

Risk Factors of Pertussis Among Older Adults in South Korea: A Nationwide Health Data-Based Case-Control Study

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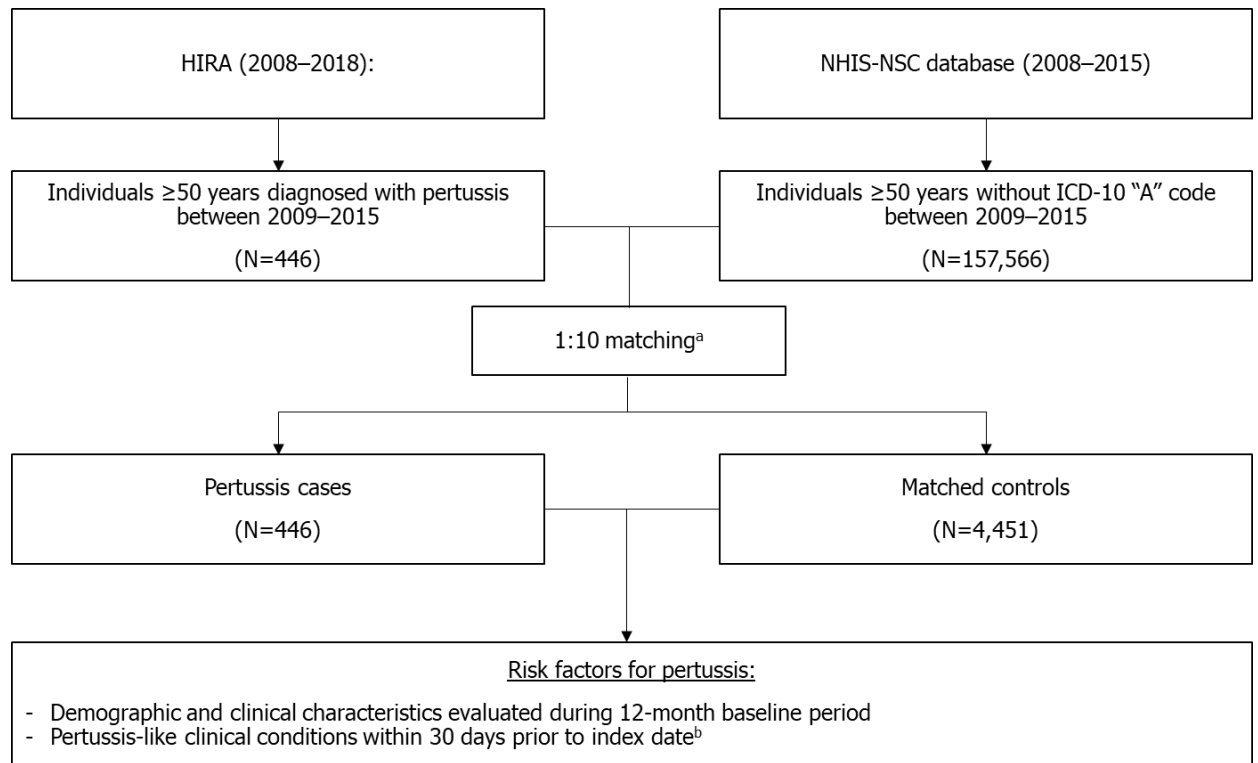
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SUPPLEMENTARY DATA

Supplementary Figure 1. Overview of sensitivity analysis



[a] Matching was based on age group (5-year band), sex, and geographic location; [b] Includes acute bronchitis, allergic rhinitis, pneumonia and URTI. HIRA: Health Insurance Review and Assessment service; ICD-10: International Statistical Classification of Diseases and Related Health Problems 10th Edition; NHIS-NSC: National Health Insurance Service – National Sample Cohort; URTI: upper respiratory tract infection.

