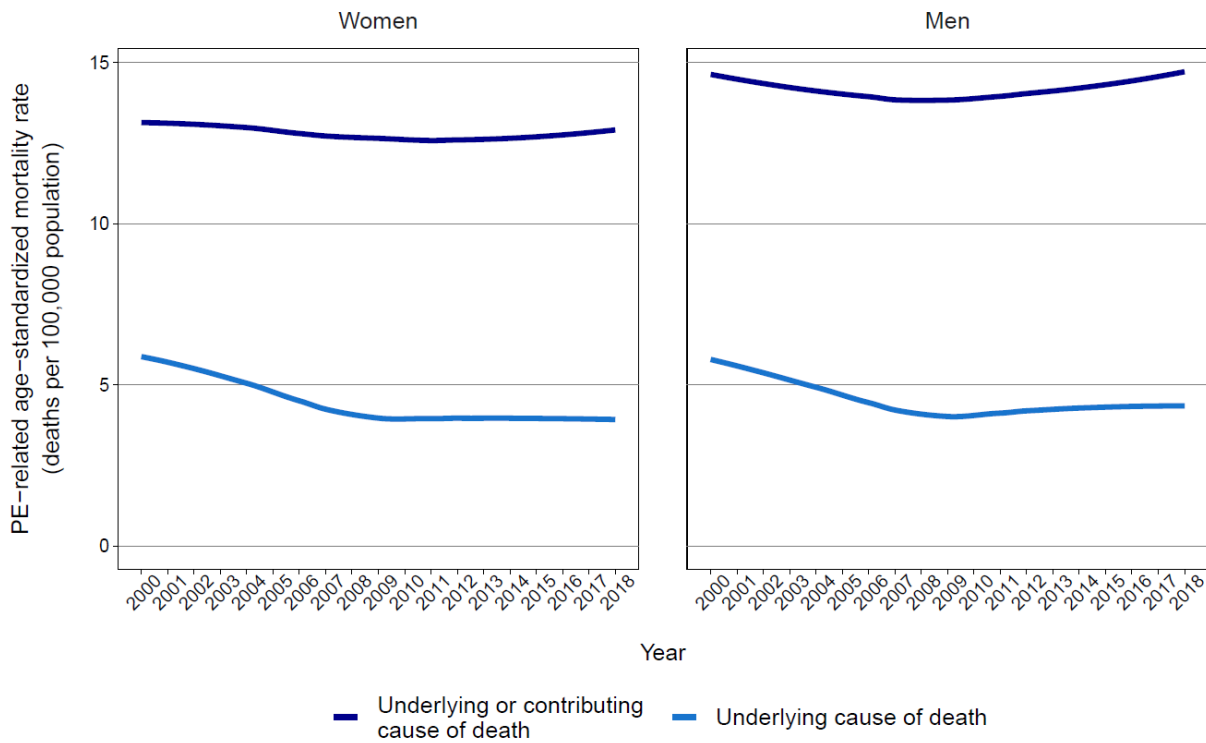
Data from the Multiple Cause of Death Database. Locally weighted scatterplot smoother (LOESS) lines for the PE-related age-standardised rate (number of deaths per 100,000 population).

Figure S3. Trends in the contribution of PE-related mortality to total mortality in the US and Canada (2000-2015).



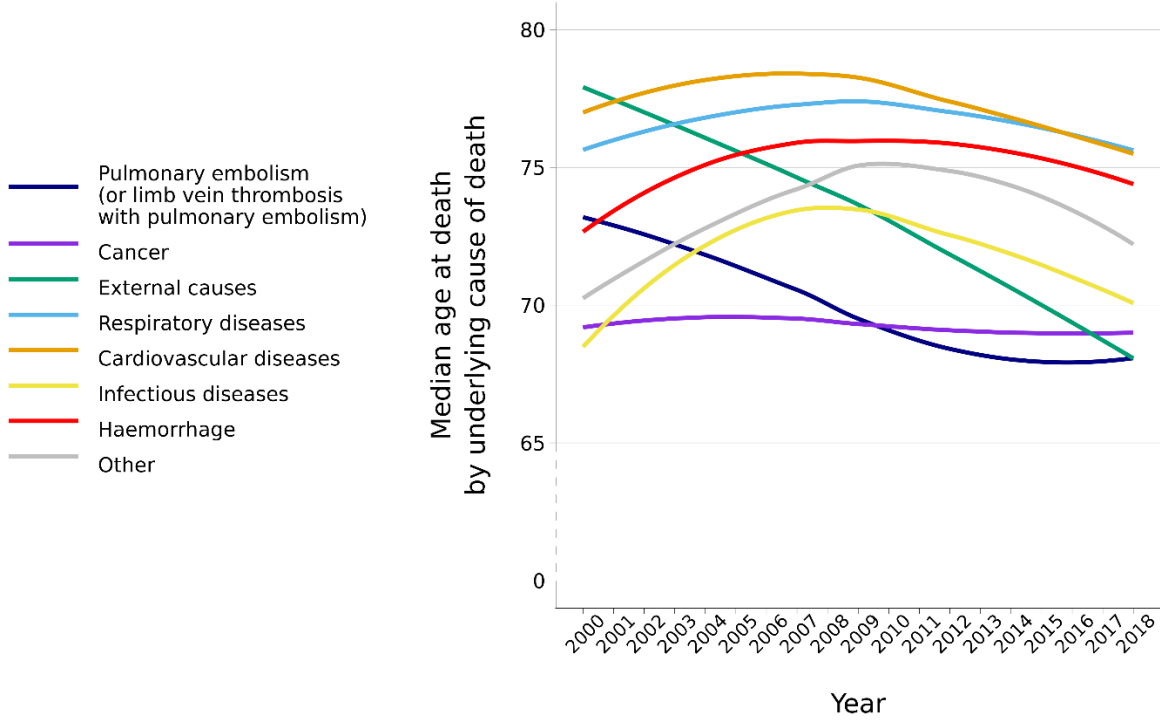
Data from the WHO Mortality Database. Mortality rate by age group (observed) and average annual number of deaths with PE as the underlying cause per 1000 total deaths.

