## Title:

# Estimated incidence of hospitalizations and deaths attributable to Respiratory Syncytial Virus infections among adults in Germany between 2015 and 2019

#### Author details:

Aleksandra Polkowska-Kramek<sup>1</sup>, Elizabeth Begier<sup>2</sup>, Robin Bruyndonckx<sup>1</sup>, Caihua Liang<sup>3</sup>, Caroline Beese<sup>4</sup>, Gordon Brestrich<sup>4</sup>, Thao Mai Phuong Tran<sup>1</sup>, Charles Nuttens<sup>5</sup>, Maribel Casas<sup>1</sup>, Lea Johanna Bayer<sup>4</sup>, Bennet Huebbe<sup>4</sup>, Worku Biyadgie Ewnetu<sup>1</sup>, Juan Luis Ramirez Agudelo<sup>1</sup>, Bradford D. Gessner<sup>3</sup>, Christof von Eiff<sup>4</sup>, Gernot Rohde<sup>6</sup>

### Affiliations:

<sup>1</sup> P95 Pharmacovigilance and Epidemiology Services, Leuven, Belgium.

<sup>2</sup>Pfizer Inc - Dublin (Ireland)

<sup>3</sup>Pfizer Inc-New York (USA)

<sup>4</sup>Pfizer Pharma GmbH - Berlin (Germany)

<sup>5</sup>Pfizer Inc - Paris (France);

<sup>6</sup> Goethe University Frankfurt, University Hospital, Medical Clinic I, Department of Respiratory Medicine, Frankfurt/Main, Germany

## **Corresponding author:**

Caihua Liang

Email: <a href="mailto:caihua.liang@pfizer.com">caihua.liang@pfizer.com</a>

Phone: 1-716-429-5598

Address: 66 Hudson Blvd E, New York, NY 10001

	ICD-10-GM				
Nominating condition	Code	Nomenclature			
	105	Rheumatic mitral valve diseases			
	106	Rheumatic aortic valve diseases			
	108.0	Rheumatic disorders of both mitral and aortic valves			
	109	Other rheumatic heart diseases			
	I11	Hypertensive heart disease			
	I13	Hypertensive heart and chronic kidney disease			
	I21-I23	I21: ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction I22: Subsequent ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction I23: Certain current complications following ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction (within 28 day period)			
	124	Other acute ischemic heart diseases			
	I25.2	Old myocardial infarction			
	I20	Angina pectoris			
Chronic cardiac disease	I25.8	Other forms of chronic ischemic heart disease			
	I27	Other pulmonary heart diseases			
	Z95.9	Presence of cardiac and vascular implant and graft, unspecified			
	Z95.1	Presence of aortocoronary bypass graft			
	I34-I39	I34: Nonrheumatic mitral valve disorders I35: Nonrheumatic aortic valve disorders I36: Nonrheumatic tricuspid valve disorders I37: Nonrheumatic pulmonary valve disorders I38: Endocarditis, valve unspecified I39: Endocarditis and heart valve disorders in diseases classified elsewhere			
	I42	Cardiomyopathy			
	I45	Other conduction disorders			
	I49	Other cardiac arrhythmias			
	150	Heart failure			

N	ICD-10-GM				
Nominating condition	Code	Nomenclature			
	I51	Complications and ill-defined descriptions of heart disease			
	170	Atherosclerosis			
	Q21	Congenital malformations of cardiac septa			
	Q24	Other congenital malformations of heart			
	Q28	Other congenital malformations of circulatory system			
	I46	Cardiac arrest			
	197.1	Other postprocedural cardiac functional disturbances			
	340	Bronchitis, not specified as acute or chronic			
	J41 J42	Simple and mucopurulent chronic bronchitis Unspecified chronic bronchitis			
	J43	Emphysema			
	J45	Asthma			
	J47	Bronchiectasis			
	344	Other chronic obstructive pulmonary disease			
	J60	Coal workers' pneumoconiosis			
	J61	Pneumoconiosis due to asbestos and other mineral fibers			
	J62	Pneumoconiosis due to dust containing silica			
Chronic respiratory diseases	J63	Pneumoconiosis due to other inorganic dust			
	J64	Pneumoconiosis, unspecified			
	J68	Respiratory conditions due to inhalation of chemicals, gases, fumes and vapors			
	J69	Pneumonitis due to solids and liquids			
	J70	Respiratory conditions due to other external agents			
	E84	Cystic fibrosis			
	J85	Abscess of lung and mediastinum			
	J81 s	Pulmonary edema			
	J84.1 J84.8	Other interstitial pulmonary disease with fibrosis Other interstitial pulmonary disease			

