

Table S1. References of excluded studies

References	Reasons for exclusion
1. Zimmerman, R. K., Dauer, K., Clarke, L., Nowalk, M. P., Raviotta, J. M., & Balasubramani, G. K. (2023). Vaccine effectiveness of recombinant and standard dose influenza vaccines against outpatient illness during 2018-2019 and 2019-2020 calculated using a retrospective test-negative design. <i>Human vaccines & immunotherapeutics</i> , 19(1), 2177461. https://doi.org/10.1080/21645515.2023.2177461	Insufficient information to determine outcomes
2. Skowronski, D. M., Chuang, E. S., Sabaiduc, S., Kaweski, S. E., Kim, S., Dickinson, J. A., Olsha, R., Gubbay, J. B., Zelyas, N., Charest, H., Bastien, N., Jassem, A. N., & De Serres, G. (2023). Vaccine effectiveness estimates from an early-season influenza A(H3N2) epidemic, including unique genetic diversity with reassortment, Canada, 2022/23. <i>Euro surveillance : bulletin European sur les maladies transmissibles = European communicable disease bulletin</i> , 28(5), 2300043. https://doi.org/10.2807/1560-7917.ES.2023.28.5.2300043	Not all strains
3. Panatto, D., Domnich, A., Chironna, M., Loconsole, D., Napoli, C., Torsello, A., Manini, I., Montomoli, E., Pariani, E., Castaldi, S., Orsi, A., Icardi, G., & On Behalf Of The It-Bive-Hosp Network Study Group (2022). Surveillance of Severe Acute Respiratory Infection and Influenza Vaccine Effectiveness among Hospitalized Italian Adults, 2021/22 Season. <i>Vaccines</i> , 11(1), 83. https://doi.org/10.3390/vaccines11010083	Adults not isolated
4. Stuurman, A. L., Levi, M., Beutels, P., Bricout, H., Descamps, A., Dos Santos, G., McGovern, I., Mira-Iglesias, A., Nauta, J., Torcel-Pagnon, L., Biccler, J., & DRIVE consortium (2023). Investigating confounding in network-based test-negative design influenza vaccine effectiveness studies-Experience from the DRIVE project. <i>Influenza and other respiratory viruses</i> , 17(1), e13087. https://doi.org/10.1111/irv.13087	Insufficient information to determine outcomes
5. Tenforde, M. W., Patel, M. M., Lewis, N. M., Adams, K., Gaglani, M., Steingrub, J. S., Shapiro, N. I., Duggal, A., Prekker, M. E., Peltan, I. D., Hager, D. N., Gong, M. N., Exline, M. C., Ginde, A. A., Mohr, N. M., Mallow, C., Martin, E. T., Talbot, H. K., Gibbs, K. W., Kwon, J. H., ... Influenza and Other Viruses in the Acutely Ill (IVY) Network (2023). Vaccine Effectiveness Against Influenza A(H3N2)-Associated Hospitalized Illness: United States, 2022. <i>Clinical infectious diseases : an official publication of the Infectious Diseases Society of America</i> , 76(6), 1030–1037. https://doi.org/10.1093/cid/ciac869	Seasons not isolated
6. Hu, W., Sjoberg, P. A., DeMarcus, L. S., & Robbins, A. S. (2021). Influenza Vaccine Effectiveness Estimates among US Department of Defense Adult Beneficiaries over Four Consecutive Influenza Seasons: A Test-Negative Design Study with Different Control Groups. <i>Vaccines</i> , 10(1), 58. https://doi.org/10.3390/vaccines10010058	Seasons not isolated
7. Maltezou, H. C., Stavros, S., Asimakopoulos, G., Pergialiotis, V., Raftopoulos, V., Talias, M. A., Pavli, A., Daskalakis, G., Sindos, M., Koutroumanis, P., Theodora, M., Antsaklis, P., Kostis, E., Stratiki, E., Kossyvakis, A., Theodoridou, M., Mentis, A., Drakakis, P., Loutradis, D., & Rodolakis, A. (2022). Effectiveness of maternal vaccination with quadrivalent inactivated influenza vaccine in pregnant women and their infants in 2019-2020. <i>Expert review of vaccines</i> , 21(7), 983–992. https://doi.org/10.1080/14760584.2022.2013820	Not RCT or TND

