

Systematic Review and Meta-Analyses of Incidence for Group B *Streptococcus* Disease in Infants and Antimicrobial Resistance, China

Appendix

Appendix Table 1. Search terms (for English papers) and search period (January 1, 2000–March 16, 2018) for PubMed/ Medline or Embase (search date: March 17, 2018)*

Search term
Infant
Outcome
Death
Mortality
Case AND Fatality AND rate
Death [MeSH terms]
Mortality [MeSH terms]
Case fatality rate [MeSH terms]
AND
Streptococcal
<i>Streptococcus</i>
Streptococci AND (Group AND B) or agalactiae
<i>Streptococcus agalactiae</i> [MeSH terms]
AND
<i>Streptococcus</i> serotype
Streptococcal serotype
<i>Streptococcus agalactiae</i> serotype [MeSH terms]

*MeSH, medical subject headings

Appendix Table 2. Search terms (for Chinese papers) and search period (January 1, 2000–March 16, 2018) for China National Knowledge Infrastructure or Wanfang med online databases (search date: March 18, 2018)

Search term
族 (Group B Streptococcal)
无乳 (<i>Streptococcus agalactiae</i>)
AND
新生儿 (Neonatal)
(Infant)
AND
血清型 (Serotype)

Appendix Table 3. Inclusion and exclusion criteria*

Characteristic	Inclusion criteria	Exclusion criteria
Population	Invasive GBS disease in infants <1–89 days of age at onset of infection	Studies containing only information on high-risk groups
Laboratory	GBS confirmed by blood, CSF, or other sterile site culture	NA
Search	No language restrictions	Foreign language papers for which it was not possible to obtain English or Chinese translations
Study	Study reporting more recent data from country or hospital	Case report, case series, reviews, conference papers; studies from the same country or hospital reporting repeated years or data.

*CSF, cerebrospinal fluid; GBS, group B *Streptococcus*; NA, not applicable.

Appendix Table 4. Characteristics of included studies for infant invasive group B *Streptococcus* (GBS) disease in children*

Reference	Region of China	Year of		Incidence	CFR	AMR	Serotype	MLST	IAP	Reporting	
		publication	Year of data collection							period, y	Study design
Chang CJ et al. (1)	Taiwan	2003	1986.1–2001.12	N	Y	N	N	N	U	<1–89	R
Chung MY et al. (2)	Taiwan	2004	1996.1.1–2002.12.31	Y	Y	N	N	N	U	<1–89	R
Jiang JH et al. (3)	Taiwan	2004	1992.1–2001.12	N	Y	N	N	N	N	<1–89	R
Wu JH et al. (4)	Taiwan	2009	2001.1–2006.12	N	Y	N	N	N	U	<1–89	P
Wang P et al. (5)	Beijing	2010	2005–2009	Y	Y	N	N	N	U	<1–6	R
Liu ZW et al. (6)	Shang Hai	2011	1999.1–2008.12	N	Y	N	N	N	U	<1–89	R
Lin CY et al. (7)	Taiwan	2011	2001.1–2008.11	Y	N	N	N	N	Y	<1–6	R
Yu HW et al. (8)	Taiwan	2011	2002.1–2005.6	Y	Y	N	N	N	Y	<1–89	R
Wu MF (9)	Guang Dong	2012	2008.1–2012.1	N	Y	N	N	N	U	<1–89	R
Dai YH et al. (10)	Guang Dong	2012	2008.6–2011.4	Y	Y	N	N	N	U	<1–89	R
Long YM et al. (11)	Guang Dong	2012	2009.7–2011.6	Y	Y	N	N	N	U	<1–89	R
Zeng SJ et al. (12)	Guang Dong	2013	2012.1–2012.12	N	Y	Y	N	N	U	<1–89	R
Luo J et al. (13)	Guang Dong	2013	2007.1–2011.12	N	Y	Y	N	N	U	7–89	R
Chen L et al. (14)	Guang Dong	2013	2010–2012	N	Y	N	N	N	U	<1–89	R
Al-Taiar A et al. (15)	Macau	2013	2006.1.1–2009.12.31	Y	N	N	N	N	U	<1–89	P
Wu YY (16)	Guang Dong	2014	2010–2013	N	Y	N	N	N	U	<1–89	R
Fan WH et al. (17)	Beijing	2014	2011.1–2013.9	N	N	Y	N	N	U	<1–89	R
Zheng Z et al. (18)	Fujian	2014	2011.10–2013.4	Y	Y	Y	N	N	Y	<1–6	R
Chen Y et al. (19)	Guang Dong	2014	2011.1–2013.10	N	Y	Y	N	N	U	<1–6	R
Wei CP et al. (20)	Shan Dong	2014	2012–2014	N	Y	N	N	N	U	<1–89	R
Huang HJ et al. (21)	Guang Dong	2014	2011.1–2012.12	N	Y	N	N	N	U	<1–89	R
Long YM et al. (22)	Guang Dong	2014	2011.1–2013.12	Y	Y	N	N	N	U	<1–89	R

Reference	Region of China	Year of		Incidence	CFR	AMR	Serotype	MLST	IAP	Reporting	
		publication	Year of data collection							period, y	Study design
Zhu ML et al. (23)	Zhe Jiang	2014	2005.1–2013.5	N	Y	Y	N	N	Y	<1–89	R
Liu X et al. (24)	Jiang Su	2015	2013.3–2015.3	N	Y	N	N	N	U	<1–89	R
Zhang S et al. (25)	Guang Dong	2015	2013.1–2014.3	N	Y	Y	N	N	U	7–89	R
Zeng SJ et al. (26)	Guang Dong	2015	2012–2014	N	N	N	Y	N	U	<1–89	R
Li K et al. (27)	Guang Dong	2015	2011.3–2014.2	N	Y	N	N	N	U	<1–89	R
Wang QQ et al. (28)	Zhe Jiang	2015	2010.4–2014.4	Y	Y	Y	N	N	Y	<1–89	R
Wang YC et al. (29)	Jiang Su	2015	2013.1–2013.12	N	Y	N	N	N	Y	<1–89	R
Luo MJ et al. (30)	Guang Dong	2015	2010–2012	N	Y	N	N	N	U	<1–6	R
Zhao N et al. (31)	Guang Dong	2015	2011.11–2014.4	N	Y	N	N	N	U	<1–89	R
Lei MF et al. (32)	Tianjin	2015	2006.12.-2014.09	N	Y	Y	N	N	U	<1–89	R
Liu H et al. (33)	Guang Dong, Hunan	2015	2013.09–2014.09	Y	Y	N	Y	Y	Y	<1–89	P
Rivera L et al. (34)	Hong Kong	2015	U	Y	Y	N	N	N	Y	<1–89	P
Zhang JS et al. (35)	Guang Dong	2015	2010–2014	N	Y	Y	N	N	U	<1–89	R
Liu ZY et al. (36)	Fu jian	2016	2011.3–2014.10	N	Y	N	N	N	U	<1–89	R
Zhang XH et al. (37)	Shan Xi (Tai Yuan)	2016	2013.1–2015.11	N	Y	N	N	N	U	<1–89	R
Li L et al. (38)	Guang Dong	2016	2008.1–2014.8	N	Y	N	N	N	U	<1–89	R
Li YH et al. (39)	Nei Menggu	2016	2013.6–2016.6	Y	Y	N	N	N	U	<1–89	R
Yang HH et al. (40)	Shang Hai	2016	2012.1–2015.5	N	Y	N	N	N	N	<1–89	R
Shen YH et al. (41)	Beijing	2016	2008.1–2014.1	N	Y	N	N	N	U	<1–89	R
Cai YF et al. (42)	Guang Dong	2016	2011.1–2014.10	N	Y	Y	N	N	U	<1–89	R
Lai JD et al. (43)	Fu Jian	2016	2010.1–2015.2	N	Y	N	N	N	U	<1–6	R
Zhao L (44)	Jiang Su	2016	2014.4–2016.4	N	Y	Y	N	N	U	<1–89	R
Ju HQ et al. (45)	Shang Hai	2016	2010.3–2015.2	N	Y	N	N	N	U	<1–89	R
Huang LF et al. (46)	Guang Dong	2016	2010.11–2014.2	N	N	Y	N	N	U	<1–89	R