Supplementary Table 1. ICD-10 and ATC codes used for data analysis

Variables	ICD-10 code or ATC code
<i>Comorbidities</i>	
Asthma	J45-J46
Cancer	C00-C43, C45-C97
Cardiovascular disease	I110, I20-I25, I42-I50, I130, I132, I70, I72, I73, I74, I77, E115, E145, E135, K550, K551, J81
Cerebrovascular disease	I60-I69, G45(excl. G454), G46
COPD	J43-J44
Diabetes	E10-E14
GERD	K21
Hyperlipidemia	E78.0-E78.5
Hypertension	I10-I15
Autoimmune disease	D59, D89, K50-K51, L40, M32-M35, M45, M79
Liver disease	B18, I85.x, I86.4, I98.2, K70-K77, Z94.4
Renal disease	E112, E132, E142, I12, I13, N00-N08, N17, N18, N19, N25-N27, Z49.0-Z49.2, Z94.0, Z99.2
<i>Pertussis-like clinical conditions</i>	
Acute bronchitis	J20-J22
Allergic rhinitis	J30
Pneumonia	J13-J18
URTI	J00-J06
<i>Medication prescriptions</i>	
immunosuppressants (excluding corticosteroids)	L04A
Cough suppressants	R05DA09, R05DB01, R05DB27, R05DB15, R05DA04, N02AA08, R05CA03
Antibiotics	J01A, J01B, J01C, J01D, J01E, J01F, J01G, J01M, J01R, J01X, S01A

ATC: Anatomical Therapeutic Chemical; COPD: chronic obstructive pulmonary disease; GERD: Gastro-esophageal reflux disease; ICD-10: International Classification of Diseases, 10th revision; URTI: Upper respiratory tract infection.

Supplementary Table 2. Multivariate logistic regression analysis of potential risk factors for pertussis among individuals aged between 50–64 years between 2009–2018

	Odds ratio (95% CI)	
	Crude	Adjusted ^a
Respiratory conditions within 12 months prior to index date		
Asthma	7.03 (5.71–8.65)	1.87 (1.41–2.48)
COPD	6.25 (3.84–10.18)	2.24 (1.18–4.29)
Pertussis-like clinical conditions within 30 days prior to index date		
Acute bronchitis	19.58 (15.83–24.21)	5.08 (3.80–6.80)
Allergic rhinitis	14.09 (11.34–17.50)	1.44 (1.04–1.99)
Pneumonia	43.04 (25.76–71.91)	5.24 (2.86–9.62)
URTI	13.37 (10.93–16.34)	3.08 (2.32–4.09)
Other medical conditions within 12 months prior to index date		
Cancer	1.90 (1.30–2.77)	1.24 (0.77–1.98)
Cardiovascular disease	2.30 (1.87–2.85)	1.22 (0.90–1.64)
Cerebrovascular disease	1.64 (1.12–2.40)	1.11 (0.70–1.08)
Diabetes	1.67 (1.33–2.09)	0.82 (0.60–1.12)
GERD	5.06 (4.22–6.07)	2.44 (1.94–3.07)
Hyperlipidemia	2.53 (2.11–3.03)	1.39 (1.06–1.83)
Hypertension	1.43 (1.19–1.72)	0.79 (0.61–1.02)
Autoimmune disease	3.37 (2.82–4.03)	1.56 (1.24–1.95)
Liver disease	2.47 (2.02–3.02)	1.14 (0.86–1.51)
Renal disease	2.04 (1.40–2.98)	1.27 (0.77–2.10)
Co-medications within 12 months prior to index date		
Immunosuppressive drugs (excluding corticosteroids)	4.50 (2.38–8.51)	1.46 (0.61–3.52)

558 pertussis cases and 5,452 matched controls were included in this analysis. [a] The multivariate model adjusted for each of the characteristics, including comorbidities, co-medications assessed within 12 months prior to index date and pertussis-like clinical conditions assessed within 30 days of index date. Significant values ($p < 0.05$) are shown in bold. CI: confidence interval; COPD: chronic obstructive pulmonary disease; GERD: gastroesophageal reflux disease; URTI: upper respiratory tract infection.

Supplementary Table 3. Multivariate logistic regression analysis of potential risk factors for pertussis among individuals aged ≥65 years between 2009–2018

