Mortality among children diagnosed with tuberculosis: Systematic review and meta-analysis - Appendix

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Contents

Search Strategy

<u>1. PUBMED</u>

"Tuberculosis"[Mesh] OR "tuberculosis"[tiab] OR "tuberculin"[tiab] OR "tuberculous"[tiab]

AND

Infant[MeSH Terms] OR Child[MeSH Terms] OR child*[tiab] OR infan*[tiab] OR neonate*[tiab] OR newborn*[tiab] OR new born*[tiab] OR baby[tiab] OR babies[tiab] OR toddler*[tiab] OR boy[tiab] OR boys[tiab] OR girl*[tiab] OR pediatric[tiab] OR "paediatric"[tiab] OR prepubescen*[tiab] OR prepuberty*[tiab]

AND

mortality[MeSH Terms] OR "survival rate"[Mesh Terms] OR prognosis[MeSH Terms] OR Mortality[tiab] OR death[tiab] OR fatal[tiab] OR "survival rate"[tiab] OR "death rate"[tiab] OR prognosis[tiab]

AND

"Health Surveys"[MeSH Terms] OR "Population"[MeSH Terms] OR "Survey"[tiab] OR "Representative"[tiab] OR "Surveillance"[tiab]

<u>2. EMBASE</u>

'tuberculosis'/exp OR 'tuberculosis':ab,ti

AND

'child'/exp OR child*:ab,ti OR infan*:ab,ti OR neonate*:ab,ti OR newborn*:ab,ti OR 'new born':ab,ti OR 'new borns':ab,ti OR baby:ab,ti OR 'babies':ab,ti OR toddler*:ab,ti OR 'boy':ab,ti OR 'boys':ab,ti OR girl*:ab,ti OR pediatric:ab,ti OR paediatric:ab,ti OR prepubescen*:ab,ti OR prepuberty*:ab,ti AND [embase]/lim
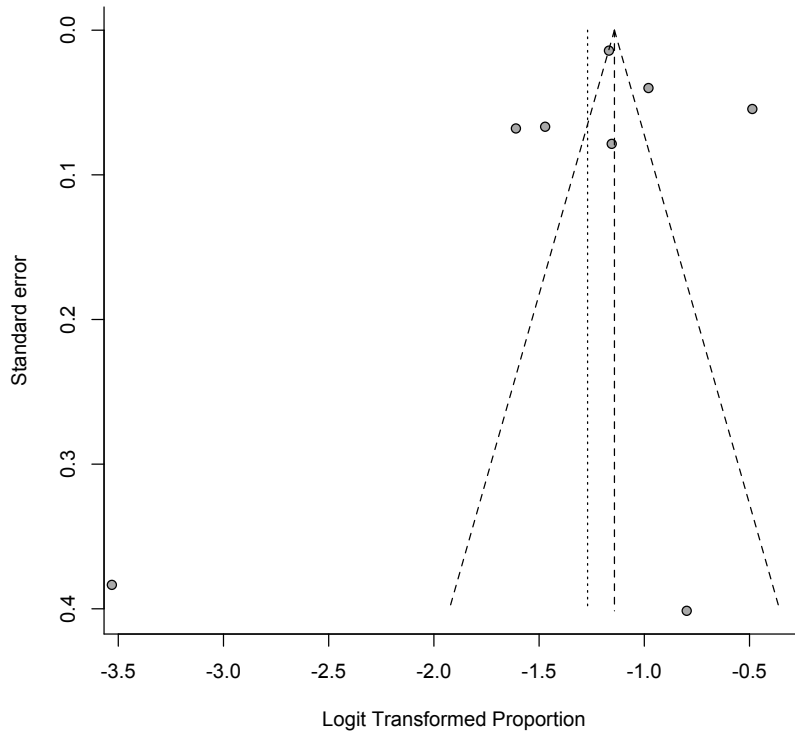
AND

'mortality'/exp OR 'survival rate'/exp OR 'prognosis'/EXP OR mortality:ab,ti OR death:ab,ti OR fatal:ab,ti OR 'survival rate':ab,ti OR 'death rate':ab,ti OR prognosis:ab,ti

AND

'health survey'/exp OR 'population'/exp OR 'disease surveillance'/exp OR survey:ab,ti OR representative:ab,ti OR surveillance:ab,ti

Figure A1 Funnel plots for the studies in the pre-treatment era. Plots are shown for studies involving (a) children aged 0-14 years, (b) children aged <5 years old, (c) children aged 5-14 years old. Grey dots indicate individual studies, the dotted line indicates the pooled estimate from the meta-analysis (and where we would expect the vertical dashed line to fall if there were no biases) and the outer dashed lines indicate the region where we would expect 95% of studies to lie if there were no biases or heterogeneity.

