Supplementary Materials

Disease burden of meningitis caused by *Streptococcus pneumoniae* among under-fives in China: A systematic review and meta-analysis

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Running Title: Pneumococcal meningitis of under-fives in China

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Appendix S1. Study Selection and Data Adjustment

Literature Search Strategy

The literature search was restricted to articles published between January, 1980 and August, 2022. Studies on meningitis published between 1980 and 2021 will be identified using standard search algorithms for systematic review in order to estimate the overall incidence, mortality and case-fatality ratio of meningitis, the distribution of pathogens in meningitis, and the distribution of *Streptococcus pneumoniae* (*S. pneumoniae*) pathogenic serotypes.

Databases searched and detailed search criteria

PubMed/Medline, Ovid-EMBASE, Biosis, Web of Science, Cochrane, and Chinese references databases (CNKI, Wanfang and ViP)

Inclusion and exclusion criteria

Included articles should contain epidemiologic information on meningitis in children younger than five years in China with a surveillance period of 12 months or longer. Articles were excluded if no original data about incidence, prevalence, morbidity, or mortality of meningitis were provided. Narrative reviews, guidelines, or articles without accessible data were also excluded. In addition, articles focusing only on specific groups of patients (e.g., patients with human immunodeficiency virus) or reporting meningitis as one of the complications were ruled out for poor representativeness. We also excluded articles with only neonatal data because the etiological distribution was different from that for older children. Considering potential risk bias, we restricted case reports to those with no less than 50 cases. Studies focusing only on viral or fungal meningitis or providing no information on overall epidemiology of meningitis should be screened out. As our study aimed to assess disease burden of *S. pneumoniae*-induced meningitis, we ruled out studies reporting only data on a specific causal organism other than *S. pneumoniae*.

Quality assessment

Validity of studies reporting on epidemiologic and etiologic characteristics of bacterial meningitis cases were independently assessed by two reviewers in terms of study design, reliability of diagnosis methods, and the possibility of leaving out potential cases. Based on these criteria, included studies were labeled as one of the three categories representing article quality: "A" papers which received approval from both reviewers that all criteria were met, "B" papers with only one approval, and "C" papers in which both reviewers judged that either criterion was not met or that data were not available to make a judgment. Prior to inclusion in the final dataset, a third quality assessment was performed on studies classified as "C" and all included studies. Studies remaining "C" quality after the third assessment were discarded.

PubMed

Access Date: 2022/08/10 21:30

Search Terms: "Meningitis" AND "China" AND "Child" AND ("Mortality" OR "Death" OR "Incidence" OR "Prevalence" OR "Morbidity" OR "Distribution")

Query: ("Meningitis"[Mesh] OR Meningitis[tw] OR Meningitides[tw] OR Pachymeningitis[tw] OR Pachymeningitides[tw]) AND ("China"[Mesh] OR China[tw] OR People's Republic of China[tw] OR Mainland China[tw] OR Sinkiang[tw] OR Inner Mongolia[tw] OR Manchuria[tw] OR Chinese[tw]) AND ("Child, Preschool"[Mesh] OR Preschool Child[tw] OR Children, Preschool[tw] OR Preschool

