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Heterogeneous and Dynamic Prevalence of Asymptomatic Influenza Virus Infections

Technical Appendix 1

Search Strategies

First Search

Influenza AND ((Asymptomatic OR Carrier OR carriage OR shedding OR symptomatic OR Subclinical OR serosurvey OR seroprevalence OR seroepidemiology) OR ((travel OR migration OR immigra*) AND (screening OR test OR testing OR detection)) OR ((“Cohort Studies”[Mesh] OR “Case-Control Studies”[Mesh]) AND “Influenza A virus”[Mesh]))

Second Search

(“influenza, human”[MeSH Terms] OR (“influenza”[All Fields] AND “human”[All Fields]) OR “human influenza”[All Fields] OR “influenza”[All Fields]) AND (“prevention and control”[Subheading] OR (“prevention”[All Fields] AND “control”[All Fields]) OR “prevention and control”[All Fields] OR “prophylaxis”[All Fields]) NOT (“vaccines”[MeSH Terms] OR “vaccines”[All Fields] OR “vaccine”[All Fields])

Manually filtered for randomized controlled trials.

Technical Appendix Table 1. Characteristics of the 55 studies included in systematic review and meta-analysis of asymptomatic and subclinical influenza infection prevalence

Authors, year	Location of the study	Influenza type or subtype	Seasonal / Pandemic	Exposure type	Diagnosis test	Definition of asymptomatic	Definition of subclinical	Asymptomatic prevalence, %	Subclinical prevalence, %
Aho M, et al., 2010	Finland	A (H1N1)	Pandemic	Military garrison	HI ≥10	No symptoms of URT infection	—	40.7	—
Belderok SM, et al., 2013	Netherlands	A, and B	Seasonal	Travel to tropical and subtropical countries	HI ≥40 and ≥4-fold increase above pre-travel titer	—	No ILI	—	90.83
Bone A, et al., 2012	France	A (H1N1)	Pandemic	Community	HI ≥40	—	No ILI	—	29.52
Buescher, et al., 1969	Thailand and Panama	A (H3N1)	Pandemic	Military garrison	HI ≥32	—	No ILI	—	77.5
Carey DE, et al., 1958	USA	A (H2N2)	Pandemic	Parish	HI ≥10	—	No 'flu'	—	24.77
Ceyhan M, et al., 2010	Turkey	A (H5N1)		Community, poultry exposure and healthcare workers	HI ≥21	—	No symptoms of avian influenza infection	—	81.25
Clover RD, et al., 1986*	USA	A (H1N1)	Seasonal	Community	Positive culture or HI ≥4-fold increase	—	No ILI	—	60
Cui F, et al., 2011	China	A (H1N1)	Pandemic	Train	rRT-PCR	—	No ARI	—	13.64
Dotan A, et al., 2014	Israel	A (H1N1)	Pandemic	Hospital	rRT-PCR	—	No URI	—	30.77
Du Ry van Beest Holle M, et al., 2005	Netherlands	A (H7N7)		Poultry	HI ≥10	—	No ILI	—	93.94
Foy HM, et al., 1987	USA	B	Seasonal	Community	HI ≥10	—	No ILI	—	32.43
Gray GC, et al., 2014	Cambodia	A (H1N1), A (H3N2), and B	Seasonal and pandemic	Community	HI ≥4-fold increase	—	No ILI	—	64.44
Guinard A, et al., 2009	France	A (H1N1)	Pandemic	School	rRT-PCR	—	No ILI	—	53.33
Hayden FG, et al., 1999*	USA	A (H1N1)	Seasonal	Experimental inoculation	Positive culture and/or HI ≥4-fold increase	—	No URT illness	—	46.15
Hayward AC, et al., 2014	UK	A (H1N1), A (H3N2), and B	Seasonal and pandemic	Community	rRT-PCR	—	No ILI	—	46.22
Hsieh YH, et al., 2014	Taiwan	A (H1N1)	Seasonal	Community and school	HI ≥4-fold increase	No symptoms	No ILI	45.15	33.33
Hudson L, et al., 2013	New Zealand	A (H1N1)	Pandemic	Healthcare workers	HI ≥40	None influenza symptoms	—	25.44	—
Ison MG, et al., 2012*	Belgium, Estonia, France, Germany, Hungary, Israel, Italy, Lithuania, Spain, UK, USA	A (H1N1), A (H3N2), and B		Transplant recipients	Positive culture and/or HI ≥4-fold increase	No symptoms	—	25	—
Jackson ML, et al., 2011	USA	A (H1N1)	Pandemic	School	HI ≥20 and ≥4-fold increase	No symptoms	No ILI	25	81.25