(a)

(b)

Standard error

Logit Transformed Proportion

(c)

Standard error

Logit Transformed Proportion
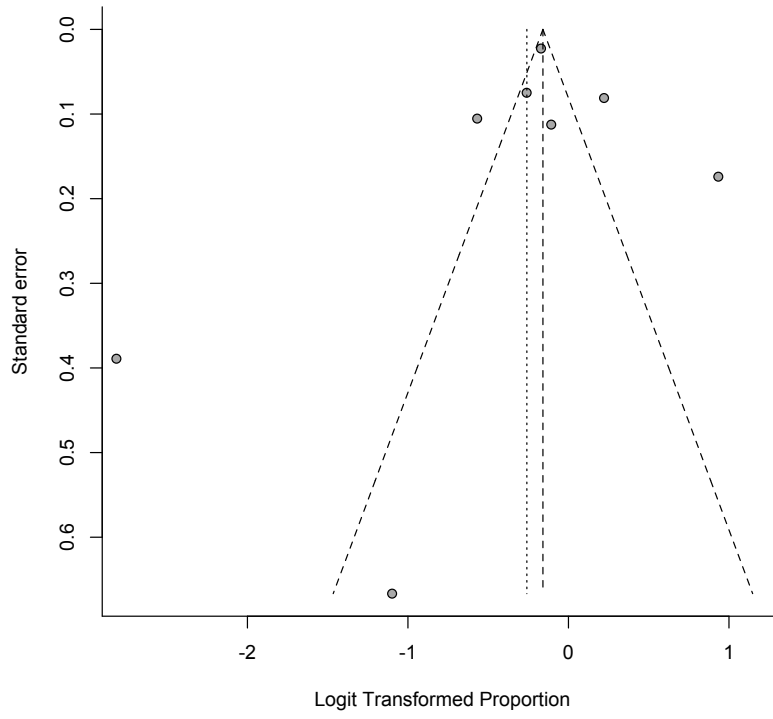
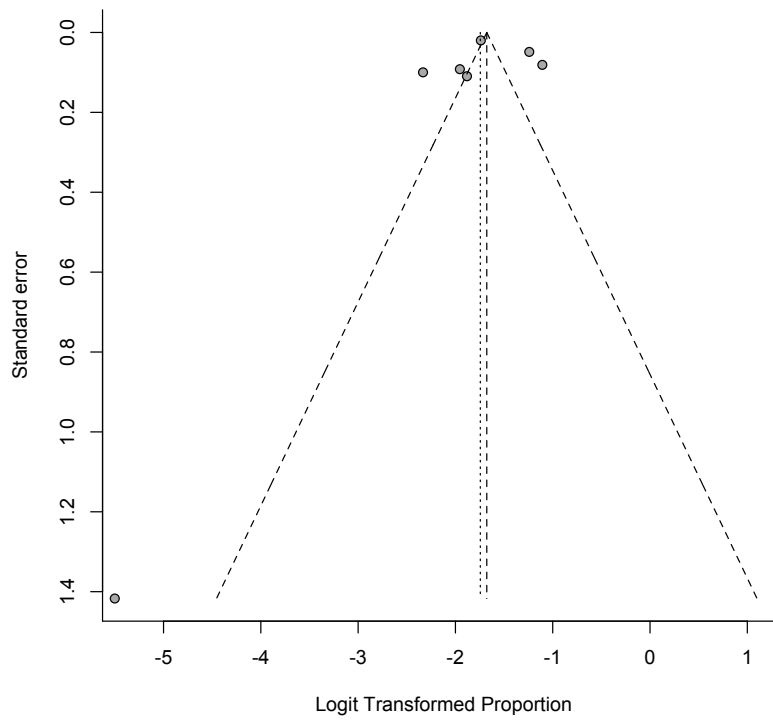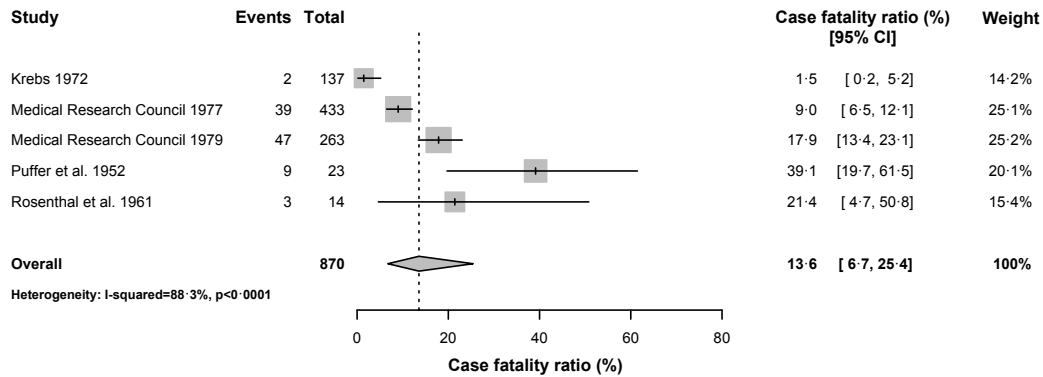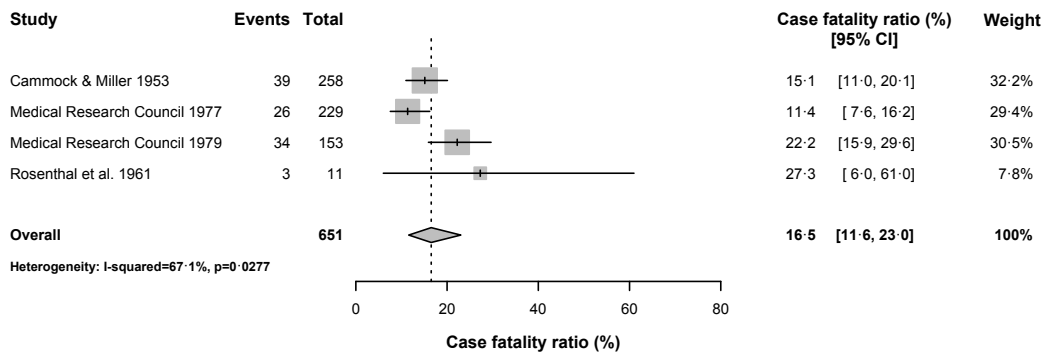**Figure A2** Forest plots for the case fatality ratios from studies in the middle-era. Results are shown for (a) children aged 0-14 years, (b) children aged <5 years old, (c) children aged 5-14 years old. Horizontal lines represent the confidence intervals around the point estimates for each study and the grey shaded areas are proportional to the weight given to each study.

