

eAPPENDIX

Case fatality risk of influenza A(H1N1pdm09): a systematic review

This appendix provides additional information on the data.

eTable: Articles excluded after reviewing the full-length text.

First Author	Journal	Year	Title	Reason for Exclusion
	J Indian Med Assoc	2009	Epidemiology of seasonal, avian and pandemic influenza	Paper not found.
	Wkly Epidemiol Rec	2009	Transmission dynamics and impact of pandemic influenza A (H1N1) 2009 virus	CFR not reported, only population-based mortality rate reported.
	Euro Surveill	2009	Progression and impact of the first winter wave of the 2009 pandemic H1N1 influenza in New South Wales, Australia	CFR not reported, only population-based mortality rate reported.
	Wkly Epidemiol Rec	2009	Considerations for assessing the severity of an influenza pandemic	CFR not reported.
	MMWR Morb Mortal Wkly Rep	2010	Deaths and hospitalizations related to 2009 pandemic influenza A (H1N1) - Greece, May 2009-February 2010	CFR not reported, only population-based mortality rate reported.
Adalja, A. A.	JAMA	2011	Comparing severity and outcomes for seasonal and 2009 H1N1 infections	Letter, not an original study.
Archer, B.	Euro Surveill	2009	Interim report on pandemic H1N1 influenza virus infections in South Africa, April to October 2009: epidemiology and factors associated with fatal cases	Only the number of cases and deaths reported, not describe explicitly as an estimate of the CFR.
Armstrong, G. L.	Clin Infect Dis	2011	Timely assessment of the severity of the 2009 H1N1 influenza pandemic	CFR not reported.
Azziz-Baumgartner, E.	Bull World Health Organ	2012	Incidence of influenza-like illness and severe acute respiratory infection during three influenza seasons in Bangladesh, 2008-2010	CFR not reported.
Azziz-Baumgartner, E.	PLoS One	2012	Mortality, Severe Acute Respiratory Infection, and Influenza-Like Illness Associated with Influenza A(H1N1)pdm09 in Argentina, 2009	CFR not reported, only population-based mortality rate reported.
Babak, A.	Clin Microbiol Infect	2010	Epidemiological and clinical characteristics of influenza A (H1N1) V infection in Isfahan, Iran, July-October 2009	Conference abstract, not an original study.
Baguelin, M.	Vaccine	2010	Vaccination against pandemic influenza A/H1N1v in England: a real-time economic evaluation	CFR not reported.
Baguelin, M.	PLoS One	2011	Age-specific incidence of A/H1N1 2009 influenza infection in England from	CFR not reported.