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- Insufficient information to determine outcomes
- Adults not isolated
- Adults not isolated
- Insufficient information to determine outcomes
- Not RCT or TND
- Adults not isolated
- Adults not isolated
- Insufficient information to determine outcomes

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- Adults not isolated
- Adults not isolated
- Adults not isolated
- Insufficient information to determine outcomes
- Adults not isolated
- Insufficient information to determine outcomes
- Adults not isolated

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40. Shang, M., Chung, J. R., Jackson, M. L., Jackson, L. A., Monto, A. S., Martin, E. T., Belongia, E. A., McLean, H. Q., Gaglani, M., Murthy, K., Zimmerman, R. K., Nowalk, M. P., Fry, A. M., & Flannery, B. (2018). Influenza vaccine effectiveness among patients with high-risk medical conditions in the United States, 2012-2016. *Vaccine*, 36(52), 8047-8053. <https://doi.org/10.1016/j.vaccine.2018.10.093>
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- Adults not isolated
- Seasons not isolated
- Adults not isolated
- Adults not isolated
- Insufficient information to determine outcomes
- Adults not isolated
- Insufficient information to determine outcomes
- Not English

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- Not English
- Adults not isolated
- Adults not isolated
- Insufficient information to determine outcomes
- Seasons not isolated
- Not all strains
- Insufficient information to determine outcomes
- Seasons not isolated
- Insufficient information to determine outcomes

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- Insufficient information to determine outcomes
- Not all strains
- Adults not isolated
- Not all strains
- Adults not isolated

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- Adults not isolated
- Insufficient information to determine outcomes
- Adults not isolated
- Adults not isolated

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- Adults not isolated
- Adults not isolated
- Adults not isolated
- Adults not isolated
- Insufficient information to determine outcomes
- Adults not isolated
- Insufficient information to determine outcomes
- Adults not isolated
- Adults not isolated

Table S2. Characteristics of the included RCT studies

(ILI: influenza like illness; ARI: Acute respiratory illness, n: sample size)

Author	Country	Season	Vaccine	Efficacy	Strain mismatch	Symptoms	Age range	Diagnostic tests
Liebowitz 2020	USA	2012-2013	QIV	43%	Matched	ILI	18-65	PCR
Madhi 2014a	South Africa	2011-2012	TIV	50.4%	Mismatched	ARI	18-38	PCR
Madhi 2014b	South Africa	2011-2012	TIV	57.7%	Unclear	ILI	18-38	PCR
Macbride 2017a	Australia	2008-2009	TIV	60.10%	Matched	ILI	18-64	PCR
Macbride 2017b	Australia	2008-2009	TIV	42%	Unclear	ILI	18-64	PCR
Steinhoff 2017a	Nepal	2011-2012	TIV	19%	Matched	ILI	15-40	PCR
Steinhoff 2017b	Nepal	2012-2013	TIV	0%	Unclear	ILI	15-40	PCR
Petrie 2016a	USA	2007-2008	TIV	70%	Matched	ILI	18-49	PCR
Petrie 2016b	USA	2007-2008	LAIIV	38 %	Matched	ILI	18-49	PCR

Table S3. Characteristics of the included TNS studies

(ILI: influenza like illness; ARI: Acute respiratory illness; RT: rapid test)

