

Appendix 1 (as supplied by the authors)

Table S1: Search strategy for observational studies of type 2 diabetes and the risk of community-acquired pneumonia – MEDLINE.

Table 1: search strategy in MEDLINE	
Search number	Search terms
1	exp Diabetes mellitus, Type 2/ (132680)
2	type 2 diabet*.mp. (134567)
3	type two diabet*.mp. (184)
4	Diabetes Mellitus/ (117098)
6	diabet*.mp. (695862)
6	insulin resistance/ (56764)
7	insulin resist*.mp. (98773)
8	glyc?emic control*.mp. (33034)
9	non insulin dependent diabet*.mp (10036)
10	t2dm.ti, ab, kw. (20698)
11	hypoglycemia/ (27321)
12	hypoglyc?emia.mp. (48884)
13	hyperglycemia/ (27918)
14	hyperglyc?emia.mp. (64499)
15	exp PNEUMONIA/ (102059)
16	community acquired pneumonia.mp. (9902)
17	respiratory tract infections/ (38391)
18	Community-Acquired Infections/ (14167)
19	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 (342105)

20	15 or 16 or 17 or 18 (785273)
21	19 and 20 (1763)

Table S2: Exposure and outcome definitions of included studies of association between type 2 diabetes and community-acquired pneumonia.

Author, year	Exposure	Exposure definition	Primary Outcome	Outcome definition
Cohort studies				
Jackson, 2004	Diabetes	Any inclusion in the Group Health Cooperative diabetes registry	Community-acquired pneumonia hospitalization	International classification for disease 9 clinical modification (ICD-9-CM) codes: 480 – 487.0, 038.0, 038.2, 041.0, 041.2, 320.1
Muller, 2005	Type 2 diabetes	International classification primary care (ICPC) code DM1 (T90.1) or DM2 (T90.2)	Pneumonia	ICPC code: pneumonia (R81)
O’Meara, 2005	Diabetes	Diabetes mellitus at baseline from fasting plasma glucose of at least 126mg/dL or the use of insulin or oral hypoglycemic agents	Pneumonia hospitalization	ICD-9-CM codes: 481.482, 486
Benfield, 2007	Diabetes	Self-reported	Pneumonia hospitalization	International classification for disease 8 (ICD-8) code : 480 – 486 ICD-10 codes : A48.1, J12 – J18
Ehrlich, 2010	Diabetes	Inclusion in the KPNC diabetes registry according to 1) pharmacy prescriptions	Pneumonia hospitalization	ICD-9 codes: 480-486

Author, year	Exposure	Exposure definition	Primary Outcome	Outcome definition
		for antidiabetic agents, 2) abnormal A1c values, primary or secondary hospital discharge of diabetes and 4) emergency department visits with a diagnosis of diabetes		
Hamilton, 2013	Type 2 diabetes	Fasting plasma glucose (>7.8 mmol/l until 1999 and >7.0 mmol/l thereafter) urine samples	Pneumonia hospitalization	ICD-9-clinical modification (CM) code :480.1, 480.2 480.8, 480.9, 481, 482.0–.9, 483.0, 485, 486 ICD-10 codes: J12.1, J12.2, J12.8, J12.9, J13, J14, J15.0, J15.1, J15.3, J15.4, J15.5, J15.6, J15.7, J15.8, J15.9, J18.0, J18.8, J18.9
Seminog LHES, 2013	Diabetes	ICD-7 code: 260, ICD-8 code: 250 ICD-9 code: 250 ICD-10 codes: E10–E14	Pneumonia	ICD-10 codes J13, pneumonia specified as <i>S. pneumoniae</i> ; A40.3, septicaemia attributable to <i>S. pneumoniae</i> ; and G00.1
Seminog ORLS1, 2013	Diabetes	Idem	Pneumonia	Idem