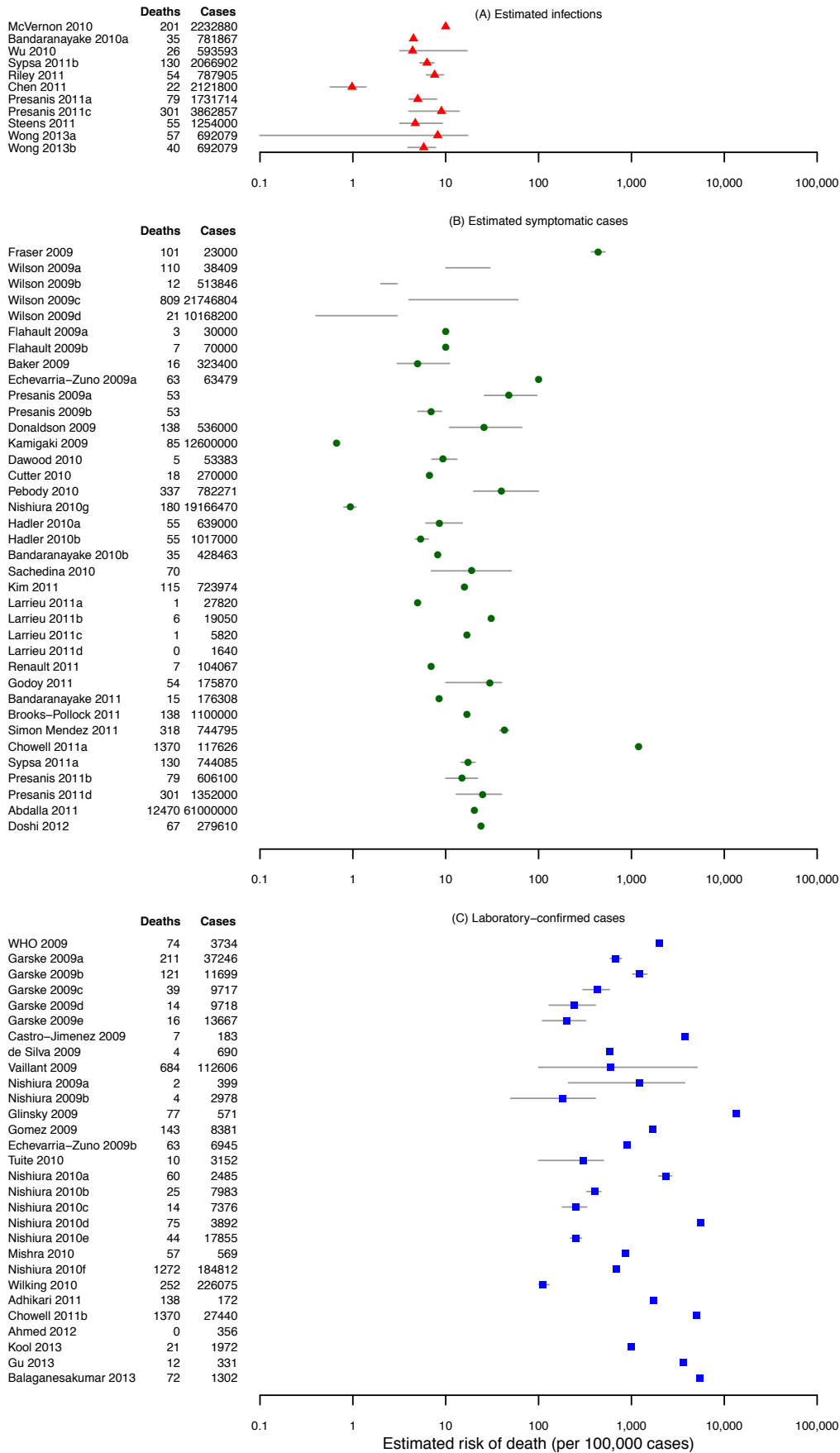
Bishop, J. F.	N Engl J Med	2009	sequential antibody prevalence data using likelihood-based estimation Australia's winter with the 2009 pandemic influenza A (H1N1) virus	CFR not reported.
Boisson, E. V.	West Indian Med J	2012	Pandemic influenza A (H1N1) 2009 in the English and Dutch-speaking Caribbean: An epidemiological overview	Conference abstract, not an original study.
Borja-Aburto, V. H.	Arch Med Res	2012	Epidemiological Characterization of a Fourth Wave of Pandemic A/H1N1 Influenza in Mexico, Winter 2011-2012: Age Shift and Severity	CFR not reported, only hospitalization fatality risk reported.
Bunthi, C.	PLoS One	2013	Influenza A(H1N1)pdm09-associated pneumonia deaths in Thailand	CFR not reported, only hospitalization fatality risk reported.
Carvalhanas, T. R. M. P.	Int J Infect Diseases	2010	Epidemiological profile of the A (H1N1) pandemic influenza in the state of Sao Paulo, Brazil, for the April-September 2009 timeframe	Conference abstract, not an original study.
Chowell, G.	PLoS Curr	2012	Recrudescence wave of pandemic A/H1N1 influenza in Mexico, winter 2011-2012: Age shift and severity	CFR not reported, only hospitalization fatality risk reported.
Chowell, G.	PLoS One	2011	Spatial and temporal characteristics of the 2009 A/H1N1 influenza pandemic in Peru	CFR not reported.
Cimolai, N.	CMAJ	2010	The severity of H1N1	Letter, not an original study.
Clark, N. M.	Semin Respir Crit Care Med	2011	Influenza: epidemiology, clinical features, therapy, and prevention	CFR reported, but not from empirical data.
Colizza, V.	PLoS Curr	2009	Estimate of Novel Influenza A/H1N1 cases in Mexico at the early stage of the pandemic with a spatially structured epidemic model	CFR not reported.
Collignon, P. J.	Med J Aust	2010	A pandemic response to a disease of predominantly seasonal intensity	Letter, not an original study.
Correia, A. M.	Rev Port Pneumol	2010	Pandemic influenza A (H1N1) in the North of Portugal: how did the autumn-winter wave behave?	CFR not reported, only population-based mortality rate reported.
Dellagi, K.	PLoS One	2011	Pandemic influenza due to pH1N1/2009 virus: estimation of infection burden in Reunion Island through a prospective serosurvey, austral winter 2009	CFR not reported.