Reference	Region of China	Year of		Incidence	CFR	AMR	Serotype	MLST	IAP	Reporting	
		publication	Year of data collection							period, y	Study design
Yue D (47)	Hu Bei	2017	2014.1–2016.1	N	Y	N	N	N	U	<1–89	R
Qiao LY et al. (48)	Shan Dong	2017	2012.1–2016.1	N	Y	N	N	N	U	7–89	R
Guan XS et al. (49)	Guang Dong	2017	2012.1–2015.12	N	Y	N	N	N	U	<1–89	R
Liu WW et al. (50)	Guang Dong	2017	2012.1–2015.12	N	Y	Y	N	N	U	<1–89	R
Lv CH (51)	Shan Dong	2017	2014.1–2015.12	N	Y	N	N	N	U	<1–89	R
Zhou YZ et al. (52)	Zhe Jiang	2017	2008.2–2016.11	N	N	Y	Y	N	U	<1–89	R
Zhang JS et al. (53)	Guang Dong	2017	2010.1.1–2015.21.31	N	Y	Y	N	N	U	<1–89	R
Zhang N et al. (54)	Shan Dong	2017	2013.1–2016.5	N	Y	Y	N	N	N	<1–89	R
Wang YJ et al. (55)	Guang Dong	2017	2011.4–2015.4	N	Y	N	N	N	U	7–89	R
Shenzhen GBS study group (56)	Guang Dong	2017	2010.1–2016.6	N	Y	N	N	N	Y	<1–89	R
Zhang S et al. (57)	Beijing	2017	2010–2014	N	Y	N	N	N	U	<1–89	R
Tan KH et al. (58)	Guang Dong	2017	2012.3–2016.3	N	N	Y	N	N	N	<1–89	R
Zhao TL (59)	Liaoning	2017	2015.1–2016.2	N	N	Y	N	N	U	<1–89	R
Ma HL et al. (60)	Si Chuan	2017	2014.1–2016.2	N	Y	N	N	N	U	<1–6	R
Huang W et al. (61)	Gong Dong, Guang Xi	2017	2013.1–2015.2	N	Y	N	N	N	U	<1–89	R
Chen IL et al. (62)	Taiwan	2017	2008.1–2013.12	N	Y	N	N	N	U	<1–89	R
Chen HY et al. (63)	Zhe Jiang	2018	2014.6.1–2017.6.31	N	Y	N	N	N	Y	<1–89	R
Guan XS et al. (64)	Guang Dong	2018	2011.1–2014.12	Y	Y	Y	Y	Y	U	<1–89	R

*AMR, antimicrobial drug resistance; CFR, case-fatality rate; GBS, group B *Streptococcus*; IAP, intrapartum antimicrobial drug prophylaxis; MLST, multilocus sequence typing; N, no; P, prospective study; R, retrospective study; U, unknown (information not available); Y, yes.

Appendix Table 5. Studies with reasons for exclusions

Reference	Year of publication	Year of data collection	Reasons for exclusion
Resiner DP et al. (65)	2000	1994.2–1997.1	Studies not from China
Chang C et al. (66)	2000	1984–1997	Investigating only specific clinical manifestations
Zhong Y et al. (67)	2002	1998.11–1999.7	Not fulfilling inclusion criteria
Liao CH et al. (68)	2002	1980.1–2000.3	No full text
Tiskumara R et al. (69)	2009	2005.1.1–2005.12.31	Studies not from China
Lin MC et al. (70)	2012	1984–2008	Investigating only specific clinical manifestations
Ye F et al. (71)	2013	2009–2011	Other topics
Zhang J et al. (72)	2013	2010.1–2011.1	Case report
Lin Z et al. (73)	2013	2009.1–2013.5	Investigating only specific clinical manifestations
Tan JF et al. (74)	2014	2011.8–2012.8	Other topics
Chu SM et al. (75)	2014	20014.1–2011.12	Other topics
Zhang J et al. (76)	2015	2009.1–2012.12	Duplicate data analysis
Li L et al. (77)	2015	2008.1–2014.8	Not fulfilling inclusion criteria
Mu L et al. (78)	2015	2011.7.2014.7	Specimen not obtained from sterile site
Zhong H et al. (79)	2015	2011–2014	Specimen not obtained from sterile site
Zhong H et al. (80)	2015	2011.1–2014.5	Duplicate data analysis
Wang P et al. (81)	2015	2008–2013	Not defined laboratory methods
Li L et al. (82)	2016	2008.1–2014.8	Not fulfilling inclusion criteria
Wang Y et al. (83)	2016	2013.9–2015.9	Specimen not obtained from sterile site
Geng H et al. (84)	2016	2010–2015	Other topics
Huang J et al. (85)	2016	2011.11–2015.9	Specimen not obtained from sterile site
Hua CZ et al. (86)	2016	2011.1–2015.12	Investigating only specific clinical manifestations
Ding Y et al. (87)	2017	2008–2015	Case report
Wang Y et al. (88)	2017	2015.10–2016.12	Specimen not obtained from sterile site
Jing L et al. (89)	2017	2009.1–2015.2	Specimen not obtained from sterile site
Wu IH et al. (90)	2017	2006.1–2013.12	Investigating only specific clinical manifestations