	Odds ratio (95% CI)	
	Crude	Adjusted ^a
Respiratory conditions within 12 months prior to index date		
Asthma	13.06 (10.38–16.43)	2.34 (1.65–3.30)
COPD	10.57 (7.64–14.62)	2.18 (1.32–3.63)
Pertussis-like clinical conditions within 30 days prior to index date		
Acute bronchitis	32.68 (25.03–42.68)	4.44 (2.98–6.62)
Allergic rhinitis	31.47 (23.93–41.37)	2.19 (1.41–3.41)
Pneumonia	145.53 (70.20–301.69)	17.39 (7.38–40.98)
URTI	19.74 (15.36–25.37)	2.64 (1.74–4.00)
Other medical conditions within 12 months prior to index date		
Cancer	5.82 (4.21–8.05)	2.35 (1.50–3.66)
Cardiovascular disease	7.23 (5.89–8.87)	2.10 (1.52–2.89)
Cerebrovascular disease	3.34 (2.57–4.34)	1.03 (0.71–1.50)
Diabetes	4.68 (3.80–5.76)	1.00 (0.73–1.38)
GERD	11.32 (9.16–13.99)	2.87 (2.15–3.84)
Hyperlipidemia	6.66 (5.43–8.17)	1.55 (1.12–2.16)
Hypertension	6.10 (4.92–7.54)	1.30 (0.93–1.81)
Autoimmune disease	6.95 (5.66–8.52)	1.34 (1.00–1.80)
Liver disease	5.97 (4.80–7.43)	1.03 (0.74–1.44)
Renal disease	5.21 (3.78–7.18)	1.75 (1.11–2.77)
Co-medications within 12 months prior to index date		
Immunosuppressive drugs (excluding corticosteroids)	8.95 (3.93–20.40)	3.82 (1.24–11.75)

446 pertussis cases and 4,258 matched controls were included. [a] The multivariate model adjusted for each of the characteristics, including comorbidities, co-medications assessed within 12 months prior to index date and pertussis-like clinical conditions assessed within 30 days of index date. Significant values ($p < 0.05$) are shown in bold. CI: confidence interval; COPD: chronic obstructive pulmonary disease; GERD: gastroesophageal reflux disease; URTI: upper respiratory tract infection.

Supplementary Table 4. Baseline characteristics of pertussis cases after matching data period between HIRA data and NHIS-NSC (2009–2015) (Sensitivity analysis)

	Pertussis ^a (n=446)		Control ^b (n=4,451)		Overall (n=4,897)	
	n	%	n	%	n	%
Age						
Mean (SD)	60.6 (8.5)		60.8 (8.6)		60.7 (8.6)	
50–54	128	28.7	1,279	28.7	1,407	28.7
55–59	111	24.9	1,110	24.9	1,221	24.9
60–64	74	16.6	739	16.6	813	16.6
65–69	58	13.0	580	13.0	638	13.0
70–74	40	9.0	400	9.0	440	9.0
75+	35	7.9	343	7.7	378	7.7
Sex						
Female	294	65.9	2,939	66.0	3,233	66.0
Male	152	34.1	1,512	34.0	1,664	34.0
Region						
Metropolitan	130	29.2	1,300	29.2	1,430	29.2
Urban area	214	48.0	2,131	47.9	2,345	47.9
Rural area	102	22.9	1,020	22.9	1,122	22.9
Comorbidities within 12 months prior to index date						
Asthma	112	25.1	515	11.6	627	12.8
Cancer	27	6.1	247	5.6	274	5.6
Cardiovascular disease	123	27.6	1,077	24.2	1,200	24.5
Cerebrovascular disease	34	7.6	401	9.0	435	8.9
COPD	27	6.1	108	2.4	135	2.8
Diabetes	91	20.4	1,062	23.9	1,153	23.6
GERD	189	42.4	1,179	26.5	1,368	27.9
Hyperlipidemia	168	37.7	1,583	35.6	1,751	35.8
Hypertension	198	44.4	2,109	47.4	2,307	47.1
Autoimmune disease	179	40.1	1,513	34.0	1,692	34.6
Liver disease	117	26.2	1,010	22.7	1,127	23.0
Renal disease	24	5.4	257	5.8	281	5.7
Co-medications						
Immunosuppressive drugs (excluding corticosteroids)	5	1.1	33	0.7	38	0.8
Pertussis-like clinical conditions within 30 days prior to index date						
Acute bronchitis	184	41.3	336	7.6	520	10.6
Allergic rhinitis	124	27.8	320	7.2	444	9.1
Pneumonia	36	8.1	27	0.6	63	1.3
URTI	183	41.0	465	10.5	648	13.2

Each pertussis case was matched up to 10 controls by age group, sex, and geographic region at index date. [a] Among 1,011 cases, 7 cases were not matched with at least one control. [b] Due to limited available data period of NHIS-NSC, controls in 2015 were matched with the cases diagnosed between 2015 and 2018. COPD: chronic obstructive pulmonary disease; GERD: gastroesophageal reflux disease; HIRA: Health Insurance Review and Assessment service; SD: standard deviation; NHIS-NSC: National Health Insurance Service – National Sample Cohort; URTI: upper respiratory tract infection.