Author, year	Exposure	Exposure definition	Primary Outcome	Outcome definition
Seminog ORLS2, 2013	Diabetes	Idem	Pneumonia	Idem
Hine, 2017	Type 2 diabetes	Diagnostic, biochemical and prescription data entered before January 1 2014 (cohort entry)	Pneumonia	read code H20-28
Lopez de Andres, 2017	Type 2 diabetes	ICD-9-CM codes: 250.x0, 250.x2	Community-acquired pneumonia hospitalization	ICD-9-CM codes: 480–488, 507.0– 507.8
Ray, 2017	Diabetes	The presence of diabetes mellitus in clinical notes	Pneumonia	medical record review of culture results
Williams, 2017	Diabetes	Read codes for diabetes at baseline	Community-acquired pneumonia	ICD-10 codes (not further specified)
Case-control studies				
Farr, 2000	Diabetes	Self-reported	Pneumonia	Acute lower respiratory tract infection for which an antibiotic was prescribed associated with new focal signs on chest examination and new radiographic pulmonary shadowing
Thomsen, 2004	Type-2 diabetes	Previous hospitalization with diabetes or earlier prescriptions for insulin or an oral antidiabetic drug	Community-acquired pneumonia	Patients older than 15 years with a first hospitalization for community-acquired

Author, year	Exposure	Exposure definition	Primary Outcome	Outcome definition
				pneumococcal bacteremia
Van de Garde, 2006	Diabetes	Recorded use of oral antidiabetic agents and/or insulin	Community-acquired pneumonia hospitalization	Primary discharge diagnosis: ICD-9-CM codes: 481, 482, 485, 486 or Patients with a signature of bacterial pneumonia (secondary discharge diagnosis) coupled with a primary pulmonary diagnosis ICD-9-CM codes: 491–493 or 496
Kornum, 2008	Type 2 diabetes	ICD-8 codes: 249– 250 ICD-10 codes: E10–E14 , O24 (diabetes in pregnancy except for O24.4	Pneumonia hospitalization	ICD-10 codes: J12.x – J18.x ICD-8 codes: not mentioned

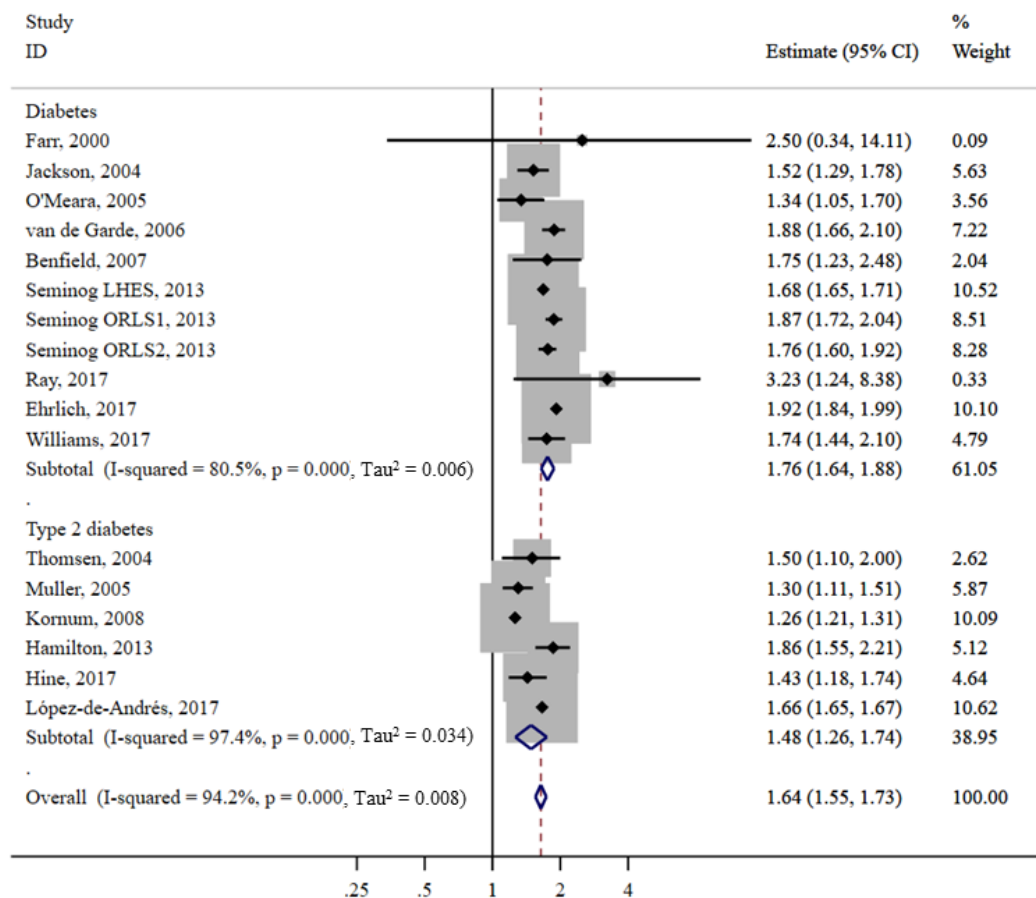
Abbreviations: KPNC: Kaiser Permanente Medical Care Program in Northern California, LHES=Linked English Hospital Statistics, ORLS=Oxford Record Linkage Study