Appendix Table 6. Results of subgroup analysis of total incidence of GBS invasive disease*

Subgroup	No. studies	Incidence (95% CI)	Heterogeneity test	
			I ² , %	Q test p value
Study design				
Retrospective	10	0.54 (0.32–0.75)	88.20	0.001
Prospective	3	0.60 (0.12–1.08)	56.80	0.10
Isolate type				
Blood	5	0.37 (0.14–0.60)	69.70	0.01
All sterile sites	1	1.17 (0.89–1.44)		
Blood plus CSF	7	0.52 (0.35–0.69)	46.00	0.09
Age of onset, y				
EOGBS	11	0.38 (0.25–0.51)	65.40	0.001
LOGBS	3	0.18 (0.11–0.25)	0.0	0.45

*CSF, cerebrospinal fluid; EOGBS; early-onset group B *Streptococcus*; LOGBS, late-onset group B *Streptococcus*.

Appendix Table 7. Relationship between group B *Streptococcus* serotypes and MLST results*

Author	No samples	Serotype	ST17	ST12	ST23	ST10	ST1	New 17-like
Liu H et al.	2	III	1	0	0	0	0	1
	3	Ib	0	2	0	1	0	0
	2	Ia	0	0	2	0	0	0
	1	V	0	0	0	0	1	0
Guan XS et al.	53	III	43	0	0	0	0	0
	10	Ib	0	5	1	1	0	0
	2	Ia	0		2	0	0	0
	3	V	0	0	0	0	3	0

*MLST, multilocus sequence typing; ST, sequence type.

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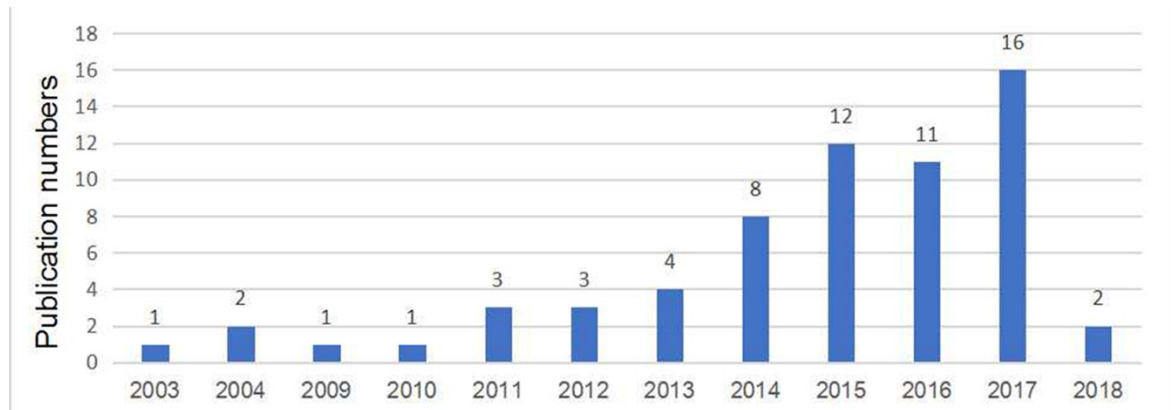
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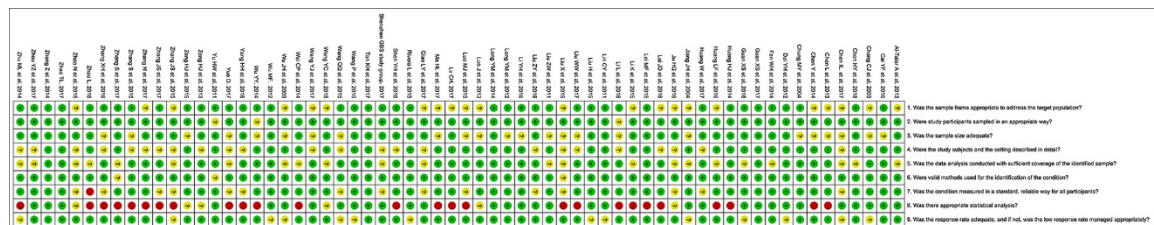
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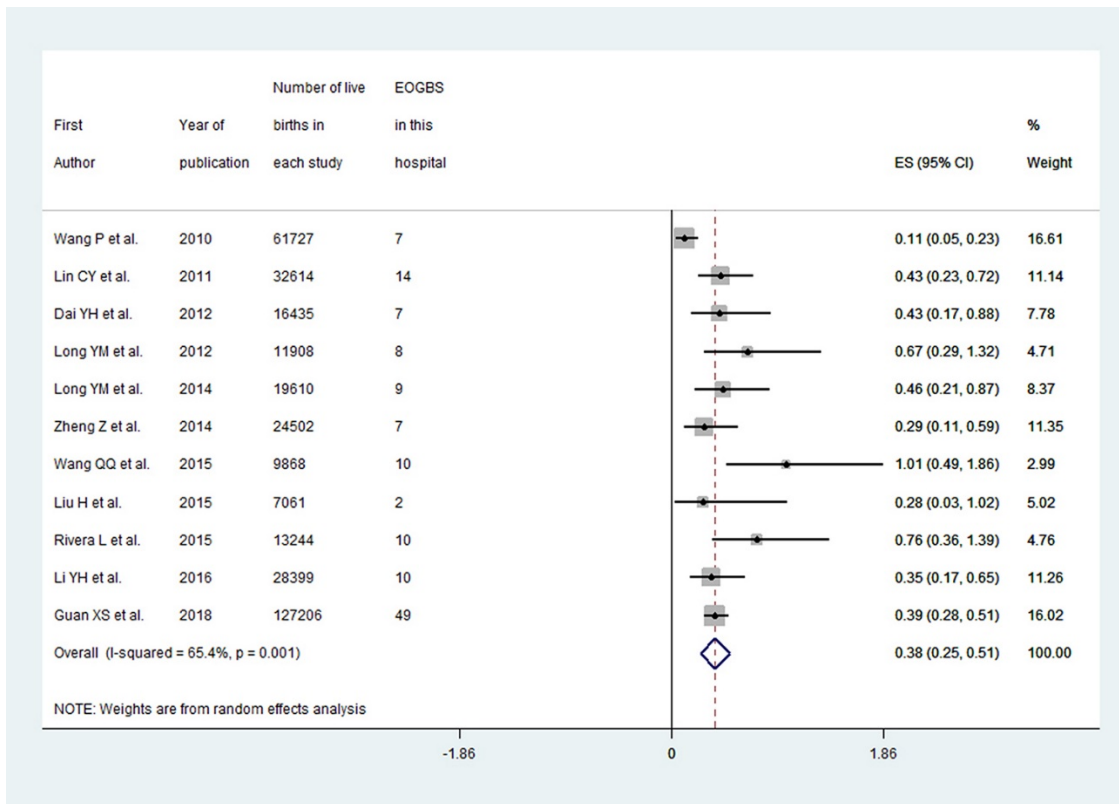
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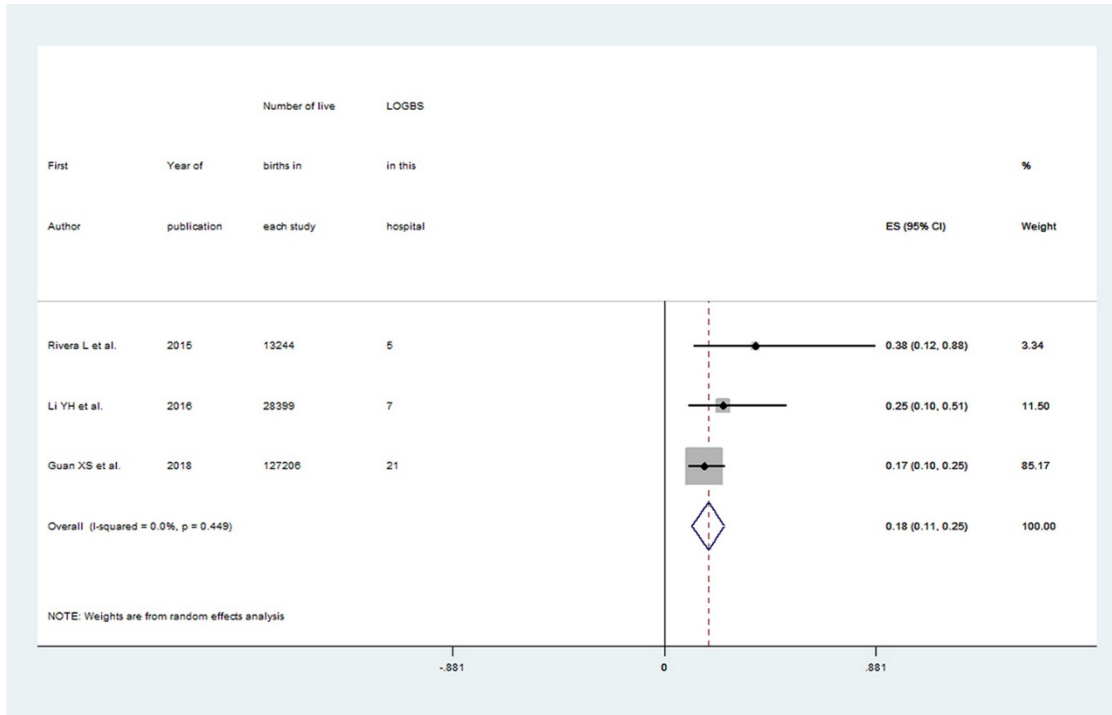
Appendix Figure 1. Publication year of included studies of infants invasive group B *Streptococcus* disease (n = 64) In 2018, we only searched articles published before March 16, 2018.