Donaldson, L. J.	BMJ (Online)	2010	Mortality from pandemic A/H1N1 2009 influenza in England: Public health surveillance study	Duplicate publication.
Donaldson, L. J.	BMJ	2010	English mortality from A/H1N1. Comparisons with recent flu mortality	Letter, not an original study.
D'Ortenzio, E.	Clin Microbiol Infect	2010	A review of the dynamics and severity of the pandemic A(H1N1) influenza virus on Reunion island, 2009	More complete report of the study published elsewhere [1].
Duque, V.	Rev Port Pneumol	2010	The early days of pandemic (H1N1) 2009 virus infection in the central region of Portugal	CFR not reported.
Falagas, M. E.	Eur J Clin Microbiol Infect Dis	2010	Epidemiological aspects of 2009 H1N1 influenza: the accumulating experience from the Northern Hemisphere	Review, not an original study.
Falagas, M. E.	Epidemiol Infect	2011	Pandemic A(H1N1) 2009 influenza: review of the Southern Hemisphere experience	Review, not an original study.
Fowler, R. A.	Lancet	2010	Paediatric mortality related to H1N1 infection in England	CFR not reported.
Fowlkes, A. L.	Clin Infect Dis	2011	Epidemiology of 2009 pandemic influenza A (H1N1) deaths in the United States, April-July 2009	CFR not reported.
Gooya, M. M.	Arch Iran Med	2010	Influenza A (H1N1) pandemic in Iran: report of first confirmed cases from June to November 2009	CFR not reported, only number of death and case reported.
Gouya, M. M.	Iran Red Crescent Med J	2011	Mortality from Pandemic Influenza A (H1N1) in Iran	CFR not reported, only hospitalization fatality risk reported.
Hardelid, P.	Health Technol Assess	2010	Assessment of baseline age-specific antibody prevalence and incidence of infection to novel influenza A/H1N1 2009	CFR not reported.
Hardelid, P.	Influenza Other Respi Viruses	2012	Mortality caused by influenza and respiratory syncytial virus by age group in England and Wales 1999-2010	CFR not reported.
Jhung, M. A.	Influenza Other Respi Viruses	2011	Preliminary results of 2009 pandemic influenza surveillance in the United States using the Aggregate Hospitalization and Death Reporting Activity	CFR not reported.
Josseran, L.	Euro Surveill	2010	Estimating the impact of the 2009 influenza A(H1N1) pandemic on mortality in the elderly in Navarre, Spain	CFR not reported.