(a)

Study	Events	Total	Case fatality ratio (%) [95% CI]	Weight
Krebs 1972	2	137	1·5 [0·2, 5·2]	14·2%
Medical Research Council 1977	39	433	9·0 [6·5, 12·1]	25·1%
Medical Research Council 1979	47	263	17·9 [13·4, 23·1]	25·2%
Puffer et al. 1952	9	23	39·1 [19·7, 61·5]	20·1%
Rosenthal et al. 1961	3	14	21·4 [4·7, 50·8]	15·4%
Overall		870	13·6 [6·7, 25·4]	100%

Heterogeneity: I-squared=88·3%, p<0·0001

Case fatality ratio (%)

(b)

Study	Events	Total	Case fatality ratio (%) [95% CI]	Weight
Cammock & Miller 1953	39	258	15·1 [11·0, 20·1]	32·2%
Medical Research Council 1977	26	229	11·4 [7·6, 16·2]	29·4%
Medical Research Council 1979	34	153	22·2 [15·9, 29·6]	30·5%
Rosenthal et al. 1961	3	11	27·3 [6·0, 61·0]	7·8%
Overall		651	16·5 [11·6, 23·0]	100%

Heterogeneity: I-squared=67·1%, p=0·0277

Case fatality ratio (%)

(c)

Study	Events	Total	Case fatality ratio (%) [95% CI]	Weight
Gothi et al. 1971	2	39	5·1 [0·6, 17·3]	8·7%
Medical Research Council 1977	13	204	6·4 [3·4, 10·7]	45·6%
Medical Research Council 1979	13	110	11·8 [6·5, 19·4]	43·5%
Rosenthal et al. 1961	0	3	0·0 [0·0, 70·8]	2·1%
Overall		356	8·3 [5·6, 12·3]	100%

Heterogeneity: I-squared=10·4%, p=0·341
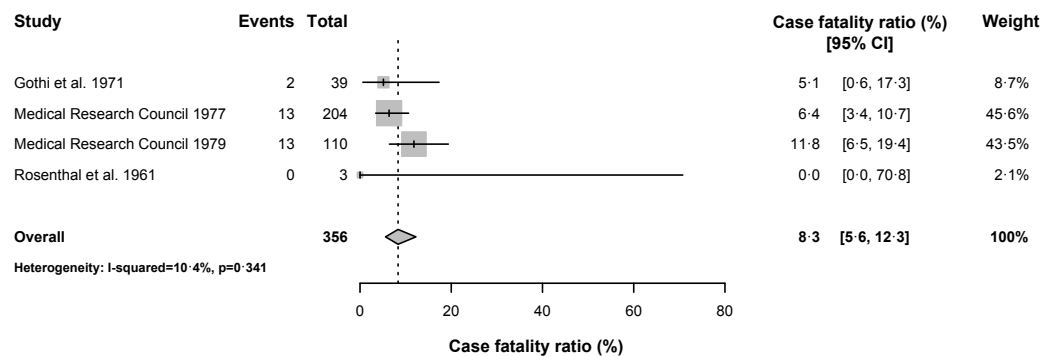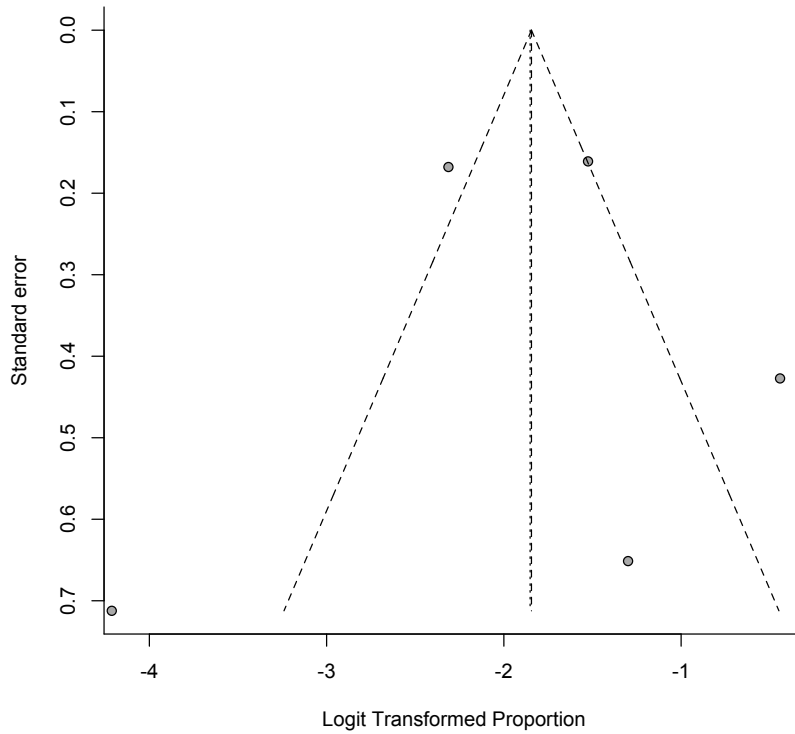
Case fatality ratio (%)

Figure A3 Funnel plots for the studies in the middle era. Plots are shown for studies involving (a) children aged 0-14 years, (b) children aged <5 years old, (c) children aged 5-14 years old. Grey dots indicate individual studies, the dotted line indicates the pooled estimate from the meta-analysis (and where we would expect the vertical dashed line to fall if there were no biases) and the outer dashed lines indicate the region where we would expect 95% of studies to lie if there were no biases or heterogeneity.

