

TITLE: Understanding the global burden of influenza in adults aged 18–64 years: A systematic literature review from 2012 to 2022.

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Table S1. Electronic database search strategy.

#	Query	Results from September 20 th 2022	
1	Influenza terms	exp influenza/	100,437
2		exp influenza A/ or exp Influenza A virus/	43,042
3		exp influenza B/ or exp Influenza B virus/	5,661
4		exp seasonal influenza/	7,036
5		(flu or influenza*).mp.	226,346
6		or/1-5	226,346
7	Clinical burden terms	exp *hospitalization/ or exp *outpatient care/ or exp *outpatient/ or exp *outpatient department/ or exp *hospital patient/ or exp *general practice/ or exp *emergency ward/ or exp *"length of stay"/	204,253
8		*epidemiology/ or *morbidity/ or *mortality/ or *prevalence/ or *incidence/	282,848
9		exp *"pharmacy (shop)"/ or exp *non prescription drug/ or exp *self medication/ or exp *clinical pathway/	23,458
10		exp *social care/ or exp *home care/ or exp *long term care/ or *nursing home/ or exp *elderly care/	245,286
11		(over adj3 counter).ti,ab.	14,762
12		breakthrough.ti,ab.	34,884
13		((social or home or elderly or follow*) adj3 care).ti,ab.	100,683
14		(hospitalization or outpatient or inpatient or (length adj5 stay) or (general adj3 practice) or (emergency adj3 (ward or department))) .ti,ab.	722,449
15		(disease adj4 (burden or impact)).ti,ab.	96,554
16		(epidemiology or morbidity or mortality or prevalence or incidence).ti.	634,276
17		or/7-16	1,908,457
18	Humanistic burden terms	exp "quality of life"/ or exp quality adjusted life year/ or exp disability-adjusted life year/ or exp absenteeism/ or exp "European Quality of Life 5 Dimensions questionnaire"/	617,188
19		("quality of life" or QoL or patient reported outcome* or ((patient or emotional or treatment) adj3 (satisfaction or dissatisfaction or response)) or "health related quality of life" or HRQoL).ti,ab.	818,866
20		(eq adj3 5d).ti,ab.	20,486
21		exp sleep quality/ or exp sleep/	270,800
22		or/18-21	1,252,181
23	Economic burden terms	exp *health economics/	290,861
24		exp *"cost of illness"/ or exp *"hospital cost"/ or exp *"hospitalization cost"/ or exp *"cost control"/ or exp	116,776

		*"drug cost"/ or exp *"health care cost"/ or exp *health care utilization/ or exp *productivity/ or exp *medical leave/	
25		exp *economic evaluation/ or exp *"cost benefit analysis"/ or exp *"cost effectiveness analysis"/ or exp *"cost utility analysis"/ or exp *cost minimization analysis/	71,275
26		(Cost* or expen* or financ* or price* or pricing or pharmaco-economic* or ((economic or societ* or socioeconomic or socio economic or illness or disease or patient* or caregiver* or carer*) adj2 burden)).ti,ab.	1,358,762
27		((resource* adj2 (utili\$ation or use*)) or productivity or hospitali#ation* or (leave adj2 (medical or sick or disability))).ti,ab.	457,344
28		(cost adj (effective* or utilit* or minimi* or benefit)).ti,ab.	236,078
29		or/23-28	1,877,725
30	Older people terms	exp aged/ or exp elderly care/ or exp pensioner/ or exp retirement/	3,459,591
31		((("65" or "70" or "75" or "80") adj3 year*).mp.	462,544
32		((old* or elder* or retire* or pensioner* or aged) adj3 (patient or person or people)).mp.	254,389
33		or/30-32	3,764,728
34	Countries of interest for economic burden (not used in subtotals)	Italy/ or Spain/ or France/ or United Kingdom/ or Germany/ or United States/ or Brazil/ or Japan/ or China/ or Mexico/ or Saudi Arabia/ or Taiwan/ or Hong Kong/ or South Africa/ or Australia/	2,920,946
35		(Italy or Spain or France or United Kingdom or England or Wales or Scotland or Germany).mp.	1,576,549
36		(United states or USA or Japan or China or Brazil or Mexico or Saudi Arabia or Taiwan or Hong Kong or South Africa or Australia).mp.	3,608,308
37		or/34-36	4,968,203
38	Animal studies	(exp Animal/ or nonhuman/) not exp human/	6,878,040
39	Unwanted study types	exp case study/ or exp case report/ or exp letter/ or exp preliminary communication/ or exp note/ or exp editorial/ or exp editor/ or exp editorial policies/ or exp newspaper/	5,466,378
40	Subtotal of influence and burden terms	6 and (17 or 22 or 29)	39,752
41	Remove animal and study types	40 not (38 or 39)	34,271
42	Conference proceedings prior to 2020	exp conference paper/ or conference abstract/ or (conference adj (abstract or paper or review or proceeding)).pt.	5,311,316
43		limit 42 to yr="1990 - 2019"	4,584,493
44	Child terms	child/	1,967,382

45		pediatrics/	87,481
46		(child* or p?ediatric or "under 18*" or "under 5*" or school or nursery).ti,ab.	2,408,843
47		or/44-46	3,067,953
48	Clinical burden without epidemiology terms	7 or 9 or 10 or 11 or 12 or 13 or 14 or 15	1,260,887
49	Influenza and clinical burden	6 and 48	13,501
50	Influenza and humanistic burden	6 and 22	8,220
51	Influenza and economic burden	6 and 29	19,395
52	Subtotal of influenza and all burden areas	49 or 50 or 51	33,907
53	Removing animal studies, unwanted study types and older conference proceedings	52 not (43 or 38 or 39)	24,399
54	Removing children	53 not 47	16,854
55	Limit to 10 years	limit 54 to yr="2012 -Current"	9,578
56	Remove older people	55 not 33	6,817
57	Remove older people (descriptive terms only)	55 not (30 or 32)	6,970

Study quality and bias assessment results

The study quality and bias assessment tables are presented below, stratified by study type: epidemiology (Table S2), cohort (Table S3), cross-sectional (Table S4), economic (Table S5), and case-control (Table S6). The green, red, orange and gray highlight indicate ‘yes’, ‘no’, ‘unclear’ or ‘NA’ response to each question in the corresponding critical appraisal checklist.