	ICD-10-GM					
Nominating condition	Code	Nomenclature				
	J84.0	Alveolar and parieto- alveolar conditions				
	J98.4	Other disorders of lung				
	E10-E14	Diabetes mellitus				
	E16	Other disorders of pancreatic internal secretion				
	G63.2	Diabetic polyneuropathy				
Diabetes mellitus	H36.0	Diabetic retinopathy				
	H35.0	Retinopathies of the ocular fundus and changes in retinal vessels				
	H28.0	Diabetic cataract				
	024	Diabetes mellitus in pregnancy, childbirth, and the puerperium				
Chronic liver disease	K70-K77	Diseases of liver				
Chronic liver disease	Q44.6	Cystic disease of liver				
	I12	Hypertensive chronic kidney disease				
	N00	Acute nephritic syndrome				
	N04	Nephrotic syndrome				
	N03	Chronic nephritic syndrome				
	N05	Unspecified nephritic syndrome				
	N17	Acute kidney failure				
	N18	Chronic kidney disease (ckd)				
Chronic kidney disease	N19	Unspecified kidney failure				
Simonia mano, albados	N26	Renal sclerosis, unspecified				
	N25	Disorders resulting from impaired renal tubular function				
	N27	Small kidney of unknown cause				
	N13.3	Unspecified hydronephrosis				
	N28.8	Other specified disorders of kidney and ureter				
	Z94.0	Kidney transplant status				
	Z49	Encounter for care involving renal dialysis				
	B20-B24	Human immunodeficiency virus [HIV] disease				
Immunosuppression	D71	Functional disorders of polymorphonuclear neutrophils				
	D72.0	Genetic anomalies of leukocytes				

Naminakina andiki	ICD-10-GM				
Nominating condition	Code	Nomenclature			
	M30	Polyarteritis nodosa and related conditions			
	M32	Systemic lupus erythematosus (SLE)			
	M35.0 H19.3	Sjögren syndrome, unspecified Sjögren syndrome with keratoconjunctivitis			
	M33.2	Polymyositis, organ involvement unspecified			
	M06	Other rheumatoid arthritis			
	Z21	Asymptomatic human immunodeficiency virus [HIV] infection status			
	Z94.0	Kidney transplant status			
	Z95.3	Presence of xenogenic heart valve			
	Z94	Transplanted organ			
	Z51.0	Encounter for antineoplastic radiation therapy			
	Z51.1	Chemotherapy session due to malignant neoplasm			
	D37-D48	Neoplasms of uncertain or unknown behaviour			
	C00-C14	Malignant neoplasms of lip, oral cavity and pharynx			
	C15-C26	Malignant neoplasms of digestive organs			
	C30-C39	Malignant neoplasms of respiratory and intrathoracic organs			
	C40-C41 C43-C44 C45-C49 C50- C50	Malignant neoplasms of bone and articular cartilage Melanoma and other malignant neoplasms of skin Malignant neoplasms of mesothelial and soft tissue Malignant neoplasms of breast			
	C51-C58 C60-63 C64-C68	Malignant neoplasms of female genital organs Malignant neoplasms of male genital organs Malignant neoplasms of urinary tract			
	C69-C72	Malignant neoplasms of eye, brain and other parts of central nervous system			
	C73-C75	Malignant neoplasms of thyroid and other endocrine glands			
	C76-C80	Malignant neoplasms of ill- defined, other secondary and			