Author	Country	Season	Vaccine	Effectiveness (95% CI) extracted from the paper	Strain mismatch	Symptoms	Age range	Diagnostic tests
Kissling 2023	Europe	2021-2022	QIV and LAIV	41 (25-64)	Mismatched	ILI and ARI	15-64	PCR
Tenforde 2023	USA	2021-2022	QIV	29 (24-33)	Mismatched	ILI	18-64	PCR
Kim 2022	Canada	2021-2022	QIV	not available	Mismatched	ILI	20-64	PCR
Price 2022	USA	2021-2022	QIV	not available	Mismatched	ILI	18-49	PCR
Richard 2022a	USA	2012-2013	LAIV	not available	Mismatched	ILI	18-64	PCR, RT, culture
Richard 2022b	USA	2013-2014	LAIV	not available	Mismatched	ILI	18-64	PCR, RT, culture
Richard 2022c	USA	2014-2015	LAIV	not available	Mismatched	ILI	18-64	PCR, RT, culture
Richard 2022d	USA	2012-2013	TIV	not available	Mismatched	ILI	18-64	PCR, RT, culture
Richard 2022e	USA	2013-2014	TIV	not available	Mismatched	ILI	18-64	PCR, RT, culture
Richard 2022f	USA	2014-2015	TIV	not available	Mismatched	ILI	18-64	PCR, RT, culture
Sominina 2021	Russia	2018-2019	TIV	62 not adjusted	Matched	ARI	18-64	PCR
Hyder 2021a	India	2018-2019	QIV	24 (-66-66)	Mismatched	ILI	18-49	PCR
Hyder 2021b	India	2018-2019	QIV	49 (-78-85)	Mismatched	ILI	50-64	PCR
Sturmann 2021a	Europe	2019-2020	TIV and QIV	29 (-3-53)	Mismatched	ARI	18-64	PCR
Stuurman 2021b	Europe	2019-2020	TIV and QIV	30 (-8-71)	Mismatched	ILI	18-64	PCR
Grijalva 2021a	USA	2019-2020	TIV and QIV	62 (27-81)	Mismatched	ARI	18-49	PCR
Grijalva 2021b	USA	2019-2020	TIV and QIV	20 (-48-57)	Mismatched	ARI	50-64	PCR
Hu 2021	USA	2019-2020	Unclear	46 (36-55)	Mismatched	ILI	18-64	PCR
Martin 2020 ^a	USA	2016-2017	QIV	31 (12.4-45)	Matched	ARI	>18	PCR
Martin 2020b	USA	2017-2018	QIV	34.2 (21.9-44.6)	Matched	ARI	>18	PCR
Stuurman 2020a	Europe	2018-2019	QIV	40 (2-63)	Matched	ARI and ILI	18-64	PCR and RT
Stuurman 2020b	Europe	2018-2019	QIV	45 (18-63)	Matched	ARI and ILI	18-64	PCR and RT
Rizzo 2020	Italy	2018-2019	QIV	40.5 (18.7-56.4)	Mismatched	ARI	18-64	PCR
Qahtami 2020	Saudi Arabia	2018-2019	TIV	42 (14-64)	Unclear	ILI	18 – working age	PCR
Redlberger-Fritz 2020a	Austria	2016-2017	QIV, TIV, aTIV, LAIV	-7 (-131-51)	Mismatched	ILI	15-64	PCR
Redlberger-Fritz 2020b	Austria	2017-2018	QIV, TIV, aTIV, LAIV	19 (-63-60)	Mismatched	ILI	15-64	PCR
Redlberger-Fritz 2020c	Austria	2018-2019	QIV, TIV, aTIV, LAIV	51 (-2-76)	Matched	ILI	15-64	PCR