Table S3: Quality assessment of studies examining the association between type 2 diabetes and risk of community-acquired pneumonia.

Study	Outcome	Confounding	Selection of participants into the study	Classification of interventions	Deviations from intended intervention	Missing data	Measurement of outcomes	Reported result	Overall
Cohort study									
Jackson, 2004	Community-acquired pneumonia hospitalization	Serious	Low	Low	Serious	Moderate	Moderate	Moderate	Serious
Muller, 2005	Infections including Pneumonia	Serious	Serious	Low	Serious	Low	Serious	Serious	Serious
O'Meara, 2005	Pneumonia hospitalization	Serious	Low	Moderate	Low	Low	Moderate	Moderate	Serious
Benfield, 2007	Pneumonia related death	Serious	Moderate	Low	Low	Low	Serious	Serious	Serious
Ehrlich, 2010	Pneumonia	Serious	Moderate	Moderate	Low	Moderate	Moderate	Moderate	Serious
Hamilton, 2013	Pneumonia	Serious	Serious	Moderate	Low	Low	Serious	Moderate	Serious
Seminog, 2013	Pneumonia	Serious	Moderate	Low	Low	Low	Serious	Moderate	Serious
Hine, 2017	Pneumonia	Serious	Moderate	Low	Low	Moderate	Serious	Serious	Serious
Lopez-de-Andres, 2017	Community-acquired pneumonia hospitalization	Serious	Low	Low	Low	Moderate	Low	Moderate	Serious
Ray, 2017	Pneumonia	Serious	Moderate	Low	Serious	Serious	Serious	Serious	Serious

Williams, 2017	Community-acquired pneumonia	Serious	Serious	Low	Low	Low	Low	Moderate	Serious
Case-control study									
Farr, 2000	Pneumonia	Serious	Moderate	Moderate	Low	Moderate	Low	Moderate	Serious
Thomsen, 2004	Hospitalization for CAP	Serious	Serious	Low	Low	Serious	Serious	Serious	Serious
van de Garde, 2006	Community-acquired pneumonia	Serious	Moderate	Low	Low	Low	Low	Moderate	Serious
Kornum, 2008	Pneumonia Hospitalization	Serious	Low	Low	Low	Low	Moderate	Moderate	Serious