Nominating condition	ICD-10-GM			
	Code	Nomenclature		
		unspecified sites		
	C81-C88	C81 Hodgkin lymphoma, C82 Follicular lymphoma, C83 Non follicular lymphoma, C84 Matu T/NK-cell lymphomas, C85 Ot specified and unspecified types non-Hodgkin lymphoma, C86 Other specified types of T/NK-lymphoma, C88 Malignant immunoproliferative diseases a certain other B-cell lymphomas		
	C90.1 C91-C95	C90.1 Plasma cell leukemia C91 Lymphoid leukemia, C92 Myeloid leukemia, C93 Monocy leukemia, C94 Other leukemia specified cell type, C95 Leuker of unspecified cell type		
	D80-D84 and D89	D80 Immunodeficiency with predominantly antibody defect D81 Combined immunodeficiencies D82 Immunodeficiency associated with other major defects D83 Common variable immunodeficiency D84 Other immunodeficiencies D89 Other disorders involving immune mechanism, not elsewhere classified		
	T86	Complications of transplanted organs and tissue		
	M32	Systemic lupus erythematosus		
	M05; M06; M08	Rheumatoid arthritis		
	L40	Psoriasis		
	M07	Enteropathic arthropathies		
	M31.5 M31.6	Giant cell arteritis with polymyalgia rheumatica Other giant cell arteritis		
	Q00-Q07	Congenital malformations of th nervous system		
Neurological disorders	G10-G14; G20-G26; G30-G32; G35-G37	Inflammatory diseases of the central nervous system, System atrophies primarily affecting the central nervous system,		
	G45-G46	G45 Transient cerebral ischem attacks and related syndromes, G46 Vascular syndromes of brain in cerebrovascular diseases		
	G70-G99	G70-G73 Diseases of myoneu junction and muscle, G80-G83		

Nominating condition	ICD-10-GM				
	Code	Nomenclature			
		Cerebral palsy and other paralytic syndromes, G90-G99 Other disorders of the nervous system			

ICD: International Classification of Diseases.

Supplementary table 2. Parameter estimates for the final Quasi-poisson regression models for respiratory hospitalizations in patients without risk factors.

	18-44 years		45-59 year	45-59 years		60-74 years		≥75 years	
Parameter	Estimate	Standard error	Estimate	Standard error	Estimate	Standard error	Estimate	Standard error	
β <sub>0</sub>	96.719	2.325	50.281	1.411	21.264	0.821	11.658	0.827	
β1	-0.031	0.013	-0.007	0.008	0.026	0.005	0.027	0.014	
β2	NA	NA	NA	NA	NA	NA	0.000	0.000	
β <sub>3</sub>	NA	NA	NA	NA	NA	NA	NA	NA	
β4	NA	NA	NA	NA	NA	NA	NA	NA	
β <sub>5</sub>	4.524	2.196	0.867	1.409	1.671	0.878	0.669	0.570	
β <sub>6</sub>	7.861	1.615	4.528	0.944	0.701	0.538	1.511	0.422	
β <sub>7</sub>	-0.799	1.615	0.070	0.959	0.737	0.549	0.145	0.414	
β8	-5.664	1.462	-0.649	0.947	-0.307	0.595	-0.168	0.372	
β <sub>9</sub>	0.165	0.054	0.133	0.033	0.094	0.020	0.046	0.015	
β <sub>10</sub>	0.084	0.085	0.072	0.052	0.044	0.031	0.070	0.024	

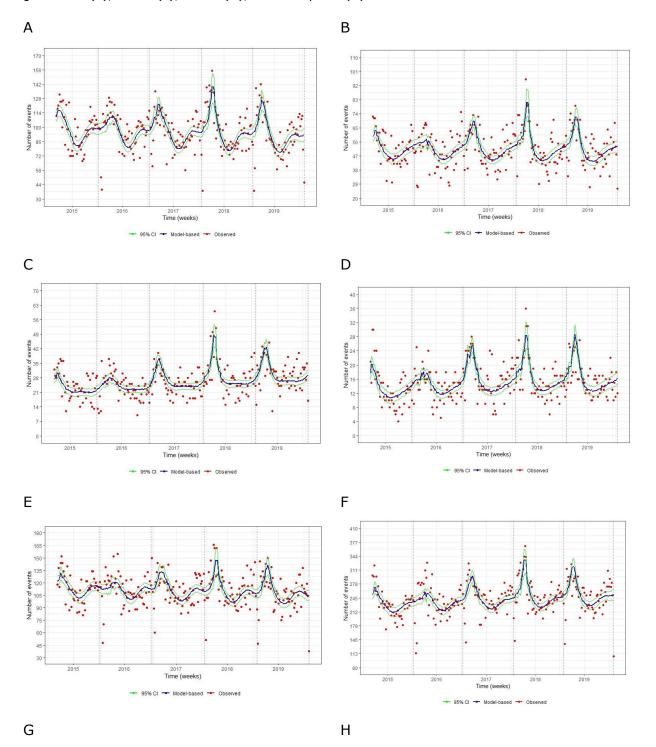
Parameter  $\beta_0$  is the coefficient associated with the baseline number of events,  $\beta_1$  to  $\beta_4$  are coefficients associated with the aperiodic time trend,  $\beta_5$  to  $\beta_8$  are coefficients associated with the periodic time trend, and  $\beta_{(8+l)}$  are coefficients associated with appropriately lagged activity of pathogen l with l=1,...,L where l=1,.