(a)

(b)

Logit Transformed Proportion

(c)

Logit Transformed Proportion

8
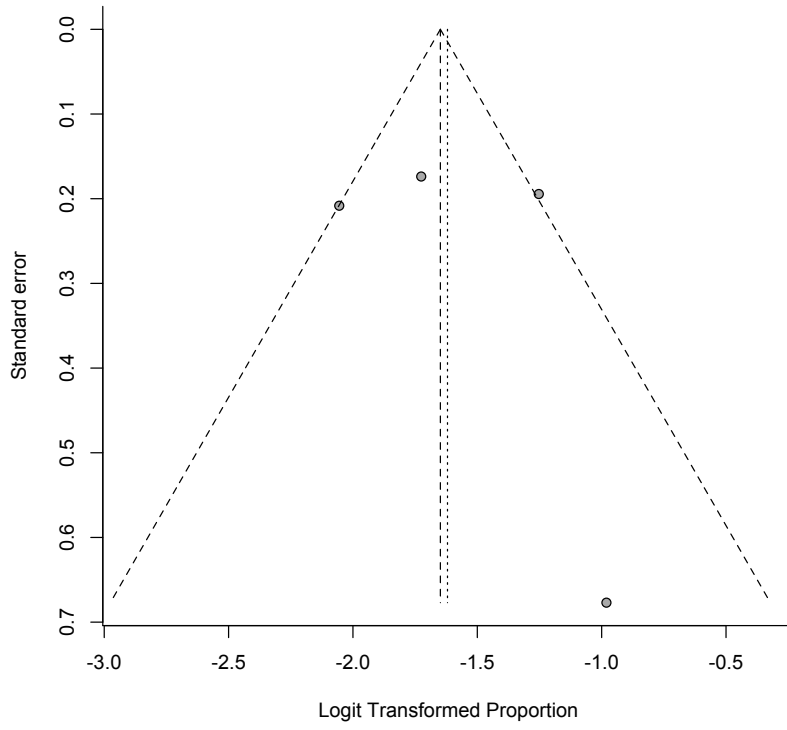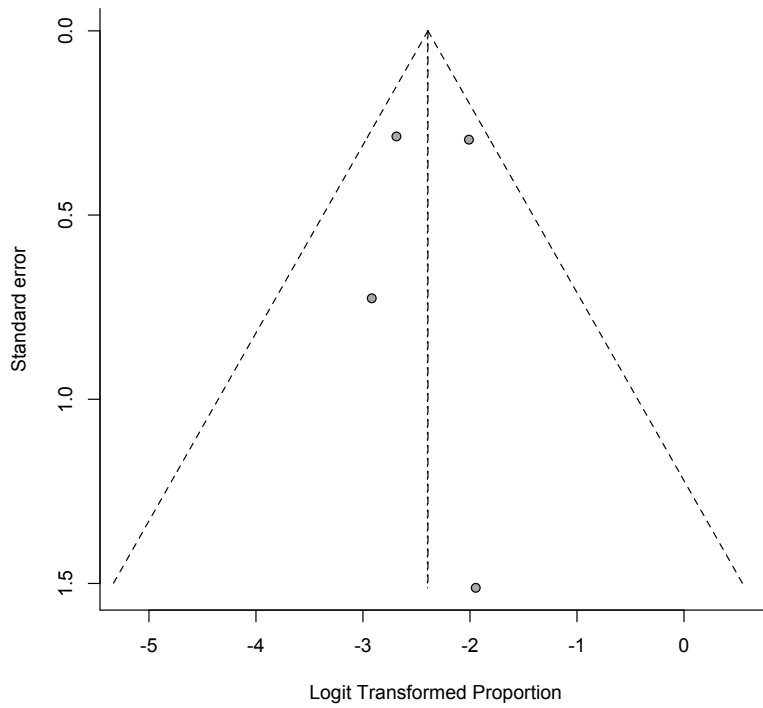
Figure A4 Forest plots for the case fatality ratios from studies in the recent-era. Results are shown for (a) children aged 0-14 years, (b) children aged <5 years old, (c) children aged 