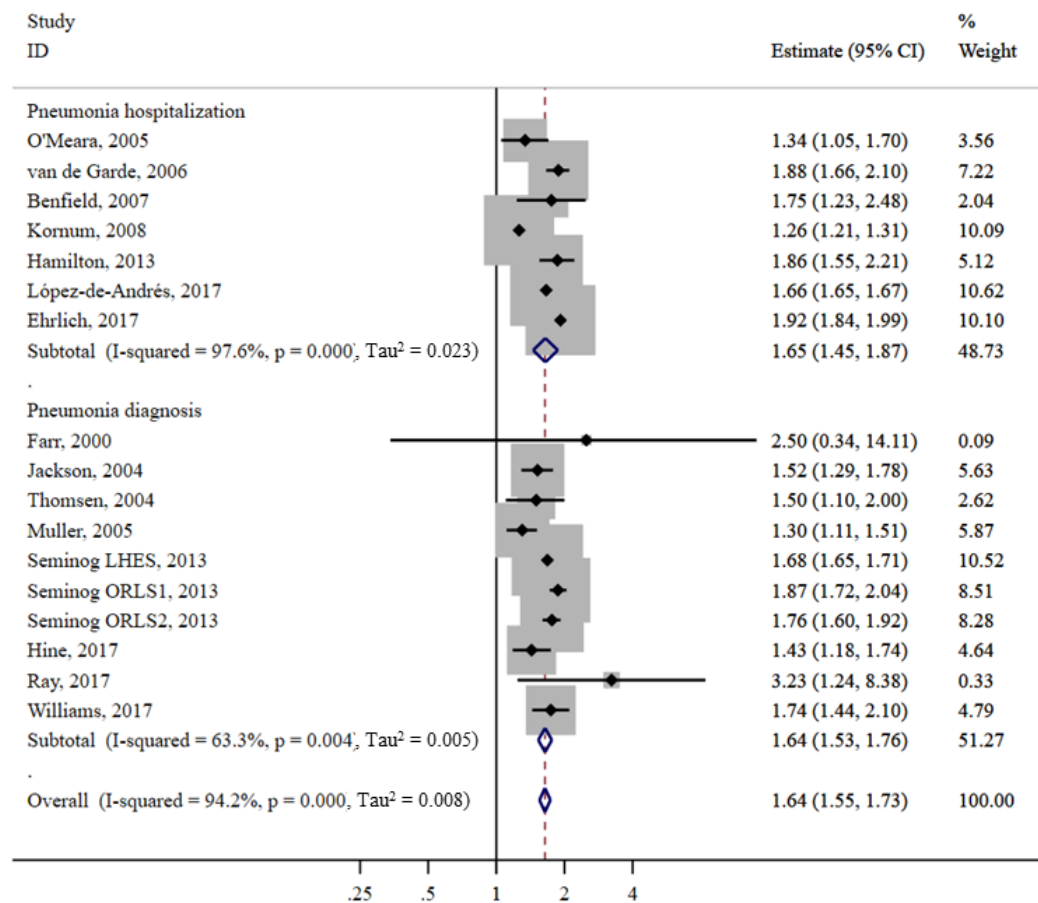
Figure S1: Forest plot of association between type 2 diabetes and risk of community-acquired pneumonia by exposure definition.



Abbreviations: LHES=Linked English Hospital, ORLS=Oxford Record Linkage Study.

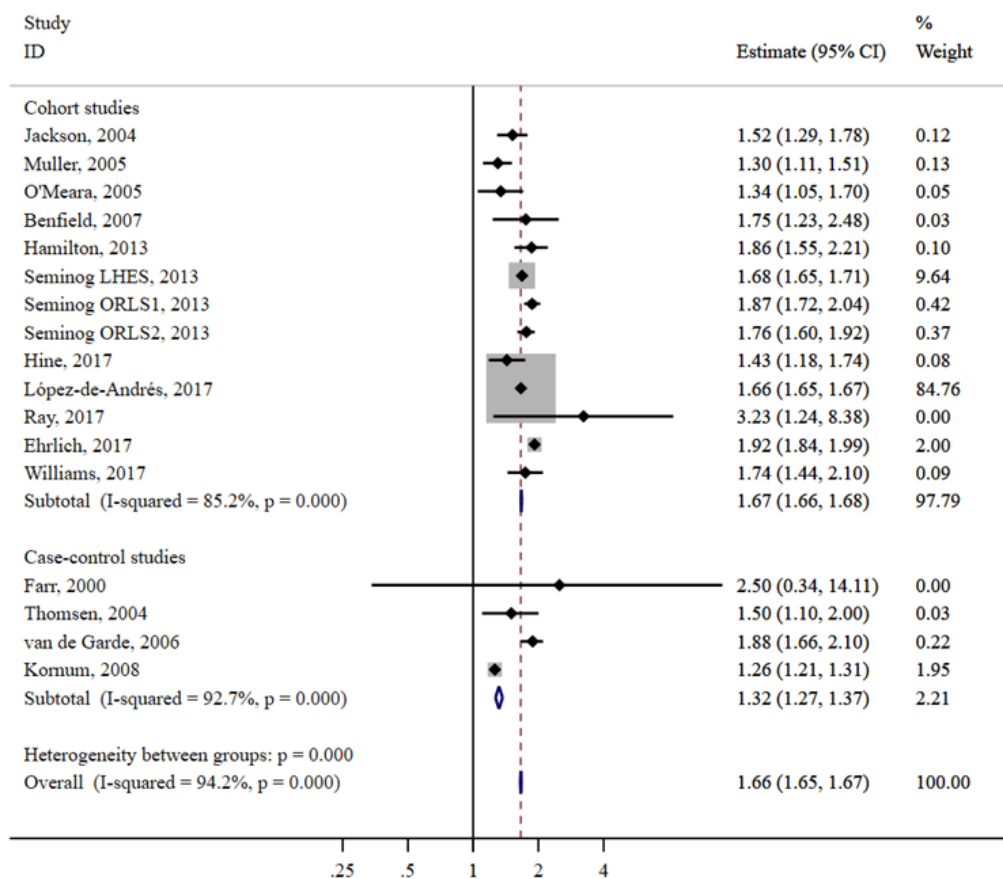
The 95% prediction intervals were 1.43, 2.17 for studies of diabetes in general and 0.90, 2.42 for studies of type 2 diabetes.