Appendix Figure 2. Risk for bias in the studies. Colored circles indicate different risks. Green, low risk; yellow, unknown risk; red, high risk.

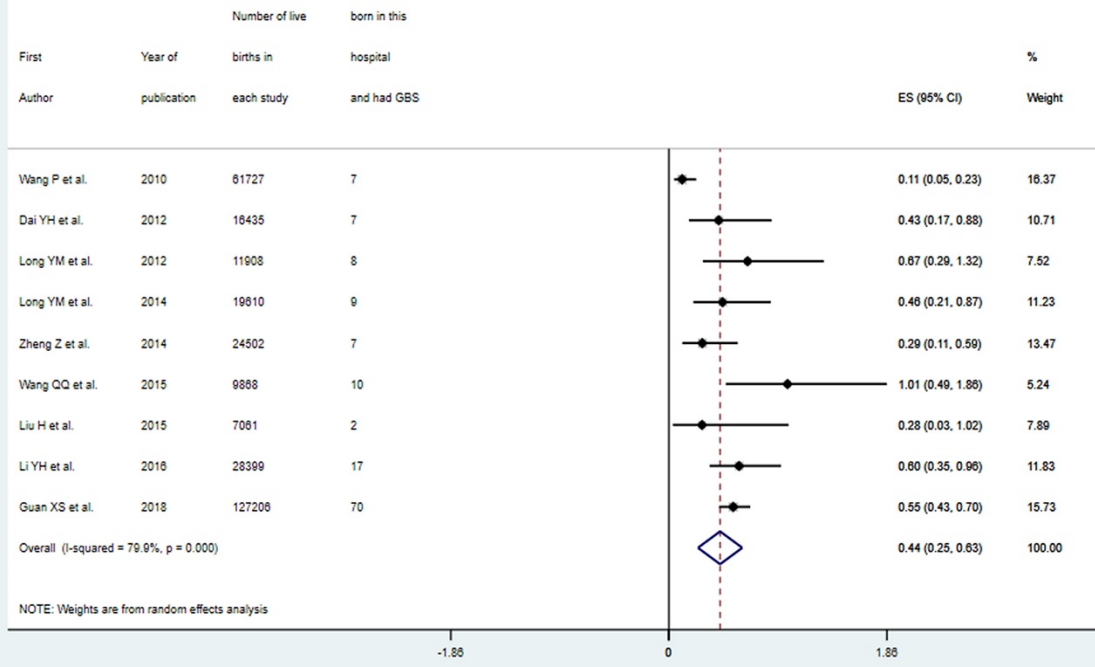


Appendix Figure 3. Incidence risk for early-onset group B *Streptococcus* (EOGBS) disease (n = 11). Vertical dashed line indicates a visual assessment of heterogeneity of the studies. If the vertical line can be drawn, forest plots indicate that all studies are similar enough to be included for meta-analysis. Error bars indicate 95% CI. ES, effect size; GBS, group B *Streptococcus* disease.