						ARI and ILI	18-64	PCR
Rose 2020	Europe	2019-2020	QIV, TIV and LAIV	36 (1-58)	Mismatched			
Ando 2019	Japan	2018-2019	QIV	43.4 (17.3-61.2)	Unclear	ILI	16-64	RT
Segaloff 2019a	USA	2014-2015	TIV	41.1 (1.7-64.7)	Mismatched	ARI	Adults	PCR
Segaloff 2019b	USA	2015-2016	TIV	68.7 (44.6-82.5)	Matched	ARI	Adults	PCR
Flannery 2019	USA	2018-2019	TIV and QIV	Not available	Mismatched	ILI	18-64	PCR
Kissling 2019	Europe	2016-2017	TIV	34 (18-46)	Mismatched	ILI	15-64	PCR
Blanchette 2019	Canada	2010-2011	TIV	34 (20-40)	Unclear	ARI	18-64	PCR
Constantino 2019	Italia	2018-2019	QIV and TIV	59.5 (0.03-83.1)	Matched	ILI	15-64	PCR
Pebody 2019	United Kingdom	2017-2018	QIV and TIV	12.2 (-16.8-34)	Unclear	ILI	15-64	PCR
Chon 2019	Japan	2015-2016	QIV	27.3 not adjusted	Unclear	ILI	19-64	PCR and RT
Molgaard-Nielsen 2019	Dinamarca	2010-2011	TIV	63.9 (29.1-81.6)	Unclear	ILI	Pregnant women	Unclear
Regan 2019	Australia	2016	QIV	31 (3-51)	Mismatched	ILI	18-64	PCR
Kissling 2019a	Dinamarca	2018-2019	QIV and TIV	55 (44-64)	Mismatched	ILI	18-64	PCR
Kissling 2019b	European Union	2018-2019	QIV and TIV	32 (-31-65)	Mismatched	ILI	18-64	PCR
Kissling 2019c	United Kingdom	2018-2019	QIV and TIV	37 (-20-67)	Mismatched	ILI	18-64	PCR
Kissling 2019d	Dinamarca	2018-2019	QIV and TIV	39 (14-67)	Mismatched	ILI	18-64	PCR
Showronski 2019	Canada	2017-2018	Unclear	63 (46-75)	Matched	ILI	20-64	PCR
Regan 2019a	Australia	2012	TIV	46% not adjusted	Unclear	ILI	18-64	PCR
Regan 2019b	Australia	2013	TIV	57% not adjusted	Unclear	ILI	18-64	PCR
Regan 2019c	Australia	2014	TIV	60% not adjusted	Unclear	ILI	18-64	PCR
Regan 2019d	Australia	2015	TIV	50% not adjusted	Unclear	ILI	18-64	PCR
Thompson 2018a	USA	2010-2011	Unclear	72 (-5-93)	Unclear	ARI	18-50	PCR
Thompson 2018b	USA	2011-2012	Unclear	47 (-98-86)	Unclear	ARI	18-50	PCR
Thompson 2018c	USA	2012-2013	Unclear	23 (-85-68)	Unclear	ARI	18-50	PCR
Thompson 2018d	USA	2013-2014	Unclear	51 (-30-82)	Unclear	ARI	18-50	PCR
Thompson 2018e	USA	2014-2015	Unclear	24 (-189-47)	Unclear	ARI	18-50	PCR
Thompson 2018f	USA	2015-2016	Unclear	40 (-33-72)	Unclear	ARI	18-50	PCR
Flannery 2018a	USA	2017-2018	QIV and TIV	19 (0-34)	Matched	ILI	18-49	PCR
Flannery 2018b	USA	2017-2018	QIV and TIV	40 (24-53)	Matched	ILI	50-64	PCR
Chan 2018	China	2017-2018	QIV and TIV	71 (42.7-85.8)	Unclear	ILI	18-64	PCR
Seki 2018	Japan	2016-2017	QIV	36.5%	Matched	ILI	15-65	RT
Wu 2018	China	2016-2017	TIV	4 (-284-76)	Mismatched	ILI	18-59	PCR
Yaron-Yakobi 2018a	Israel	2014-2015	QIV, TIV, LAIV	-53.7 (-116.8-91.4)	Mismatched	ILI	18-64	PCR
Yaron-Yakobi 2018b	Israel	2015-2016	QIV, TIV, LAIV	39.1 (7.8-59.8)	Mismatched	ILI	18-64	PCR
Showronski 2018	Canada	2017-2018	QIV and TIV	31 (6-49)	Unclear	ILI	20-64	PCR