Figure S2: Forest plot of association between type 2 diabetes and risk of community-acquired pneumonia by outcome definition.



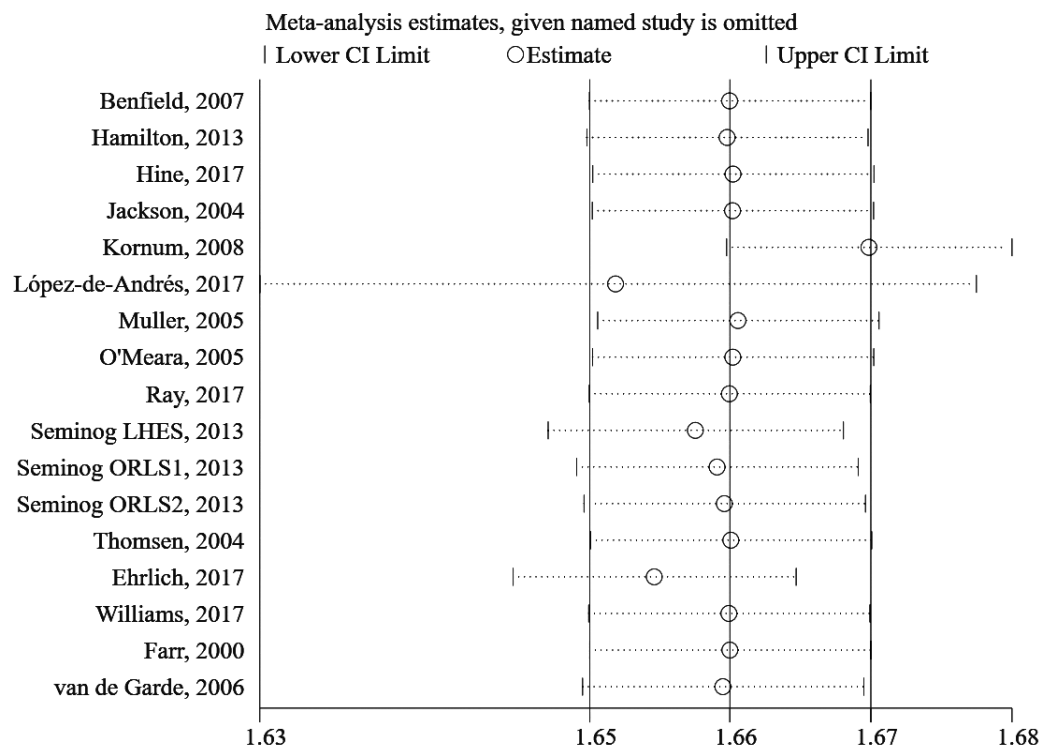
Abbreviations: LHES=Linked English Hospital, ORLS=Oxford Record Linkage Study The 95% prediction intervals were 1.10, 2.47 for studies with the outcome defined by pneumonia hospitalization and 1.34, 2.00 for studies with the outcome defined by a diagnosis of pneumonia.

Figure S3: Forest plot of association between type 2 diabetes and risk of community-acquired pneumonia using fixed-effects model.