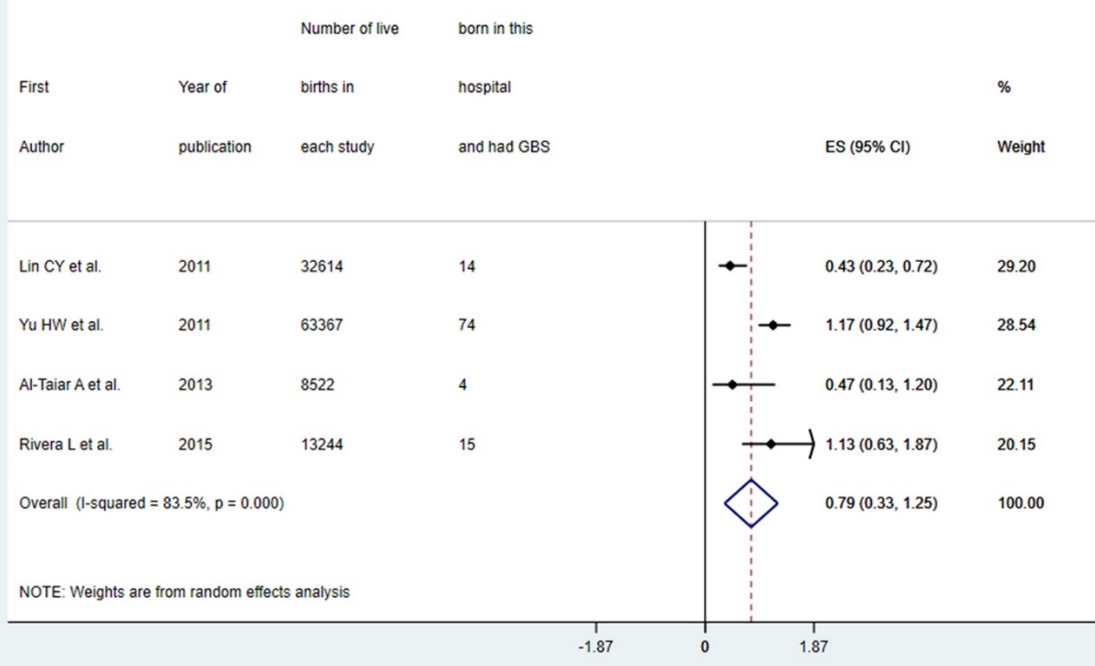


Appendix Figure 4. Incidence risk for late-onset (age 7–89 days) group B *Streptococcus* (LOGBS) disease (n = 3). Vertical dashed line indicates a visual assessment of heterogeneity of the studies. If the vertical line can be drawn, forest plots indicate that all studies are similar enough to be included for meta-analysis. Shaded areas indicate relative weight that each individual study contributes to the overall pooled effect. Error bars indicate 95% CI. ES, effect size.

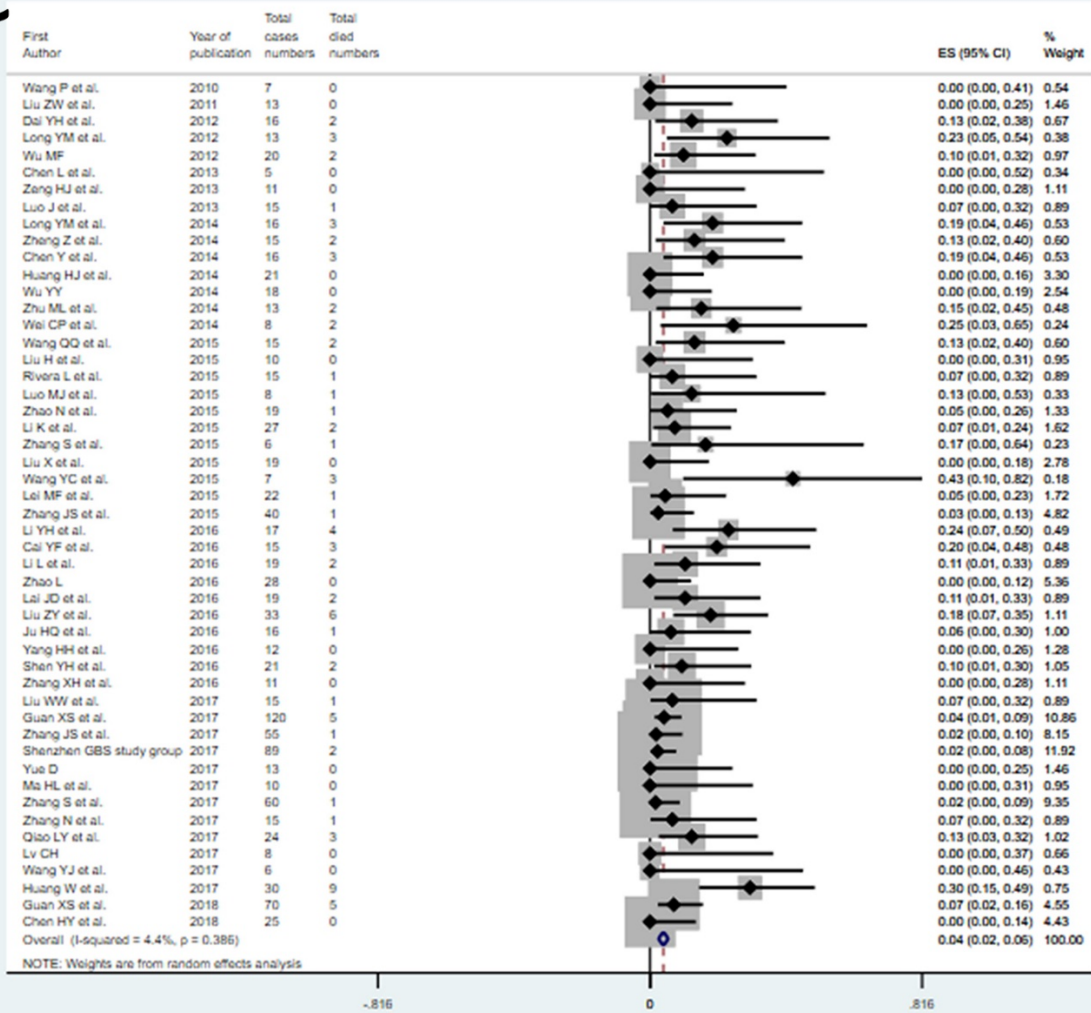
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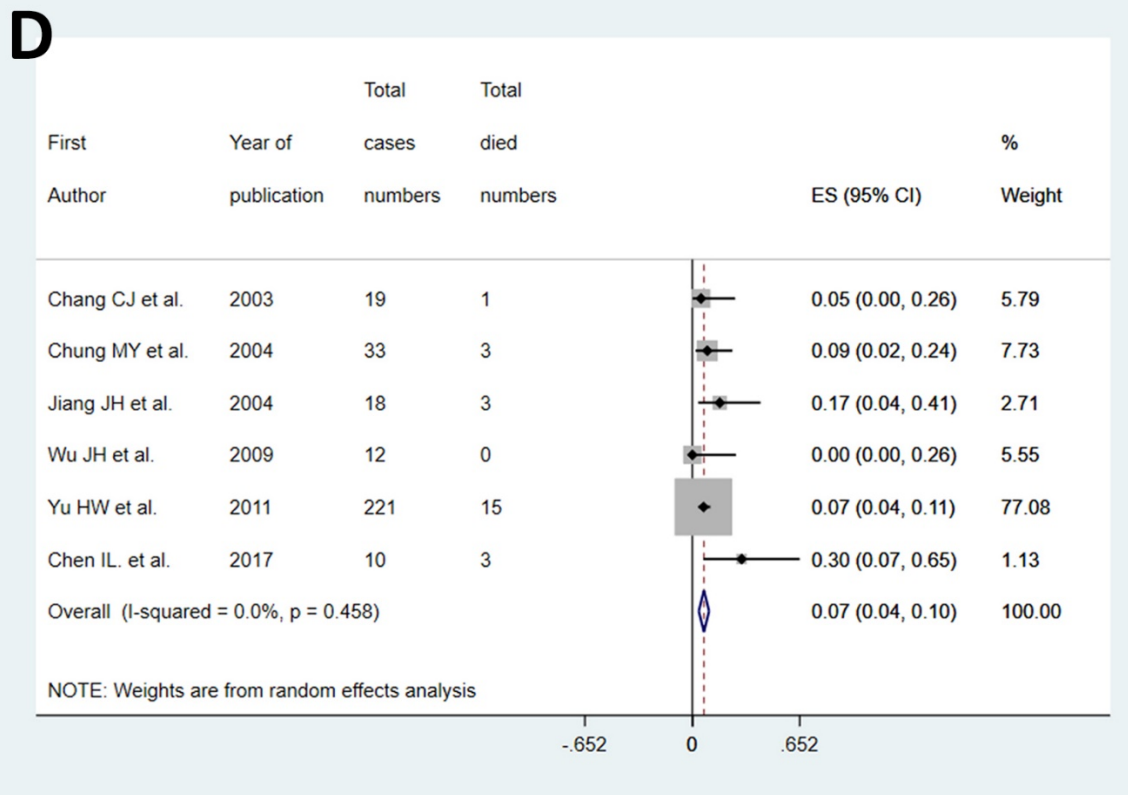