Supplementary Table 5. Multivariate logistic regression analysis of potential risk factors for pertussis among individuals 50–64 years after matching data period between HIRA data and NHIS-NSC (2009–2015; sensitivity analysis)

	Odds ratio (95% CI)	
	Crude	Adjusted ^a
Respiratory conditions within 12 months prior to index date		
Asthma	2.65 (1.99–3.51)	1.39 (1.00–1.95)
COPD	2.93 (1.53–5.63)	2.43 (1.13–5.20)
Pertussis-like clinical conditions within 30 days prior to index date		
Acute bronchitis	9.31 (7.17–12.09)	4.90 (3.53–6.79)
Allergic rhinitis	5.28 (3.99–6.99)	1.00 (0.69–1.46)
Pneumonia	12.38 (6.62–23.13)	3.45 (1.66–7.16)
URTI	6.61 (5.14–8.50)	3.02 (2.21–4.14)
Other medical conditions within 12 months prior to index date		
Cancer	1.05 (0.63–1.76)	1.03 (0.58–1.82)
Cardiovascular disease	1.07 (0.80–1.43)	1.18 (0.84–1.67)
Cerebrovascular disease	0.67 (0.67–1.21)	0.69 (0.36–1.33)
Diabetes	0.69 (0.50–0.95)	0.62 (0.42–0.91)
GERD	1.94 (1.53–2.48)	1.59 (1.21–2.09)
Hyperlipidemia	1.06 (0.83–1.35)	1.06 (0.77–1.46)
Hypertension	0.87 (0.68–1.10)	0.90 (0.67–1.20)
Autoimmune disease	1.35 (1.06–1.71)	1.02 (0.78–1.34)
Liver disease	1.12 (0.86–1.48)	1.08 (0.78–1.51)
Renal disease	0.82 (0.46–1.45)	0.87 (0.45–1.68)
Co-medications within 12 months prior to index date		
Immunosuppressive drugs (excluding corticosteroids)	1.54 (0.54–4.45)	1.33 (0.41–4.28)

239 pertussis cases and 2,389 matched controls were included in this analysis. [a] The multivariate model adjusted for each of the characteristics, including comorbidities, co-medications assessed within 12 months prior to index date and pertussis-like clinical conditions assessed within 30 days of index date. Significant values ($p < 0.05$) are shown in bold. CI: confidence interval; COPD: chronic obstructive pulmonary disease; GERD: gastroesophageal reflux disease; HIRA: Health Insurance Review and Assessment service; NHIS-NSC: National Health Insurance Service – National Sample Cohort; URTI: upper respiratory tract infection.

Supplementary Table 6. Multivariate logistic regression analysis of potential risk factors for pertussis among individuals ≥65 years after matching data period between HIRA data and NHIS-NSC (2009–2015; sensitivity analysis)

	Odds ratio (95% CI)	
	Crude	Adjusted ^a
Respiratory conditions within 12 months prior to index date		
Asthma	2.42 (1.60–3.64)	1.46 (0.89–2.38)
COPD	2.42 (1.34–4.38)	1.97 (0.98–3.95)
Pertussis-like clinical conditions within 30 days prior to index date		
Acute bronchitis	7.14 (4.78–10.68)	4.39 (2.59–7.43)
Allergic rhinitis	4.29 (2.76–6.67)	0.89 (0.48–1.63)
Pneumonia	19.34 (7.95–47.03)	7.74 (2.88–20.80)
URTI	4.66 (3.14–6.91)	2.34 (1.37–4.00)
Other medical conditions within 12 months prior to index date		
Cancer	1.18 (0.60–2.34)	1.16 (0.55–2.44)
Cardiovascular disease	1.44 (1.01–2.06)	1.60 (1.03–2.47)
Cerebrovascular disease	0.97 (0.60–1.56)	0.98 (0.57–1.69)
Diabetes	1.04 (0.72–1.52)	0.76 (0.48–1.21)
GERD	2.31 (1.61–3.31)	1.94 (1.29–2.91)
Hyperlipidemia	1.18 (0.82–1.69)	1.01 (0.64–1.59)
Hypertension	0.91 (0.63–1.31)	0.76 (0.49–1.18)
Autoimmune disease	1.20 (0.84–1.73)	0.75 (0.49–1.14)
Liver disease	1.42 (0.96–2.09)	1.09 (0.68–1.77)
Renal disease	1.12 (0.58–2.14)	0.93 (0.43–2.03)
Co-medications within 12 months prior to index date		
Immunosuppressive drugs (excluding corticosteroids)	1.43 (0.17–11.67)	2.49 (0.29–21.61)