Authors, year	Location of the study	Influenza type or subtype	Seasonal / Pandemic	Exposure type	Diagnosis test	Definition of asymptomatic	Definition of subclinical	Asymptomatic prevalence, %	Subclinical prevalence, %
Jaeger JL, et al., 2011	USA	A (H1N1)	Pandemic	Hospital	HI ≥20	—	No ARI or ILI	—	66.66
Johnson S, et al., 2011	UK	A (H1N1)	Pandemic	Boarding school	HI ≥8	—	No ILI	—	68.35
Khakpour M, et al., 1969	Iran	A (H3N2)	Pandemic	Prisoners	HI	—	No ILI	—	23.53
Khaokham CB, et al., 2013	USA	A (H1N1)	Pandemic	Navy vessel	rRT-PCR or HI ≥4-fold increase	No symptoms	No ILI	52.11	88.03
Khuntirat B, et al., 2014	Thailand	A (H1N1)	Pandemic	Community	rRT-PCR and HI ≥4-fold increase	—	No ILI	—	83.33
Kumar S, et al., 2010	USA	A (H1N1)	Pandemic	Community	rRT-PCR	No symptoms	No ILI	10	32
Kumar S, et al., 2011	USA	A (H1N1)	Pandemic	Healthcare workers	HI ≥40	No symptoms	No ILI	35	30
Kuster SP, et al., 2013	Canada	A (H1N1)	Pandemic	Community and healthcare workers	HI ≥40	—	No ARI	—	13.04
Lau LLH, et al., 2010	Hong Kong	A (H1N1), A (H3N2), and B	Seasonal	Community	rRT-PCR	No symptoms	—	25.42	—
Levy JW, et al., 2013	Thailand	A (H1N1), A (H3N2), and B	Seasonal and pandemic	Community	rRT-PCR	No symptoms	—	2.54	—
Li T, et al., 2011	China	A (H1N1)	Pandemic	Boarding school	rRT-PCR and HI ≥40	No symptoms	—	30.89	—
Mikulska M, et al., 2013	Italy	A (H1N1), A (H3N2), and B	Seasonal	Allogeneic haematopoietic stem cell recipients	rRT-PCR	No symptoms	No ILI	10	45
Neatherlin J, et al., 2013	USA	A (H1N1)	Pandemic	Airplane	MN ≥40 and HI ≥20	—	No ARI/ILI	—	75
Oker-Blom N, et al., 1970*	Finland	A (H3N2)	Pandemic	Community	HI ≥4-fold increase	—	No respiratory illness	—	18
Pang X, et al., 2011	China	A (H1N1)	Pandemic	Community	rRT-PCR	—	No ILI	—	4.62
Papenburg J, et al., 2010	Canada	A (H1N1)	Pandemic	Community	Microneutralization ≥40 or ≥4-fold increase	No symptoms	—	9.43	—
Pascalis H, et al., 2012	Reunion Island	A (H1N1)	Pandemic	Community	rRT-PCR	No symptoms	No ILI	1.61	30.65
Pasco JA, et al., 2012	Australia	A (H1N1)	Pandemic	Community	HI ≥40	—	No ILI	—	75.97
Paton NI, et al., 2011*	Singapore	A (H1N1), A (H3N2), and B	Seasonal	Community	HI ≥4-fold increase	—	No clinical influenza (ILI)	—	51.72
Priest PC, et al., 2013	New Zealand	A, and B	Seasonal	Airport	rRT-PCR	No symptoms	—	6.67	—
Qi W, et al., 2014	China	A (H10N8)	Pandemic	Poultry exposure	HI ≥20	—	No influenza symptoms	—	100
Redlberger-Fritz M, et al., 2014	Austria	A (H1N1)	Pandemic	Attended hospital	rRT-PCR	—	No respiratory symptoms	—	60.72

Authors, year	Location of the study	Influenza type or subtype	Seasonal / Pandemic	Exposure type	Diagnosis test	Definition of asymptomatic	Definition of subclinical	Asymptomatic prevalence, %	Subclinical prevalence, %
Robinson JL, et al., 2007	Canada	A (H3N2)		Community	HI ≥32	—	No ILI	—	77.78
Salez N, et al., 2014	France, Reunion Island, UK	C		Community	HI, ELISA and rRT-PCR	—	No ILI	—	50
Shafir SC, et al., 2011	USA	A (H1N1)		University campus	HI ≥40	—	No ILI	—	54.43
Shankar AG, et al., 2014	UK	A (H1N1)	Pandemic	Airplane	rRT-PCR	—	No ILI	—	0
Smit PM, et al., 2012	Netherlands	A (H1N1)	Seasonal	Healthcare workers	rRT-PCR	—	No ILI	—	0
Sridhar S, et al., 2014	UK	A (H1N1)	Pandemic	Community	HI ≥32	—	No ILI	—	84.15
Suess T, et al., 2012	Germany	A (H1N1), A (H3N2), and B	Seasonal and pandemic	Community	rRT-PCR	No symptoms	No ILI	4.76	17.99
Thai PQ, et al., 2014	Vietnam	A (H1N1)	Pandemic	Community	rRT-PCR	No symptoms	—	45.45	—
Toyokawa T, et al., 2011	Japan	A (H1N1)	Pandemic	Healthcare workers	HI ≥40	—	No fever	—	92.86
Vilella A, et al., 2012	Dominican Republic	A (H1N1)	Pandemic	Community	rRT-PCR	No symptoms	—	5.13	—
Wang TE, et al., 2010	Taiwan	A (H1N1), A (H3N2)	Seasonal	School	HI ≥4-fold increase	No symptoms	—	62.5	—
Woods CW, et al., 2013	USA and UK	A (H1N1), A (H3N2)	Seasonal	Experimental inoculation	Positive culture or rRT-PCR	—	Jackson score <6	—	56.1
Yan L, et al., 2012	China	A (H1N1)	Pandemic	School	rRT-PCR or HI ≥40	—	No ARI	—	64.49
Zaman M, et al., 2011	Pakistan	A (H5N1)	Pandemic	Hospital	rRT-PCR	No symptoms	—	25	—

*Only control or placebo group included; ARI, acute respiratory illness; HI, hemagglutination inhibition; ILI, influenza-like illness; LRT, lower respiratory tract; rRT-PCR, real-time reverse transcription PCR; URT, upper respiratory tract.

Technical Appendix 2 Table. Included studies (N = 55), by influenza type/subtype

Type	Subtype	No. of studies	References
A	H10N8	1	*1*
	H7N7	1	*2*
	H5N1	2	*3,4*
	H3N2	11	*5–15*
	H2N2	1	*16*
	H1N1	38	*5,8,9,12–15,17–47*
B		5	*5,8,12,48,49*
C		1	*50*
Mixed		6	*49,51–55*

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