Figure S4. Trends in PE-related age-standardized mortality rates in the US.

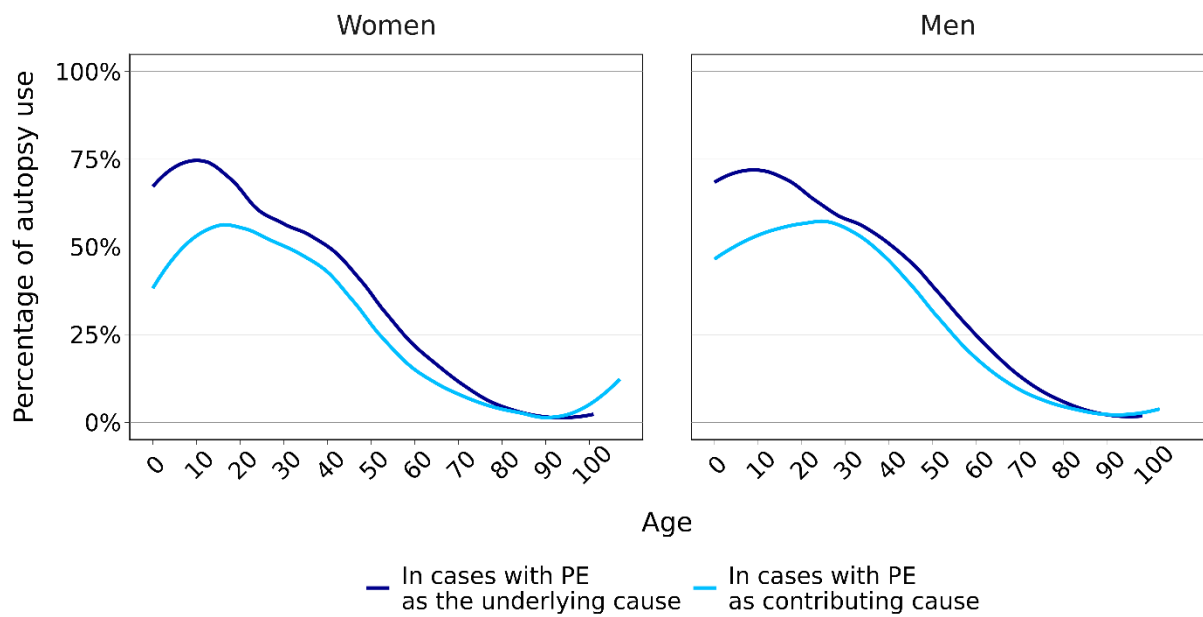


Data from the Multiple Cause of Death database. Locally weighted scatterplot smoother (LOESS) lines for the PE-related age-standardised mortality rate (number of deaths per 100,000 population) related to PE listed as the underlying cause of death or in any position of the death certificate.

Figure S5. Median age at death by underlying cause of death.



Data from the Multiple Cause of Death database.

Figure S6. Use of autopsy in patients with PE in the US.

Data from the Multiple Cause of Death database. Between 2003 (the first year with available information on autopsy) and 2018, autopsy was performed after 21,782 (17.9%) of 121,416 deaths with PE as the underlying cause of death; the use of autopsy remained stable from 2003 to 2018 (beta coefficient -0.07%; 95%CI -0.16%, +0.02%). Of 356,786 deaths with PE as a contributing cause of death, autopsy was performed in 44,813 (12.6%) cases (beta coefficient -0.18%; 95%CI -0.22%, -0.13%). Autopsy was performed more often in men than in women, irrespective of whether PE was listed as the underlying cause of death (absolute difference +4.3%, 95%CI +3.9%; +4.7%) or as a contributing cause of death (absolute difference +3.6%; 95%CI +3.4%; +3.9%), and in younger patients.

Addendum

Statistical source code used to generate estimates can be obtained from the study statistician (Dr. Luca Valerio, luca.valerio@uni-mainz.de).

Source data can be downloaded at https://www.who.int/healthinfo/mortality_data/en/ (WHO Mortality data) and https://www.cdc.gov/nchs/data_access/vitalstatsonline.htm (US Centers for Disease Control and Prevention, National Center for Health Statistics: Mortality Multiple Cause Files).