5-14 years old. Includes HIV infected, HIV uninfected and HIV status unknown children. Horizontal lines represent the confidence intervals around the point estimates for each study and the grey shaded areas are proportional to the weight given to each study.
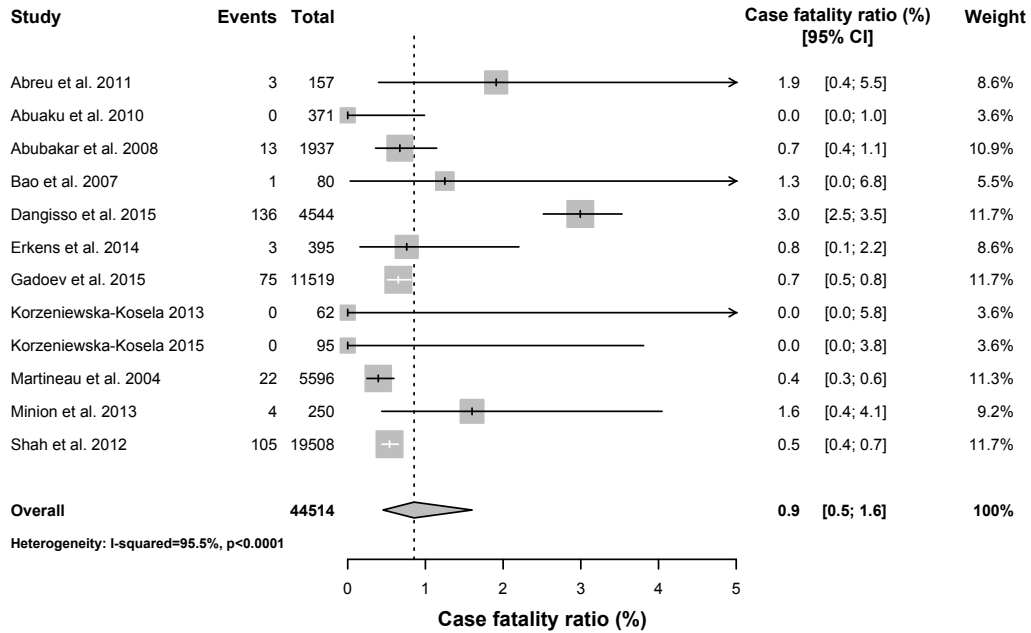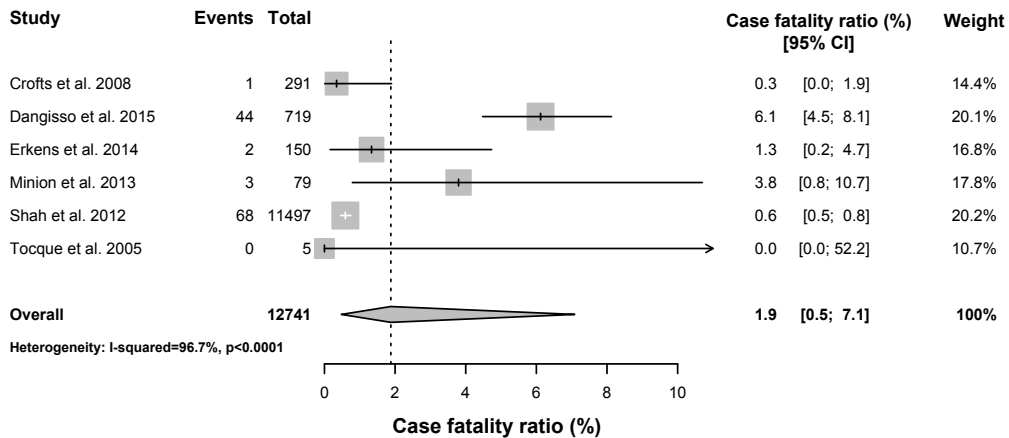
(a)