Table S2. JBI quality appraisal of included epidemiology studies

	Was the sample frame appropriate to address the target population?	Were study participants sampled in an appropriate way?	Was the sample size adequate?	Were the study subjects and the setting described in detail?	Was the data analysis conducted with sufficient coverage of the identified sample?	Were valid methods used for the identification of the condition?	Was vaccination confirmation measured in a standard, reliable way for all participants?	Was there appropriate statistical analysis?	Was the response rate adequate, and if not, was the low response rate managed appropriately?	Overall appraisal
Zimmerman et al. 2022(6)										Low risk of bias
Ono et al. 2016(29)										Low risk of bias
Yandrapalli et al. 2018(5)										Low risk of bias

Valenzuela-Mendez et al. 2022(63)										Low risk of bias
Lemaitre et al. 2021(32)										Low risk of bias
Vandroux et al. 2020(46)										Low risk of bias
Joya Montosa et al. 2020(36)										Low risk of bias
Cohen et al. 2012(64)										Low risk of bias
Fuller et al. 2022(3)										Low risk of bias
Tripathi et al. 2020(65)										Low risk of bias
Gounder et al. 2014(26)										Low risk of bias

San-Roman-Montero et al. 2019(27)											Low risk of bias
Boddington et al. 2017(53)											Low risk of bias
Goettler et al. 2022(31)											Low risk of bias
Mohammad et al. 2019(66)											Low risk of bias

Table S3. JBI quality appraisal of included cohort studies

Study	Were the two groups similar and recruited from the same population?	Were the exposures measured similarly to assign people to both exposed and unexposed groups?	Was the exposure measured in a valid and reliable way?	Were confounding factors identified?	Were strategies to deal with confounding factors stated?	Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	Were the outcomes measured in a valid and reliable way?	Was the follow up time reported and sufficient to be long enough for outcomes to occur?	Was follow up complete, and if not, were the reasons to loss to follow up described and explored?	Were strategies to address incomplete follow up utilized?	Was appropriate statistical analysis used?	Overall appraisal
Li et al. 2022(33)												Low risk of bias
Yoshino et al. 2021(43)												Low risk of bias
Schoen et al. 2019(34)												Low risk of bias
Ortiz et al. 2014(4)												Low risk of bias
Benoit et al. 2012(67)												Low risk of bias
Vos et al. 2021Vos, 2021 #986}												Low risk of bias

Chaves et al. 2013(38)												Low risk of bias
Ishida et al. 2022(35)												Low risk of bias
Nam et al. 2020(37)												Low risk of bias
Komeda et al. 2021(68)												Low risk of bias
Hosogaya et al. 2021(49)												Low risk of bias
Yamana et al. 2021(1)												Low risk of bias
Wallick et al. 2021(69)												Low risk of bias

Table S4. JBI quality appraisal of included cross-sectional studies

	Were criteria for inclusion in the sample clearly defined?	Were the study subjects and the setting described in detail?	Was the exposure measured in a valid and reliable way?	Were objective, standard criteria used for measurement of the condition?	Were confounding factors identified?	Were strategies to deal with confounding factors stated?	Were the outcomes measured in a valid and reliable way?	Was appropriate statistical analysis used?	Overall appraisal
Collins et al. 2019(70)									Low risk of bias
Dal Negro et al. 2018(30)									Low risk of bias
Tsuzuki et al. 2020(42)									Unclear
Ahmed et al. 2020(50)									Low risk of bias
Tsai et al. 2014. (47)									Low risk of bias
Chung et al. 2022. (71)									Low risk of bias

Derqui et al. 2022. (2)											Low risk of bias
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Table S5. JBI quality appraisal of included economic evaluation studies

	Is there a well-defined question?	Is there comprehensive description of alternatives?	Are all important and relevant costs and outcomes for each alternative identified?	Has clinical effectiveness been established?	Are costs and outcomes measured accurately?	Are costs and outcomes valued credibly?	Are costs and outcomes adjusted for differential timing?	Is there an incremental analysis of costs and consequences?	Were sensitivity analyses conducted to investigate uncertainty in estimates of costs or consequences?	Do study results include all issues of concern to users?	Are the results generalizable to the setting of interest in the review?	Overall appraisal
Tempia et al. 2019(44)												Low risk of bias
De Miguel et al. 2022(28)												Low risk of bias
Karve et al. 2013(51)												Low risk of bias

Table S6. JBI quality appraisal of included case-control studies

	Were the groups comparable other than the presence of disease in cases or the absence of disease in controls?	Were cases and controls matched appropriately?	Were the same criteria used for identification of cases and controls?	Was exposure measured in a standard, valid and reliable way?	Was exposure measured in the same way for cases and controls?	Were confounding factors identified?	Were strategies to deal with confounding factors stated?	Were outcomes assessed in a standard, valid and reliable way for cases and controls?	Was the exposure period of interest long enough to be meaningful?	Was appropriate statistical analysis used?	Overall appraisal
Samson et al. 2019(39)											Low risk of bias
Tinsley et al. 2019(40)											Low risk of bias

