

Deaths Associated with Pneumonic Plague, 1946–2017

Appendix

Articles Citing a 50% Mortality in Pneumonic Plague

Many articles that quote a treated mortality of 50% cite a 2000 Lancet paper by Ratsitorahina et al. (1), which describes a small outbreak of primary pneumonic plague in Madagascar in 1997. The mortality is not explicitly stated in the article, but the data show an overall mortality of 50%. However, the mortality amongst treated confirmed/probable cases is reported as only 10%. On reviewing publications that cited Ratsitorahina et al., we identified 9 that referenced a treated mortality of 50%, one of 40%, and none referencing other values (2–11). None of the articles explained how they derived this figure. One of these citations was a review paper published in the Lancet in 2007 (11). This review paper was also itself cited 9 times in relation to a treated mortality of 50% (12–19). Through examination of these publications' references, we identified a further 6 publications where a treated mortality of 50% was stated but not referenced (20–25), and only one publication mentioning a lower mortality (14%; source unreferenced) (26).

In the Ratsitorahina et al. paper, there were 18 cases in total. One patient (case 10) did not have plague. Therefore, there were 17 cases with plague. Of these, 10 appear to have received treatment (cases 6, 7, 8, 9, 11, 12, 13, 14, 15, 16 – as “eight patients with pneumonic syndrome were transferred” . . . “The patients were suspected to have pneumonic plague and thus were treated with streptomycin,” and “The healer’s brother died a few hours after admission”). Only 1 died out of these 10 (case 6). Eight patients did not receive treatment, and all died (cases 1, 2, 3, 4, 5, 17, 18). Therefore, the treated mortality is 10%, the untreated mortality is 100%, and the overall mortality is 53%.

Methods

We detailed whether confirmed cases alone, confirmed and probable cases together, or confirmed, probable, and suspected cases together were reported (and extracted numerical

data on the most specific classification available). Likewise, we noted whether articles included only primary pneumonic or undifferentiated pneumonic cases (defined by article authors using the term 'primary') and extracted data on the most specific measurement. Data on secondary pneumonic cases were not included. We defined antibiotic treatment as one or more doses of antibiotics currently or previously used for the treatment of plague: aminoglycosides, quinolones, tetracyclines, sulphonamides (alone), septrin, and chloramphenicol. Where data were duplicated in more than one publication, the largest of the overlapping cohorts that detailed antibiotic use were used. Data were reported as missing for each variable when they were not available in the article. Authors were not contacted for missing data. Where data were duplicated in more than one publication, the largest of the overlapping cohorts that detailed antibiotic use were used.

Descriptive statistics are presented as frequencies for categorical variables, means and standard deviations for normally distributed data, and median with range for other continuous variables.

Results

Antibiotics given included aminoglycosides (90 courses), quinolones (24 courses), sulphonamides (23 courses), chloramphenicol (16 courses), tetracyclines (15 courses), and septrin (3 courses). Six articles described the time to antibiotic administration in some detail, but the non-standardised way this was reported precluded stratification by this measure.