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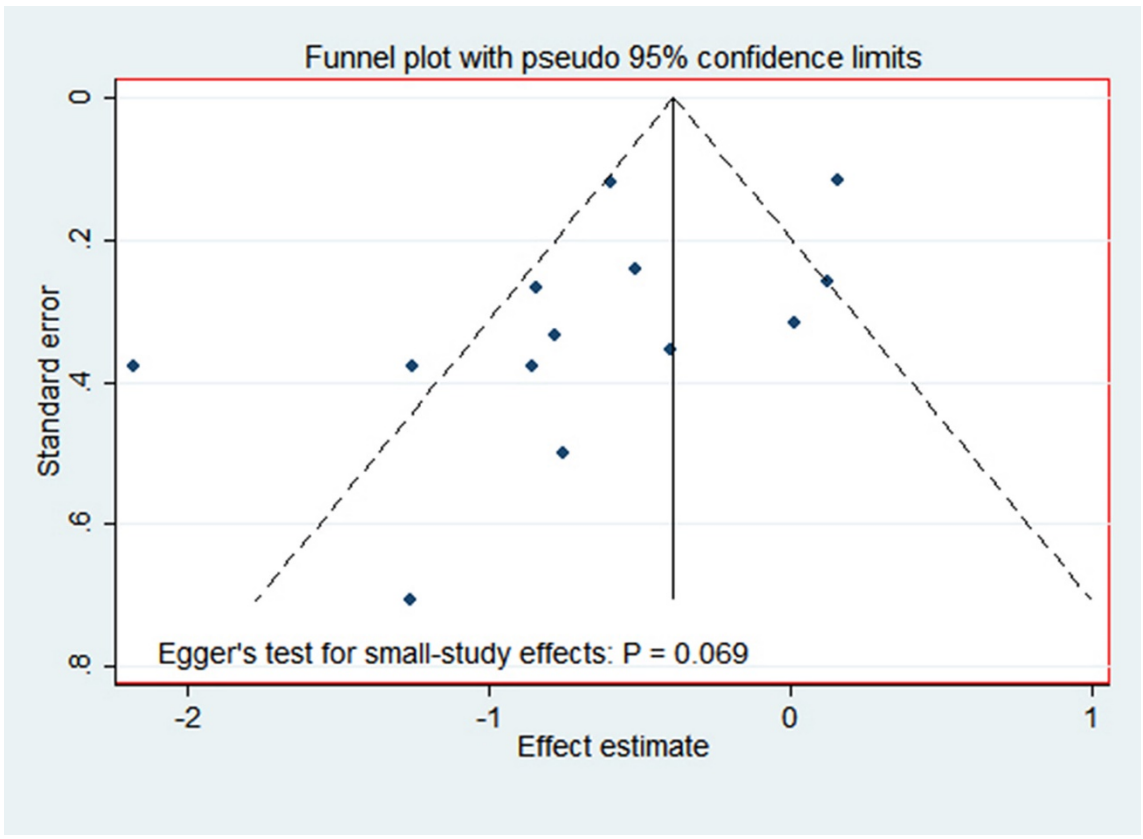