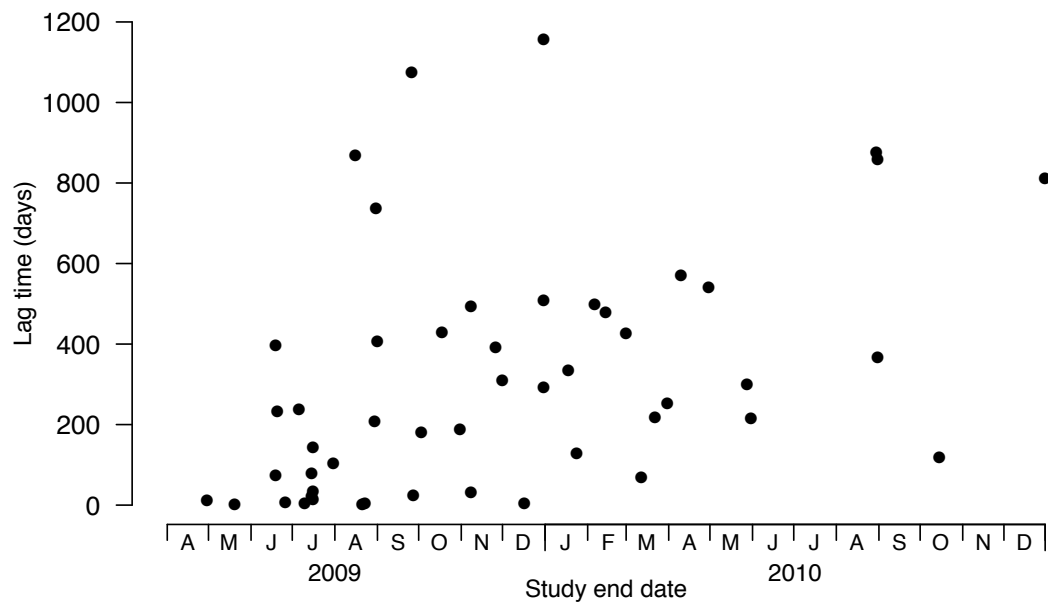
Kao, T. M.	Emerg Infect Dis	2010	Rapid diagnostic tests and severity of illness in pandemic (H1N1) 2009, Taiwan	CFR not reported.
Karpova, L. S.	Vopr Virusol	2012	[An influenza pandemic in Russia as a part of a global spread of the influenza A(H1N1)pdm09 in 2009-2011]	Paper not found
Khan, G.	Emerg Infect Dis	2011	Pandemic (H1N1) 2009, Abu Dhabi, United Arab Emirates, May 2009-March 2010	CFR not reported, only population-based mortality rate reported.
Khandaker, G.	Influenza Other Respi Viruses	2011	Systematic review of clinical and epidemiological features of the pandemic influenza A (H1N1) 2009	Review, not an original study.
Larrauri Camara, A.	Rev Esp Salud Publica	2010	[Surveillance of influenza pandemic (H1N1)2009 in Spain]	More complete report of the study published elsewhere [2].
McLeish, N. J.	PLoS One	2011	Sero-prevalence and incidence of A/H1N1 2009 influenza infection in Scotland in winter 2009-2010	CFR not reported.
Molbak, K.	Vaccine	2011	Burden of illness of the 2009 pandemic of influenza A (H1N1) in Denmark	CFR not reported.
Moral, L.	Enferm Infecc Microbiol Clin	2011	Burden of severe 2009 pandemic influenza A (H1N1) infection in children in Southeast Spain	CFR not reported.
Muscatello, D. J.	Emerg Infect Dis	2010	All-cause mortality during first wave of pandemic (H1N1) 2009, New South Wales, Australia, 2009	CFR not reported.
Nishiura, H.	Lancet Infect Dis	2010	Case fatality ratio of pandemic influenza	CFR reported, but not from empirical data.
Offenstadt, G.	Crit Care Med	2011	Severity of pH1N1 influenza A	Letter, not an original study.
Petrovic, V.	Croat Med J	2011	Overview of the winter wave of 2009 pandemic influenza A(H1N1)v in Vojvodina, Serbia	CFR not reported, only hospitalization fatality risk reported.
Poeppl, W.	Infection	2011	Clinical aspects of 2009 pandemic influenza A (H1N1) virus infection in Austria	CFR not reported, only hospitalization fatality risk reported.
Poggensee, G.	BMC Infect Dis	2010	The prior to the end of the prior to the end of the first year of the pandemic of pandemic influenza (H1N1) 2009 in Germany: from initiation to acceleration	CFR not reported.
Ponnambalam, L.	Intl J Infect Diseases	2012	Age-stratified transmission dynamic models to assess severity of influenza	Conference abstract, not an original study.