207 pertussis cases and 2,062 matched controls were included in this analysis. [a] The multivariate model adjusted for each of the characteristics, including comorbidities, co-medications assessed within 12 months prior to index date and pertussis-like clinical conditions assessed within 30 days of index date. Significant values ($p < 0.05$) are shown in bold. CI: confidence interval; COPD: chronic obstructive pulmonary disease; GERD: gastroesophageal reflux disease; HIRA: Health Insurance Review and Assessment service; NHIS-NSC: National Health Insurance Service – National Sample Cohort; URTI: upper respiratory tract infection.

Supplementary Table 7. Baseline characteristics and multivariate logistic regression analysis of potential risk factors for pertussis between 2009–2018 (sensitivity analysis using separate models for chronic and acute medical events)

	Pertussis ^a (n=1,004)		Control ^b (n=9,710)		Adjusted odds ratio (95% CI) ^c	
	n	%	n	%		
Age						
Mean (SD)	64.2 (10.4)		65.0 (10.6)			
50–54	214	21.3	2,112	21.8	-	-
55–59	195	19.4	1,916	19.7	-	-
60–64	149	14.8	1,424	14.7	-	-
65–69	137	13.7	1,300	13.4	-	-
70–74	106	10.6	996	10.3	-	-
75+	203	20.2	1,962	20.2	-	-
Sex						
Female	614	61.2	5,968	61.5	-	-
Male	390	38.8	3,742	38.5	-	-
Region						
Metropolitan	219	21.8	2,088	21.5	-	-
Urban area	386	38.5	3,774	38.9	-	-
Rural area	399	39.7	3,848	39.6	-	-
Respiratory conditions within 12 months prior to index date						
Asthma	371	37.0	577	5.9	4.59 (3.86–5.45)	
COPD	106	10.6	129	1.3	1.56 (1.19–2.05)	
Pertussis-like clinical conditions within 30 days prior to index date						
Acute bronchitis	464	46.2	339	3.5	14.66 (11.83–18.16)	
Allergic rhinitis	401	39.9	323	3.3	3.24 (2.63–4.00)	
Pneumonia	169	16.8	27	0.3	13.15 (8.89–19.45)	
URTI	438	43.6	468	4.8	1.07 (0.86–1.31)	
Other medical conditions within 12 months prior to index date						
Cancer	97	9.7	297	3.1	1.70 (1.43–2.01)	
Cardiovascular disease	381	38.0	1,281	13.2	1.19 (0.93–1.53)	
Cerebrovascular disease	121	12.1	493	5.1	1.77 (1.29–2.44)	
Diabetes	296	29.5	1,260	13.0	1.02 (0.85–1.21)	
GERD	542	54.0	1,365	14.1	3.28 (2.83–3.81)	
Hyperlipidemia	482	48.0	1,867	19.2	2.07 (1.77–2.42)	
Hypertension	494	49.2	2,557	26.3	0.70 (0.60–0.82)	
Autoimmune disease	495	49.3	1,703	17.5	2.08 (1.79–2.42)	
Liver disease	324	32.3	1,134	11.7	2.79 (2.33–3.33)	
Renal disease	96	9.6	300	3.1	1.89 (1.40–2.55)	
Co-medications within 12 months prior to index date						
Immunosuppressive drugs (excluding corticosteroids)	25	2.5	43	0.4	1.37 (0.78–2.42)	

Each pertussis case was matched up to 10 controls by age group, sex, and geographic region at index date. [a] Among 1,011 cases, 7 cases were not matched with at least one control. [b] Due to limited available data period of NHIS-NSC, controls in 2015 were matched with the cases diagnosed between 2015 and 2018. [c] Separate multivariate models adjusted for comorbidities and co-medications assessed within 12 months prior to index date, and pertussis-like clinical conditions assessed within 30 days prior to index date. CI: confidence interval; COPD: chronic obstructive pulmonary disease; GERD: gastroesophageal reflux disease; NHIS-NSC: National Health Insurance Service – National Sample Cohort; SD: standard deviation; URTI: upper respiratory tract infection.