Study	Events	Total	Case fatality ratio (%) [95% CI]	Weight
Abreu et al. 2011	3	157	1.9 [0.4; 5.5]	8.6%
Abuaku et al. 2010	0	371	0.0 [0.0; 1.0]	3.6%
Abubakar et al. 2008	13	1937	0.7 [0.4; 1.1]	10.9%
Bao et al. 2007	1	80	1.3 [0.0; 6.8]	5.5%
Dangisso et al. 2015	136	4544	3.0 [2.5; 3.5]	11.7%
Erkens et al. 2014	3	395	0.8 [0.1; 2.2]	8.6%
Gadoev et al. 2015	75	11519	0.7 [0.5; 0.8]	11.7%
Korzeniewska-Kosela 2013	0	62	0.0 [0.0; 5.8]	3.6%
Korzeniewska-Kosela 2015	0	95	0.0 [0.0; 3.8]	3.6%
Martineau et al. 2004	22	5596	0.4 [0.3; 0.6]	11.3%
Minion et al. 2013	4	250	1.6 [0.4; 4.1]	9.2%
Shah et al. 2012	105	19508	0.5 [0.4; 0.7]	11.7%
Overall		44514	0.9 [0.5; 1.6]	100%

Heterogeneity: I-squared=95.5%, p<0.0001

Case fatality ratio (%)

(b)

Study	Events	Total	Case fatality ratio (%) [95% CI]	Weight
Crofts et al. 2008	1	291	0.3 [0.0; 1.9]	14.4%
Dangisso et al. 2015	44	719	6.1 [4.5; 8.1]	20.1%
Erkens et al. 2014	2	150	1.3 [0.2; 4.7]	16.8%
Minion et al. 2013	3	79	3.8 [0.8; 10.7]	17.8%
Shah et al. 2012	68	11497	0.6 [0.5; 0.8]	20.2%
Tocque et al. 2005	0	5	0.0 [0.0; 52.2]	10.7%
Overall		12741	1.9 [0.5; 7.1]	100%

Heterogeneity: I-squared=96.7%, p<0.0001

Case fatality ratio (%)

(c)

Study	Events	Total		Case fatality ratio (%) [95% CI]		Weight
Crofts et al. 2008	1	565		0.2	[0.0; 1.0]	12.7%
Dangisso et al. 2015	92	3825		2.4	[1.9; 2.9]	22.5%
Erkens et al. 2014	1	245		0.4	[0.0; 2.3]	12.6%
Minion et al. 2013	1	171		0.6	[0.0; 3.2]	12.6%
Shah et al. 2012	37	8011		0.5	[0.3; 0.6]	22.2%
Shen et al. 2009	0	33		0.0	[0.0; 10.6]	8.7%
Tocque et al. 2005	0	23		0.0	[0.0; 14.8]	8.7%
Overall		12873		0.8	[0.3; 2.1]	100%