Presanis, A. M.	PLoS Curr	2009	pandemics in real-time The severity of pandemic H1N1 influenza in the United States, April - July 2009	More complete report of the study published elsewhere [3].
Reyes, L.	Influenza Other Respi Viruses	2010	Population-based surveillance for 2009 pandemic influenza A (H1N1) virus in Guatemala, 2009	CFR not reported, only hospitalization fatality risk reported.
Rodriguez-Valero, M.	J Infect Dev Ctries	2012	Difference between early clinical features of swine origin A H1N1 influenza confirmed and not confirmed infection in Mexico	CFR not reported, only hospitalization fatality risk reported.
Roriz-Cruz, M.	J Am Geriatr Soc	2010	Lower mortality from H1N1 influenza in older Argentineans: men more affected	CFR not reported.
Shen, J.	Virology J	2012	Epidemiologic parameters and evaluation of control measure for 2009 novel influenza a (H1N1) in Xiamen, Fujian Province, China	CFR not reported.
Shrestha, S. S.	Clin Infect Dis	2011	Estimating the burden of 2009 pandemic influenza A (H1N1) in the United States (April 2009-April 2010)	CFR not reported, only hospitalization fatality risk reported.
Smoljanovic, M.	Croat Med J	2011	Predicting AH1N1 2009 influenza epidemic in Southeast Europe	CFR not reported.
Van Kerkhove, M. D.	Influenza Other Respi Viruses	2011	Epidemiologic and virologic assessment of the 2009 influenza A (H1N1) pandemic on selected temperate countries in the Southern Hemisphere: Argentina, Australia, Chile, New Zealand and South Africa	CFR not reported, only hospitalization fatality risk reported.
Van Kerkhove, M. D.	Influenza Other Respi Viruses	2013	Estimating age-specific cumulative incidence for the 2009 influenza pandemic: a meta-analysis of A(H1N1)pdm09 serological studies from 19 countries	Meta-analysis, not an original study.
von Kries, R.	PLoS One	2011	Post-pandemic seroprevalence of pandemic influenza A (H1N1) 2009 infection (swine flu) among children <18 years in Germany	CFR not reported.
Wu, J. T.	PLoS Med	2011	Estimating infection attack rates and severity in real time during an influenza pandemic: analysis of serial cross-sectional serologic	CFR not reported.

Wu, J. T.	Influenza Other Respi Viruses	2011	surveillance data A serial cross-sectional serologic survey of 2009 Pandemic (H1N1) in Hong Kong: implications for future pandemic influenza surveillance	Duplicate publication.
Wu, J. T.	Intl J Infect Diseases	2012	Characterizing the transmission dynamics and severity of 2009 H1N1 influenza pandemic in Hong Kong	Conference abstract, not an original study.
Yoshikura, H.	Jpn J Infect Dis	2011	A new method for monitoring and forecasting the case-fatality rate in ongoing epidemics and its evaluation using published data of SARS in 2003, H1N1 pandemic in 2009/2010, hand-foot-mouth disease in China in 2009/2010, and cholera in Haiti in 2010	CFR not reported.
Zhang, X.	PLoS One	2011	Serologic survey of the pandemic H1N1 2009 virus in Guangdong Province, China: a cross sectional study	CFR not reported.



eFigure 1: Overall estimated risk of death, by definition of cases.



eFigure 2: Lag time between end of study period to publication date.

APPENDIX REFERENCES

1. Renault P, Thouillot F, Do C, et al. [Epidemic of influenza A(H1N1) 2009 in Reunion Island: epidemiological data]. *Bull Soc Pathol Exot* 2011;104(2):108-13. doi:10.1007/s13149-010-0113-5.
2. Simon Mendez L, de Mateo Ontanon S, Larrauri Camara A, et al. [Transmissibility and severity of the pandemic influenza A (H1N1) 2009 virus in Spain]. *Gac Sanit* 2011;25(4):296-302. doi:10.1016/j.gaceta.2011.02.008.
3. Presanis AM, De Angelis D, Hagy A, et al. The severity of pandemic H1N1 influenza in the United States, from April to July 2009: a Bayesian analysis. *PLoS Med* 2009;6(12):e1000207. doi:10.1371/journal.pmed.1000207.



PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2, 3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4,5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	NA
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6, 7
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6, 7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	6
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6, 7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	8
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	NA
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	8



PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	NA
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	NA
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	NA
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Table 3
Synthesis of results	21	Present the main results of the review. If meta-analyses are done, include for each, confidence intervals and measures of consistency.	Tables 2-4
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	NA
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	NA
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	11
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	14, 16
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	17, 18
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	19

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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