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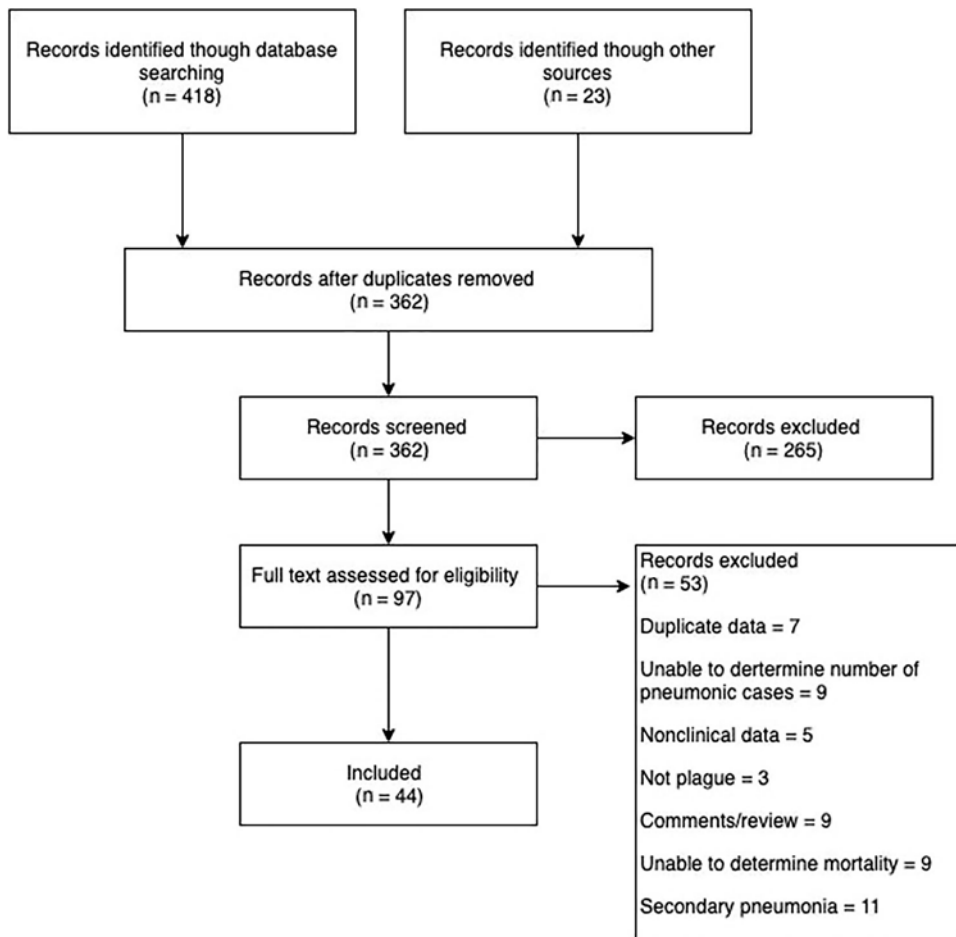
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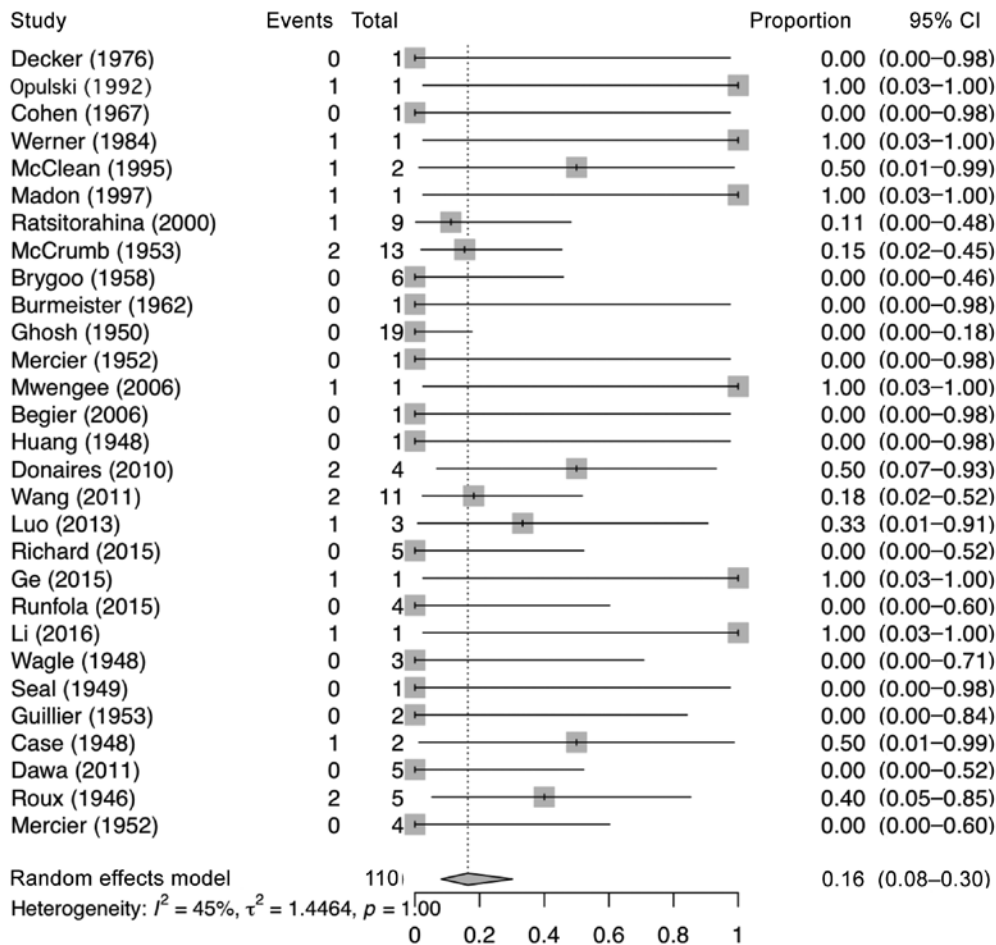
Appendix Table. Reports of pneumonic plague, 1946–2017*