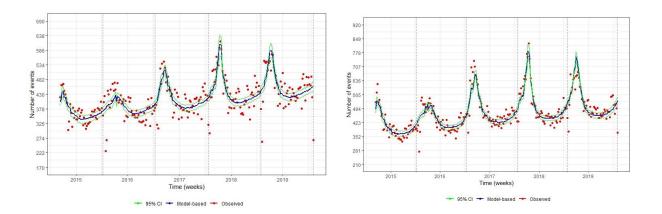
Supplementary table 3. Parameter estimates for the final Quasi-poisson regression models for respiratory hospitalizations in patients with risk factors.

	18-44 years		45-59 years		60-74 years		≥75 years	
Parameter	Estimate	Standard error	Estimate	Standard error	Estimate	Standard error	Estimate	Standard error
β <sub>0</sub>	111.266	2.590	224.215	4.659	345.516	6.048	372.397	8.309
$\beta_1$	-0.032	0.015	0.075	0.027	0.375	0.036	0.752	0.138
β2	NA	NA	NA	NA	NA	NA	-0.001	0.000
β3	NA	NA	NA	NA	NA	NA	NA	NA
β4	NA	NA	NA	NA	NA	NA	NA	NA
β <sub>5</sub>	-0.051	2.695	4.902	4.653	13.480	6.093	31.633	5.642
β <sub>6</sub>	4.809	1.643	10.253	3.145	10.719	4.149	22.234	4.249
β <sub>7</sub>	-2.247	1.701	-1.329	3.195	1.340	4.189	7.674	4.164
β8	-3.539	1.853	-4.447	3.165	-2.893	4.144	-2.003	3.758
β9	0.156	0.056	0.370	0.105	0.757	0.142	1.109	0.147
β <sub>10</sub>	0.168	0.090	0.308	0.168	0.622	0.223	1.020	0.226

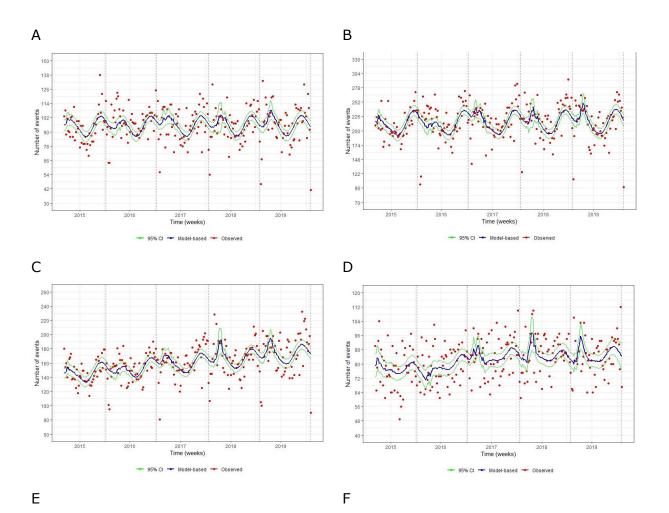
Parameter  $\beta_0$  is the coefficient associated with the baseline number of events,  $\beta_1$  to  $\beta_4$  are coefficients associated with the aperiodic time trend,  $\beta_5$  to  $\beta_8$  are coefficients associated with the periodic time trend, and  $\beta_{(8+l)}$  are coefficients associated with appropriately lagged activity of pathogen l with l=1,...,L where l=1,.