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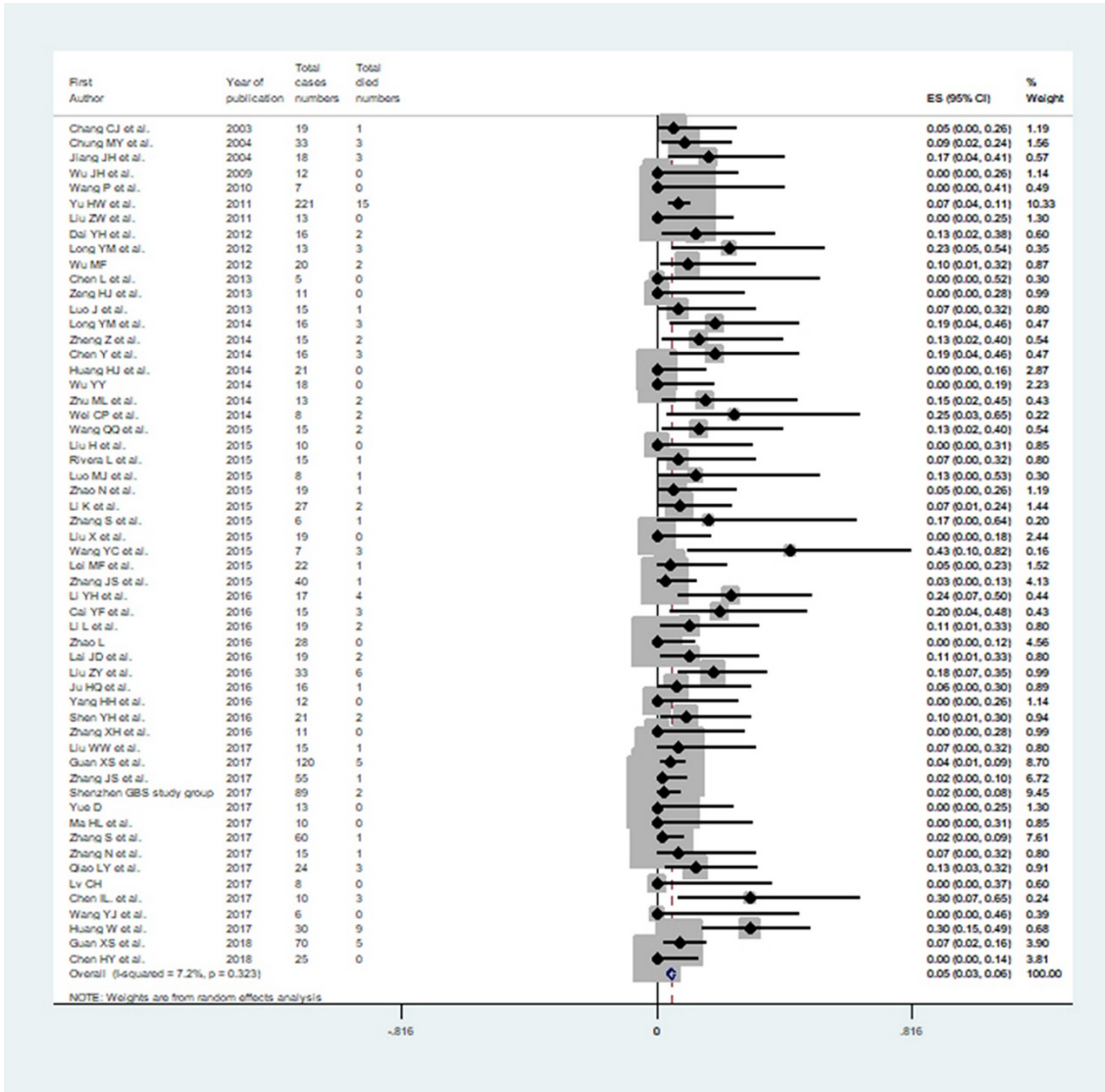




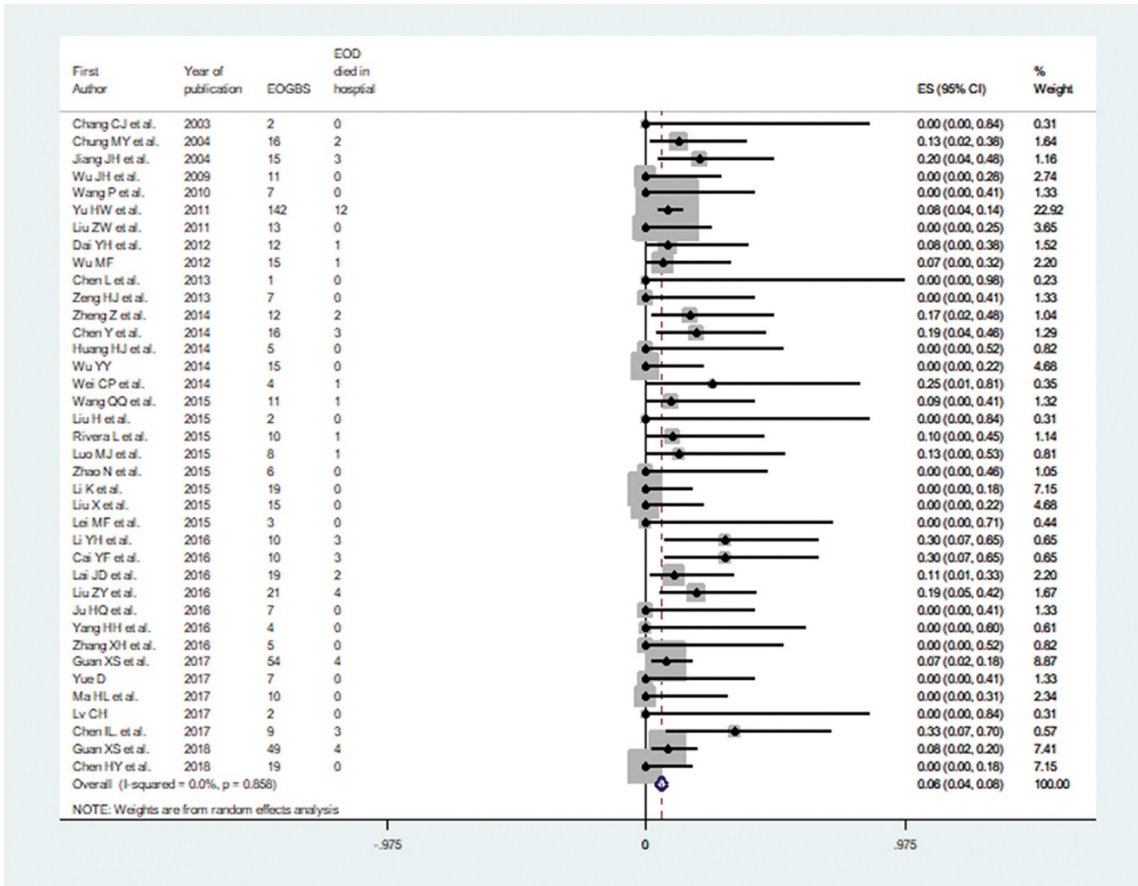
Appendix Figure 5. Sensitivity analysis of GBS invasive diseases incidence studies. A) Total incidence of GBS invasive disease in Mainland China; B) total incidence of GBS invasive disease in Taiwan, Hong Kong, and Macau; C) total CFR of GBS invasive disease in Mainland China; D) total CFR of GBS invasive disease in Taiwan, Hong Kong, and Macau. Vertical dashed line indicates a visual assessment of heterogeneity of the studies. If the vertical line can be drawn, forest plots indicate that all studies are similar enough to be included for meta-analysis. Shaded areas indicate relative weight that each individual study contributes to the overall pooled effect. ES, effect size; GBS, group B *Streptococcus* disease.