Author/year	First year cases described	Country	Total		Antimicrobial drug use unknown		Treated patients		Untreated patients	
			Deaths	Patients	No. patient deaths	No. patients with unknown use	No. deaths	No. treated	No. deaths	No. patients
Begier (2006) (27)	2004	Uganda	1	2			0	1	1	1
Brygoo 1958) (28)	1957	Madagascar	35	41			0	6	35	35
Burmeister (1962) (29)	1959	USA	0	1			0	1		
de Ribes 1997) (30)	1989	Madagascar	52	91	52	91				
Cohen (1967) (31)	1966	Vietnam	0	1			0	1		
Cramer (1995) (32)	1995	USA	0	1	0	1				
Dawa (2011) (33)	2010	Tibet	0	5			0	5		
Decker (1976) (34)	1975	Zimbabwe	0	1			0	1		
Donaires (2010) (20)	2010	Peru	2	4			2	4		
Forrester (2017) (35)	2008	Uganda	8	18	8	18				
Gage (2000) (36)	1977	USA	2	5	2	5				
Ge (2015) (37)	2014	China	1	1			1	1		
Ghosh (1950) (38)	1950	India	0	19			0	19		
Guillier (1953) (39)	1948	Madagascar	0	2			0	2		
Gupta (2007) (40)	2002	India	4	16	4	16				
Huang (1948) (41)	1947	China	0	1			0	1		
Joshi (2009) (42)	2002	India	5	30						
Kamugisha (2007) (43)	1986	Tanzania	121	427	121	427				
Lewin (1948) (44)	1947	South Africa	1	2			1	2		
Li (2016) (45)	2014	China	3	3			1	1	2	2
Luo (2013) (46)	2005	China	2	5			1	3	1	2
Madon (1997) (47)	1995	USA	1	1			1	1		
McClellan (1995) (48)	1993	Zambia	2	3			1	2	1	1
McCrum (1953) (49)	1953	Madagascar	2	13			2	13		
Mercier (1952) (50)	1952	Madagascar	4	8			0	4	4	4
Mercier (1952) (51)	1951	Madagascar	0	1			0	1		
Mwengee (2006) (9)	2002	Tanzania	1	1			1	1		
Ogen-Odoi (2009) (52)	2006	Uganda	11	12	11	12				
Opulski (1992) (53)	1992	USA	1	1			1	1		
Ramasindrazana (2017) (54)	2015	Madagascar	6	14						
Ratsitorahina (2000) (1)	1997	Madagascar	7	17			1	9	7	7
Richard (2015) (55)	2011	Madagascar	15	20			0	5	15	15
Roux (1946) (56)	1946	Algeria	2	4			2	4		
Runfoia (2015) (57)	2014	USA	0	3			0	3		
Seal (1949) (58)	1948	India	11	12	11	12				
Seal (1949) (59)	1948	India	13	14			0	1	13	13
Tieh (1948) (60)	1946	China	36	39					36	39
Trong (1967) (61)	1965	Vietnam	18	43	18	43				
Wagle (1948) (62)	1948	India	0	3			0	3		
Wang (2011) (63)	2009	China	3	12			2	11	1	1
Werner (1984) (64)	1980	USA	1	1			1	1		
Wong (2009) (65)	2007	USA	1	1					1	1
Wu (2011) (66)	2000	China	9	26	9	26				
Zhu (1993) (67)	1958	China	98	182	98	182				