Stein 2017a	Israel	2016-2017	QIV and TIV	12.5 (-108.7-63.7)	Matched	ILI	18-44	PCR
Stein 2017b	Israel	2016-2017	QIV and TIV	58.8 (.8-82.9)	Matched	ILI	45-64	PCR
Pelody 2017	United Kingdom	2017-2018	QIV and TIV	12.2 not adjusted	Mismatched	ILI	18-64	PCR
Showronski 2017a	Canada	2015-2016	TIV	not available	Matched	ILI	20-49	PCR
Showronski 2017b	Canada	2015-2016	TIV	not available	Matched	ILI	50-64	PCR
Kuliese 2017	Lithuania	2015-2016	TIV	61 (-345-97)	Unclear	ARI	18-64	PCR
Ma 2017	China	2014-2015	TIV	60 (-415-50)	Mismatched	ILI	18-59	PCR
Seki 2017a	Japan	2013-2014	QIV	56.3 (20.9-75.9)	Unclear	ILI	15-65	RT
Seki 2017b	Japan	2014-2015	QIV	7.7 (-64-48.1)	Unclear	ILI	15-65	RT
Seki 2017c	Japan	2015-2016	QIV	52.9 (20-72.3)	Matched	ILI	15-65	RT
McAnerney 2016	South Africa	2015	TIV	54.4 (-14.1-81.8)	Unclear	ILI	18-64	PCR
Fielding 2016	Australia	2015	TIV	52 (37-63)	Mismatched	ILI	18-64	PCR
Petrie 2016a	USA	2014-2015	QIV	67.4 (10.5-88.1)	Mismatched	ARI	18-49	PCR
Petrie 2016b	USA	2014-2015	QIV	9.7 (-126.5-64)	Mismatched	ARI	50-64	PCR
Rizzo 2016	Italy	2014-2015	TIV	-6.3 (-133.6-51.6)	Mismatched	ILI	15-64	PCR
Lytras 2016	Greece	2014-2015	TIV	not available	Mismatched	ARI	15-59	PCR
Rondy 2016	Europe	2013-2014	TIV	not available	Matched	ILI	18-64	PCR
Gherasim 2016	Spain	2014-2015	TIV	not available	Mismatched	ILI	15-64	PCR
Redlberger-Fritz 2016	Austria	2014-2015	TIV	54 (-13-82)	Mismatched	ILI	15-64	PCR
Kelly 2016a	Australia	2011	TIV	not available	Matched	ILI	18-64	PCR
Kelly 2016b	Australia	2011	TIV	not available	Matched	ILI	18-64	PCR
Kelly 2016c	Australia	2012	TIV	not available	Mismatched	ILI	18-64	PCR
Kelly 2016d	Australia	2012	TIV	not available	Mismatched	ILI	18-64	PCR
Kelly 2016e	Australia	2013	TIV	not available	Mismatched	ILI	18-64	PCR
Kelly 2016f	Australia	2013	TIV	not available	Mismatched	ILI	18-64	PCR
Bissielo 2016a	New Zealand	2015	TIV	27 (-8-51)	Mismatched	ILI	18-64	PCR
Bissielo 2016b	New Zealand	2015	TIV	46 (1-70)	Mismatched	ARI	19-64	PCR
Cheng 2015	Australia	2014	TIV	49.7 (35.3-60.8)	Matched	ARI	16-64	PCR
Levy 2015a	Thailand	2009-2010	TIV	not available	Mismatched	ILI	18-64	PCR
Levy 2015b	Thailand	2010-2011	TIV	not available	Matched	ILI	18-64	PCR
Levy 2015c	Thailand	2011-2012	TIV	not available	Matched	ILI	18-64	PCR
Levy 2015d	Thailand	2012-2013	TIV	not available	Mismatched	ILI	18-64	PCR
McLean 2015	USA	2012-2013	TIV	47	Matched	ARI	18-64	PCR
McAnerney 2015a	South Africa	2010	TIV	48.4 (-22.2-78.2)	Matched	ILI	18-64	PCR
McAnerney 2015b	South Africa	2011	TIV	58.7 (9.7-81.1)	Matched	ILI	18-64	PCR
McAnerney 2015c	South Africa	2012	TIV	67.1 (-15.6-90.6)	Mismatched	ILI	18-64	PCR