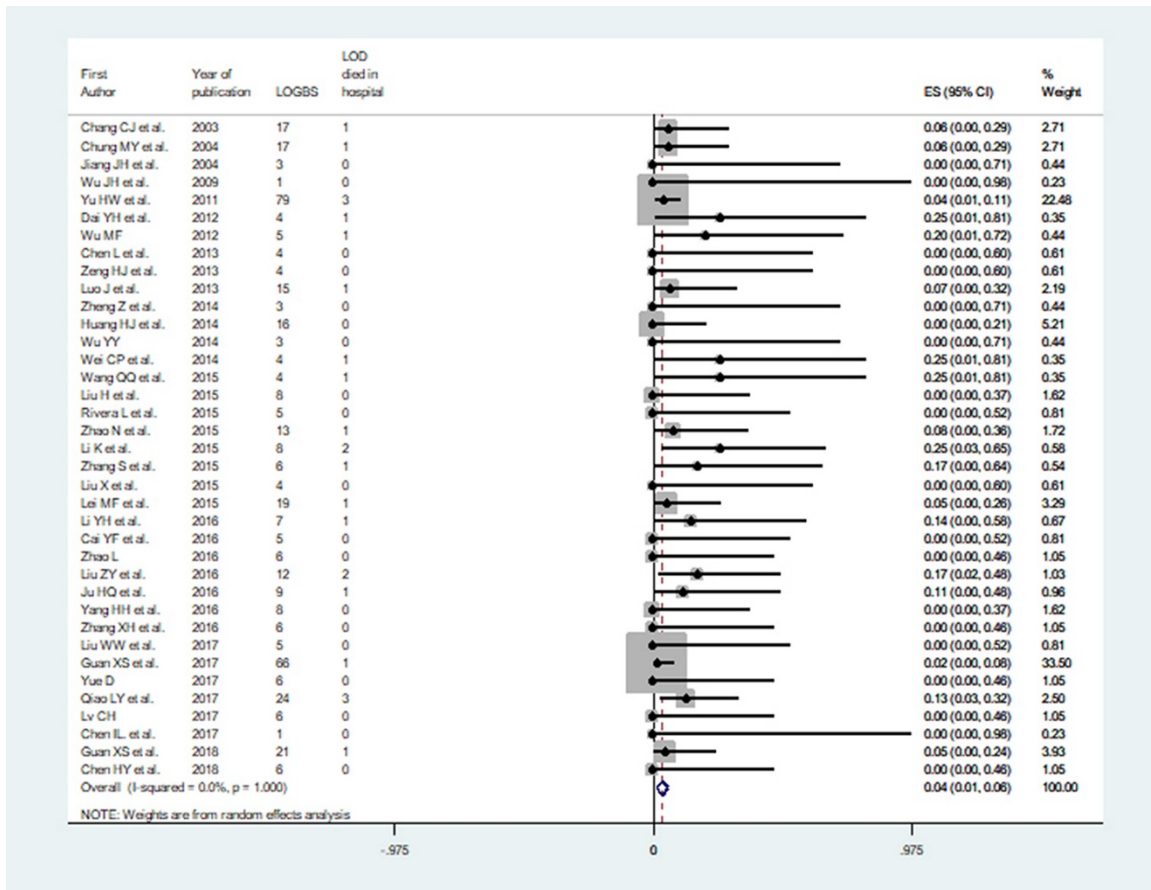
Appendix Figure 6. Funnel plot showing publication bias for group B *Streptococcus* disease.



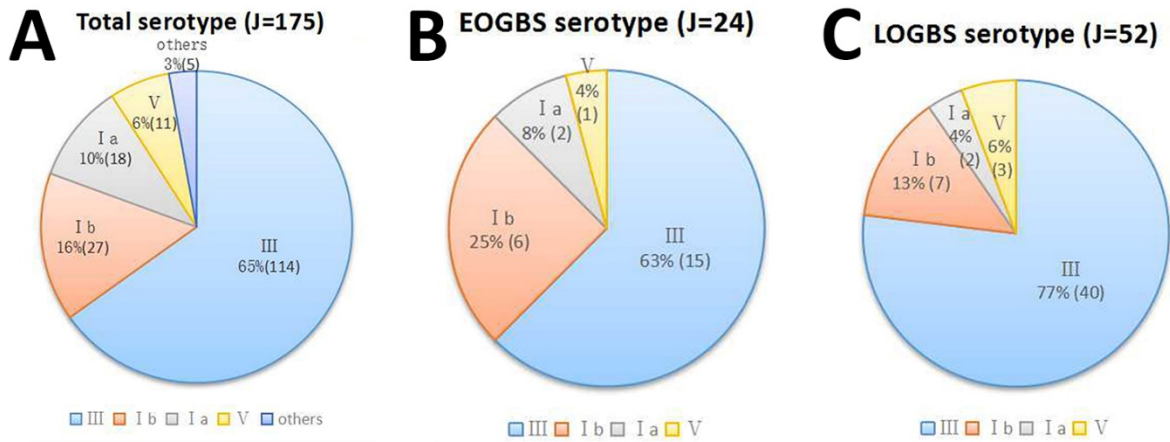
Appendix Figure 7. Case-fatality rate of group B *Streptococcus* (GBS) disease in infants <1–89 days of age (n = 56). Vertical dashed line indicates a visual assessment of heterogeneity of the studies. If the vertical line can be drawn, forest plots indicate that all studies are similar enough to be included for meta-analysis. Shaded areas indicate relative weight that each individual study contributes to the overall pooled effect. CFR, case-fatality rate; ES, effect size; GBS, group B *Streptococcus* disease.



Appendix Figure 8. Case-fatality rate (CFR) of early-onset group B *Streptococcus* (EOGBS) disease (n = 38). Vertical dashed line indicates a visual assessment of heterogeneity of the studies. If the vertical line can be drawn, forest plots indicate that all studies are similar enough to be included for meta-analysis. Shaded areas indicate relative weight that each individual study contributes to the overall pooled effect. EOD, patient died in the hospital; ES, effect size.



Appendix Figure 9. Case fatality rate (CFR) of late-onset group B *Streptococcus* (LOGBS) disease in children 7–89 days of age (n = 37). Vertical dashed line indicates a visual assessment of heterogeneity of the studies. If the vertical line can be drawn, forest plots indicate that all studies are similar enough to be included for meta-analysis. Shaded areas indicate relative weight that each individual study contributes to the overall pooled effect. LOD, patient died in the hospital; ES, effect size.



Appendix Figure 10. Serotype distribution of group B *Streptococcus* (GBS) in infants <1–89 days of age with invasive disease. A) Overall serotype distribution of GBS; B) distribution of early-onset GBS disease; C) distribution of late-onset GBS disease. EOGBS, early-onset GBS disease; LOGBS, late-onset GBS disease.