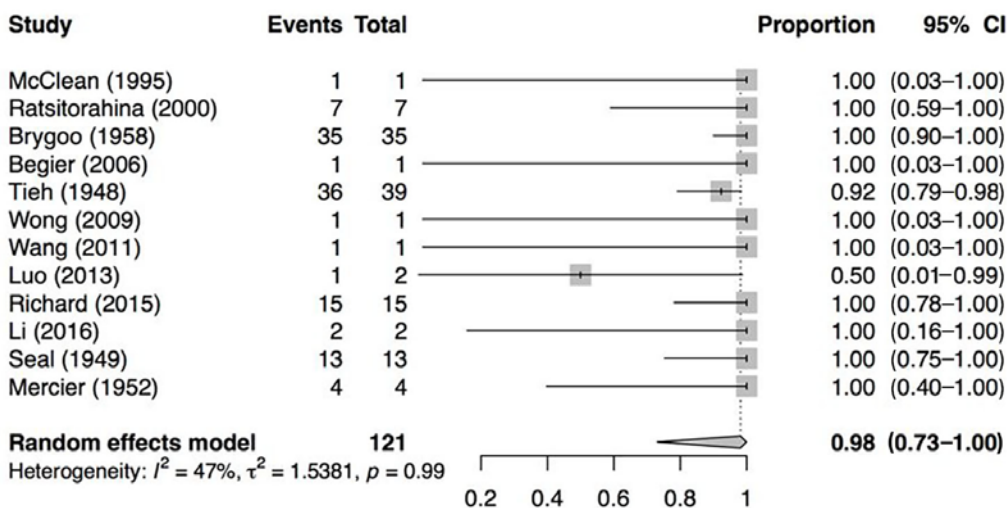
*Blank cells indicate data not available.



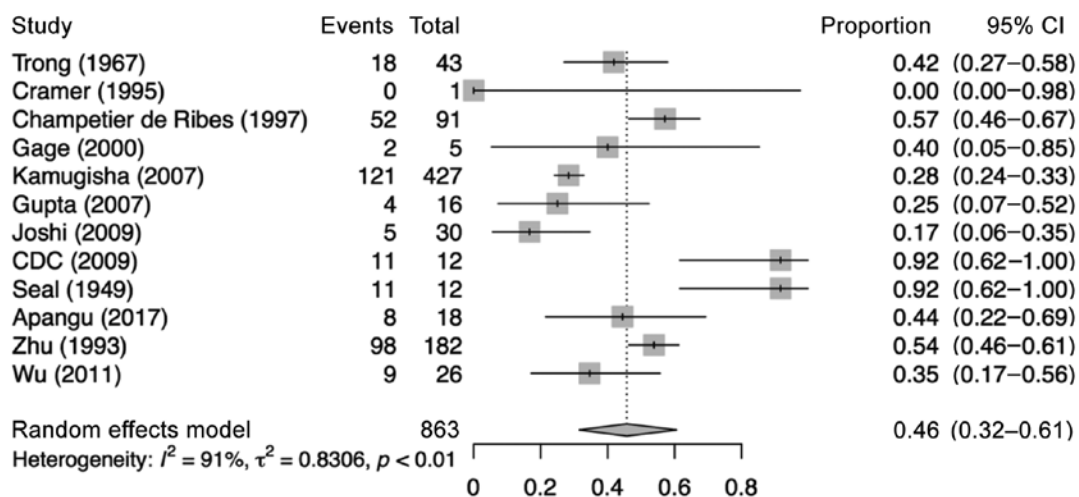
Appendix Figure 1. Overview of 362 reports of pneumonic plague, 1946–2017.



Appendix Figure 2. Forrest plot for death of all patients receiving antibiotics treatment for pneumonic plague in various countries, 1946–2015.



Appendix Figure 3. Forest plot for death of all patients with untreated pneumonic plague in various countries, 1967–2017.



Appendix Figure 4. Forest plot for pneumonic plague patients where antibiotic status was unknown, 1949–2016. Refer to Appendix Table for full citations.