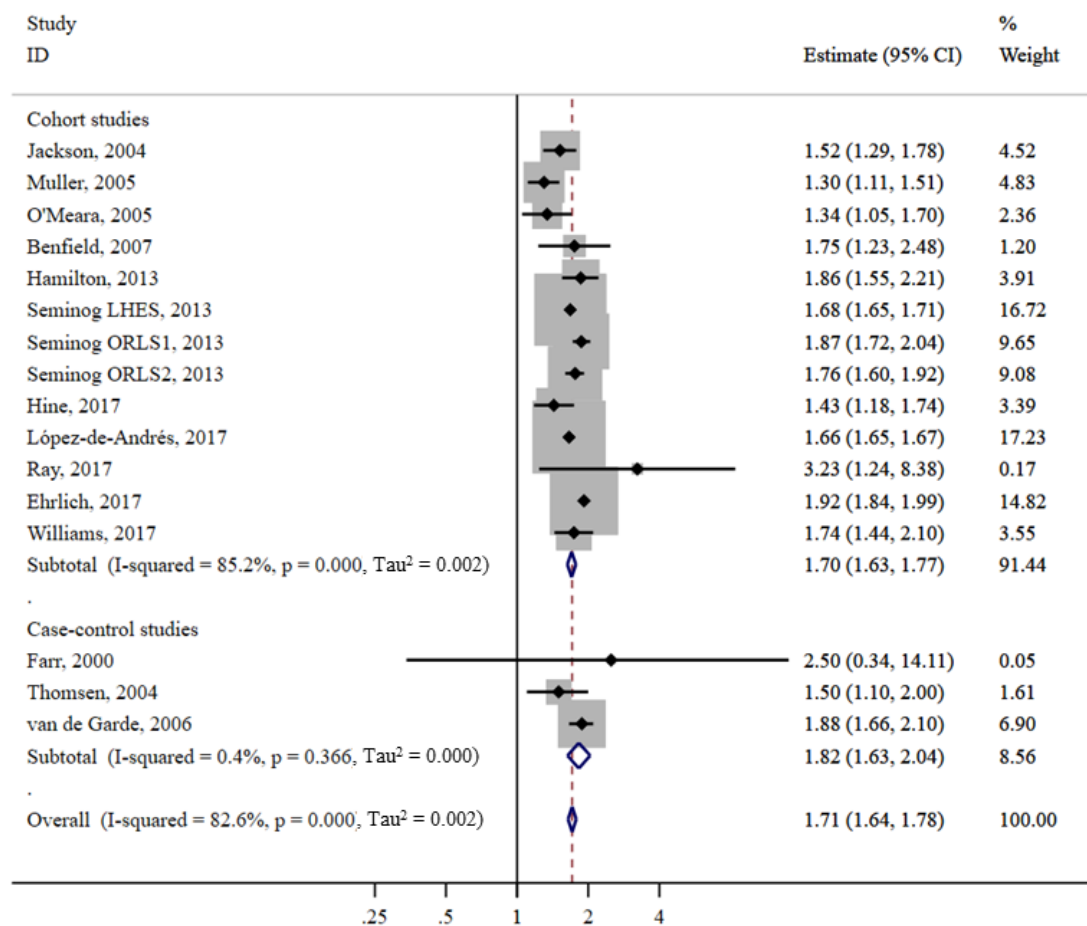
Abbreviations: LHES=Linked English Hospital, ORLS=Oxford Record Linkage Study

Figure S4: Influence analysis



Abbreviations: CI= confidence interval, LHES=Linked English Hospital, ORLS=Oxford Record Linkage Study

Figure S5: Forest plot of association between type 2 diabetes and risk of community-acquired pneumonia excluding study by Kornum et al. (2008).



Abbreviations: LHES=Linked English Hospital, ORLS=Oxford Record Linkage Study

The 95% prediction intervals were 1.51, 1.92 for cohort studies, 1.59, 2.11 for case-control studies, and 1.51, 1.93 overall.

Figure S6: Funnel plot for assessment of small-study effects (publication bias) of included studies on type 2 diabetes and community-acquired pneumonia.