McAnerney 2015d	South Africa	2013	TIV	90.7 (36.8-98.6)	Matched	ILI	18-64	PCR
McAnerney 2015e	South Africa	2014	TIV	42.7 (-106.7-84.1)	Mismatched	ILI	18-64	PCR
Rondy 2015	Europe	2012-2013	TIV	not available	Mismatched	ILI	Adultos	PCR
McLean 2015	USA	2012-2013	TIV	not available	Matched	ARI	18-64	PCR
Filipovic 2014	Croatia	2010-2011	TIV	-19.5 (-240.6-58.1) not adjusted	Matched	ILI	18-64	PCR
Turner 2014a	New Zeland	2014	TIV	not available	Unclear	ARI	18-64	PCR
Turner 2014b	New Zeland	2014	TIV	not available	Unclear	ILI	18-64	PCR
Levy 2014a	Australia	2010	TIV	60 (-1-84)	Matched	ILI	18-64	PCR
Levy 2014b	Australia	2011	TIV	40 (-22-70)	Matched	ILI	18-64	PCR
Levy 2014c	Australia	2012	TIV	47 (19-65)	Matched	ILI	18-64	PCR
Yang 2014	China	2012-2013	TIV	not available	Matched	ILI	18-59	Vírus isolation
Sullivan 2014	Australia	2012	TIV	12 (-22-36)	Mismatched	ILI	18-64	PCR
Skowronski 2014a	Canada	2011-2012	TIV	56 (26-74)	Mismatched	ILI	18-64	PCR
Skowronski 2014b	Canada	2013-2014	TIV	not available	Matched	ILI	18-64	PCR
Skowronski 2014c	Canada	2012-2013	TIV	not available	Mismatched	ILI	18-64	PCR
Kavanagh 2013	Scotland	2010-2011	TIV	100 (-349-100)	Matched	ILI	18-64	PCR
Castilla 2013	Spain	2011-2012	TIV	44 (-11-72)	Matched	ILI	15-59	PCR

Table S4. ROBINS-I overall assessment of the included TND studies by domain

(0: No information; 1: Low; 2: Moderate; 3: Serious; 4: Critical)

Thompson M. et al	2018	1	1	0	1	1	0	1	0
Flannery B. et al	2018	1	1	3	1	1	1	1	3
Chan Y. et al	2018	1	1	4	1	1	4	1	4
Seki Y. et al	2018	1	1	0	1	1	1	1	0
Wu S. et al	2018	1	1	0	1	1	1	1	0
Yaron-Yakobi H. et al	2018	1	1	4	1	1	1	1	4
Showronski D et al	2018	1	1	3	1	1	1	1	3
Stein Y. et al	2017	1	1	4	1	1	1	1	4
Pelody R. et al	2017	4	1	4	1	1	1	1	4
Showronski D et al	2017	4	1	4	1	1	1	1	4
Kuliese M. et al	2017	1	1	1	1	3	1	1	3
Ma C. et al	2017	1	1	1	1	1	1	1	1
Seki Y. et al	2017	1	1	1	1	1	1	1	1
McAnerney J. et al	2016	1	1	3	1	1	1	1	3
Fielding J. et al	2016	1	1	3	1	1	1	1	3
Petrie J. et al	2016	1	1	4	1	1	1	1	4
Rizzo C. et al	2016	1	1	4	1	1	1	1	4
Lytras t. et al	2016	4	1	4	1	1	1	1	4
Rondy A. Et al	2016	4	1	3	1	1	1	1	4
Gherasim A. Et al	2016	4	4	3	1	1	1	1	4
Redlberger-Fritz M. et al	2016	1	1	0	1	1	1	1	0
Kelly H. et al	2016	4	1	3	1	1	1	1	4
Bissielo A. et al	2016	1	1	1	1	1	1	1	1
Cheng et al	2015	1	1	3	1	4	1	1	4
Levy et al	2015	4	1	4	1	1	1	1	4
McAnerney et al	2015	1	1	3	1	1	1	1	3
McAnerney et al	2015	1	1	3	1	1	1	1	3
Rondy et al	2015	4	1	3	1	1	1	1	4
Filipovic et al	2015	4	3	3	1	1	1	1	4
McLean et al	2015	4	1	1	1	1	1	1	4
Turner et al	2014	4	1	3	1	1	1	1	4
Levy et al	2014	1	1	3	1	1	1	1	3
Yang et al	2014	4	1	4	1	1	1	1	4
Sullivan et al	2014	1	1	0	1	1	1	1	0
Skowronski et al	2014	4	1	4	1	1	4	1	4

Skowronski et al	2014	4	1	0	1	1	1	1	0
Skowronski et al	2014	2	1	4	1	1	1	1	4
Kavanagh et al	2013	1	1	1	1	1	1	1	1
Castilla et al	2013	1	1	1	1	1	1	1	1