Heterogeneity: I-squared=92.5%, p<0.0001
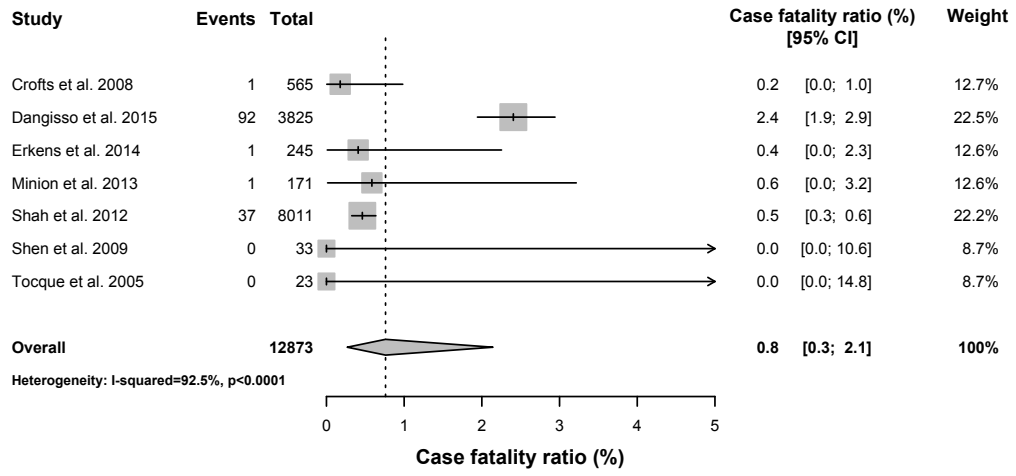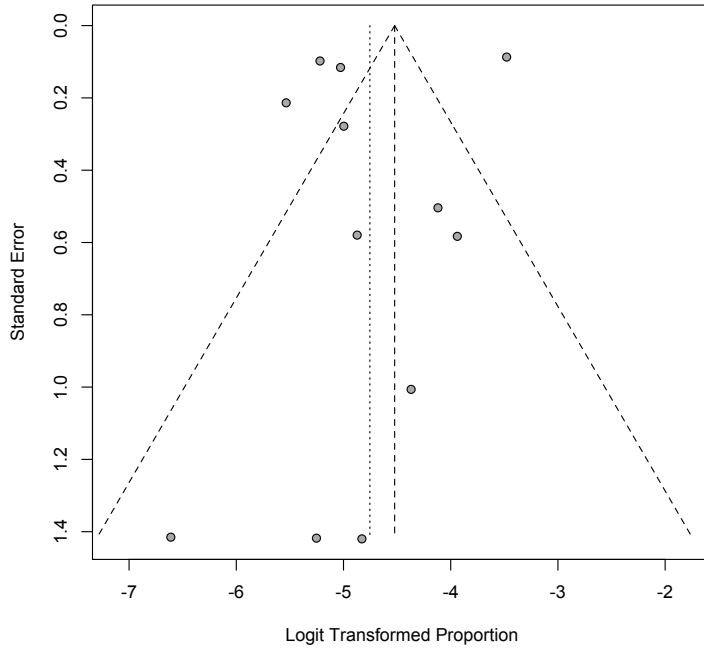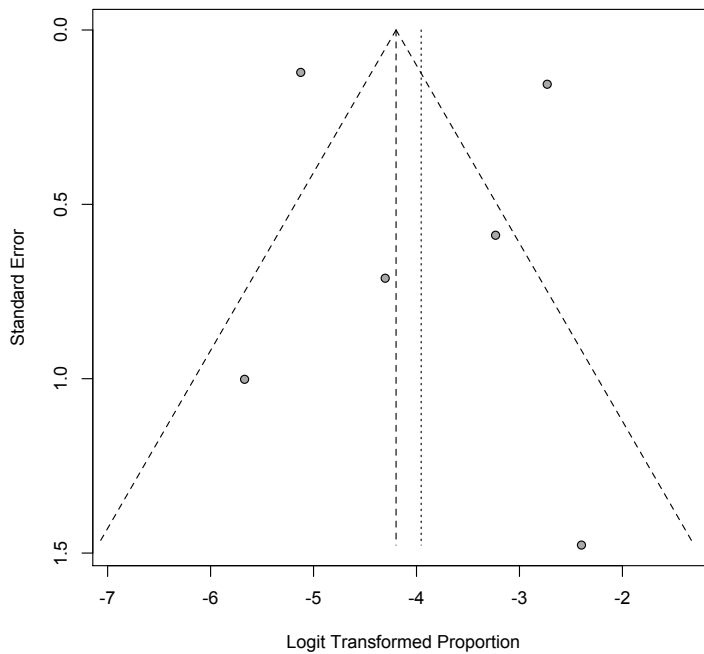

Case fatality ratio (%)

Figure A5 Funnel plots for the studies in the recent era. Plots are shown for studies involving (a) children aged 0-14 years, (b) children aged <5 years old, (c) children aged 5-14 years old. Includes HIV-infected, HIV-uninfected and HIV status unknown children. Grey dots indicate individual studies, the dotted line indicates the pooled estimate from the meta-analysis (and where we would expect the vertical dashed line to fall if there were no biases) and the outer dashed lines indicate the region where we would expect 95% of studies to lie if there were no biases or heterogeneity.

(a)

(b)

(c)