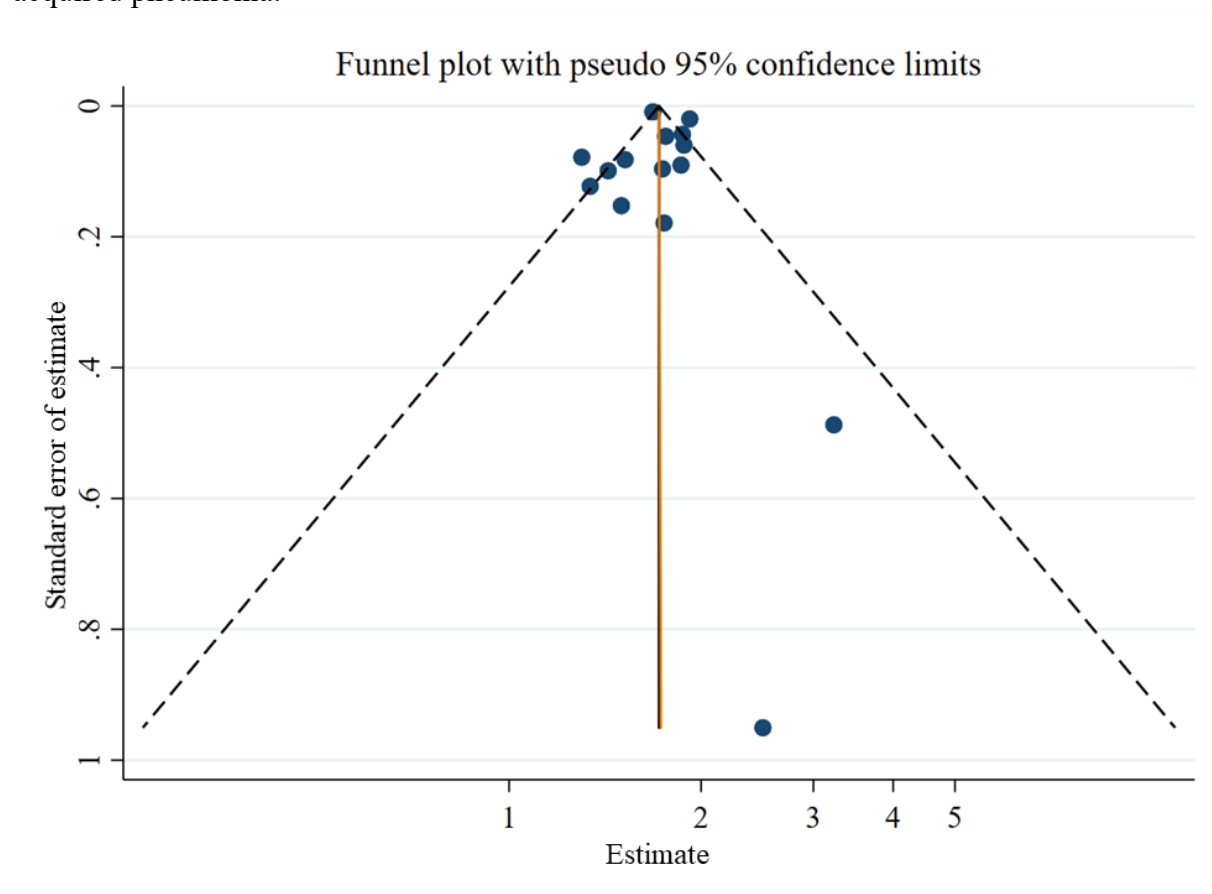


Table S4: Sensitivity analysis converting odds ratios to risk ratios using the approach described by the Cochrane collaboration. ¹