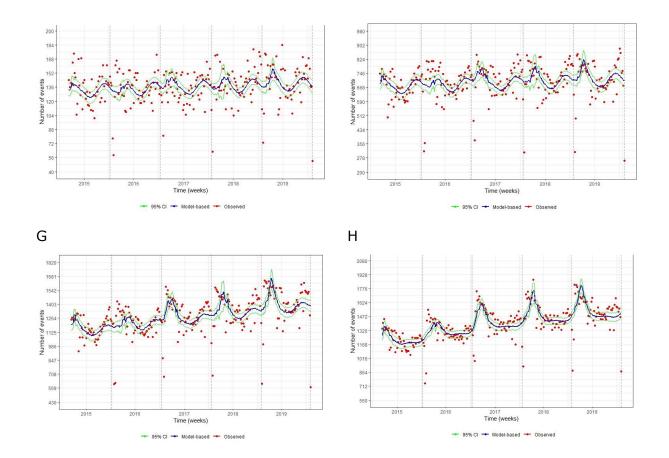
Supplementary figure 1. Weekly estimated versus observed all respiratory hospitalized cases in people aged 18-44 (A), 45-59 (B), 60-74 (C), and  $\geq$ 75 years (D) without risk factors and in people aged 18-44 (E), 45-59 (F), 60-74 (G), and  $\geq$ 75 years (H) with risk factors





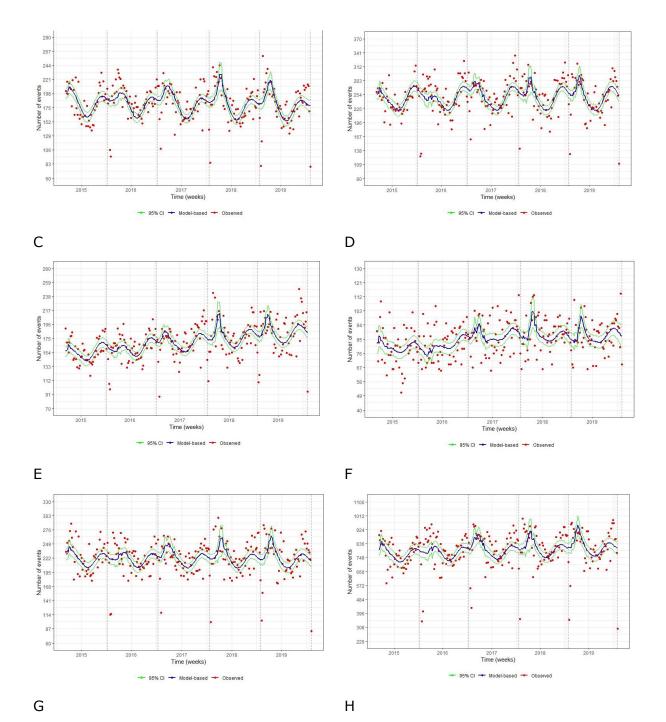
Supplementary figure 2. Weekly estimated versus observed all cardiovascular hospitalized cases in people aged 18-44 (A), 45-59 (B), 60-74 (C), and  $\geq$ 75 years (D) without risk factors and in people aged 18-44 (E), 45-59 (F), 60-74 (G), and  $\geq$ 75 years (H) with risk factors

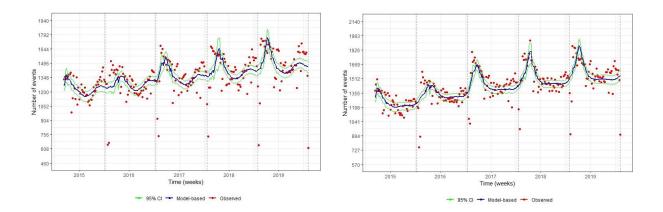




Supplementary figure 3. Weekly estimated versus observed all cardiorespiratory hospitalized cases in people aged 18-44 (A), 45-59 (B), 60-74 (C), and  $\geq$ 75 years (D) without risk factors and in people aged 18-44 (E), 45-59 (F), 60-74 (G), and  $\geq$ 75 years (H) with risk factors

A B





Supplementary figure 4. Weekly estimated versus observed deaths within 28-day of cardiorespiratory hospitalization in people aged 18-44 (A), 45-59 (B), 60-74 (C) and  $\geq$ 75 years (D) with risk factors, 2015-2019, Germany