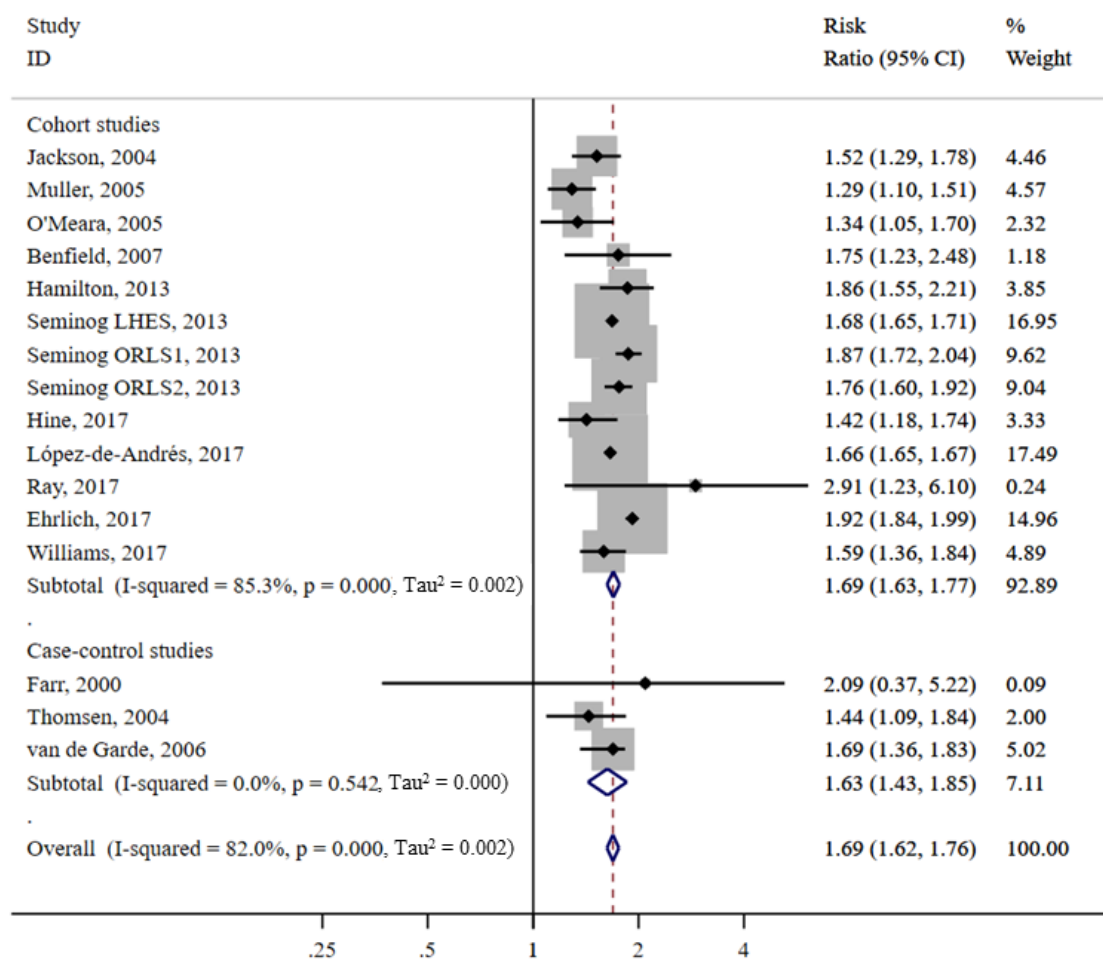
Author, Year	Reported OR (95% CI)	Calculated RR (95% CI)
Farr, 2000	2.50 (0.34, 14.11)	2.10 (0.32, 10.82)
Thomsen, 2004	1.50 (1.1, 2.00)	1.44 (1.09, 1.84)
Muller, 2005	1.30 (1.11, 1.52)	1.29 (1.10, 1.51)
van de Garde, 2006	1.88 (1.66, 2.10)	1.85 (1.64, 2.01)
Kornum, 2008	1.26 (1.21, 1.31)	1.23 (1.19, 1.27)
Hine, 2017	1.43 (1.18, 1.74)	1.42 (1.18, 1.74)
Ray, 2017	3.23 (1.24, 8.38)	2.91 (1.23, 6.10)
Williams, 2017	1.74 (1.44, 2.10)	1.71 (1.40, 1.95)

Abbreviations: CI= confidence interval, OR=odds ratio, RR=relative risk

References:

- 1) Deeks JJ, H.J., Altman DG, Chapter 10: Analysing data and undertaking meta-analyses., in Cochrane Handbook for Systematic Reviews of Interventions version 6.0 T.J. Higgins JPT, Chandler J, Cumpston M, Li T, Page MJ, Welch VA, Editor. 2019, Cochrane
- 2) Grant, R.L., Converting an odds ratio to a range of plausible relative risks for better communication of research findings. *BMJ : British Medical Journal*, 2014. 348: p. f7450.

Figure S7: Forest plot of association between type 2 diabetes and risk of community-acquired pneumonia after converting odds ratios to risk ratios.



Abbreviations: LHES=Linked English Hospital, ORLS=Oxford Record Linkage Study. The 95% prediction intervals were 1.50, 1.91 for cohort studies, 1.39, 1.91 for case-control studies, and 1.50, 1.91 overall.