Children[tw] OR "Child"[Mesh] OR Child[tw] Children[tw] OR "Infant"[Mesh] Infant[tw] OR Infants[tw] OR "Infant, Newborn"[Mesh] OR Infants, Newborn[tw] OR Newborn Infant[tw] OR Newborn Infants[tw] OR Newborns[tw] OR Newborn[tw] OR Neonate[tw] OR Neonates[tw] OR pediatric[tw] OR underage[tw] OR baby[tw] OR babies[tw] OR neonate[tw] OR neonates [tw] OR toddler[tw] OR toddlers[tw] OR underage[tw] OR boy[tw] OR boys[tw] OR girl[tw] OR girls[tw] OR kid[tw] OR kids[tw] OR minor[tw] OR minors[tw]) AND (("Mortality"[Mesh] OR Mortality[tw] OR Mortalities[tw] OR Case Fatality Rate[tw] OR Case Fatality Rates[tw] OR Rate, Case Fatality[tw] OR Rates, Case Fatality[tw] OR CFR Case Fatality Rate[tw] OR Case Fatality Ratio[tw] OR Case Fatality Ratios[tw] OR Crude Death Rate[tw] OR Crude Death Rates[tw] OR Death Rate, Crude[tw] OR Rate, Crude Death[tw] OR Crude Mortality Rate[tw] OR Crude Mortality Rates[tw] OR Mortality Rate, Crude[tw] OR Rate, Crude Mortality[tw] OR Death Rate[tw] OR Death Rates[tw] OR Rate, Death[tw] OR Mortality Rate[tw] OR Mortality Rates[tw] OR Rate, Mortality[tw] OR Mortality, Excess[tw] OR Excess Mortality[tw] OR Excess Mortalities[tw] OR Decline, Mortality[tw] OR Mortality Declines[tw] OR Mortality Decline[tw] OR Mortality Determinants[tw] OR Determinants, Mortality[tw] OR Determinant, Mortality[tw] OR Mortality Determinant[tw] OR Mortality, Differential[tw] OR Differential Mortality[tw] OR Differential Mortalities[tw] OR Age-Specific Death Rate[tw] OR Age-Specific Death Rates[tw] OR Death Rate, Age-Specific[tw] OR Rate, Age-Specific Death[tw] OR Age Specific Death Rate[tw] OR "Death"[Mesh] OR Death[tw]) OR ("Incidence"[Mesh] OR Incidence[tw] OR Incidences[tw] OR Secondary Attack Rate[tw] OR Attack Rate, Secondary[tw] OR Rate, Secondary Attack[tw] OR Secondary Attack Rates[tw] OR Incidence Proportion[tw] OR Incidence Proportions[tw] OR Proportion, Incidence[tw] OR Attack Rate[tw] OR Attack Rates[tw] OR Rate, Attack[tw] OR Cumulative Incidence[tw] OR Cumulative Incidences[tw] OR Incidence, Cumulative[tw] OR Incidence Rate[tw] OR Incidence Rates[tw] OR Rate, Incidence[tw] OR Person-time Rate[tw] OR Person time Rate[tw] OR Person-time Rates[tw] OR Rate, Person-time[tw]) OR ("Prevalence"[Mesh] OR Prevalence[tw] OR Prevalences[tw] OR Period Prevalence[tw] OR Period Prevalences[tw] OR Prevalence, Period[tw] OR Point Prevalence[tw] OR Point Prevalences[tw] OR Prevalence, Point[tw] OR "Morbidity"[Mesh] OR Morbidity[tw] OR Distribution[tw] OR Etiology[tw] OR Epidemic[tw]))
Filter: Publication date from 1980/01/01 to 2022/08/09.
Result: 203

Ovid-EMBASE
Access Date:
Step 1: exp meningitis/ OR meningitis.tw.
Step 2: exp China/ OR China.tw. OR exp Chinese/ OR Chinese.tw.
Step 3: 1 AND 2
Step 4: exp child/ or exp childhood disease/ or exp infant disease/ or (babies or baby or boy? or boyfriend or boyhood or girlfriend or girlhood or child* or girl? or infan* or kid? or minors or minors* or neonat* or neo-nat* or neo-nat* or newborn* or new-born* or paediatric* or peadiatric* or pediatric* or perinat* or preschool* or toddler? or underage? or under-age?).tw.
Step 5: 3 AND 4
Step 6:
Step 6: limit 3 to (infant <to one year> or child <unspecified age> or preschool child <1 to 6 years>)
Step 7: 5 OR 6
Step 8: exp mortality/ or exp incidence/ or exp prevelence/ or exp mortality rate/ or exp incidence rate/

or exp prevelance rate/ or exp etiology/ or exp epidemic/ or (mortality or mortalities or "case fatality rate" or "case fatality rates" or CFR or "case fatality ratio" or "case fatality ratios" or "crude death rate" or "death rate" or "crude mortality rate" or "mortality rate" or "crude death rates" or "death rates" or "crude mortality rates" or "mortality rates" or "excess mortality" or "excess mortalities" or "decline" or "mortality determinant" or "declines" or "mortality determinants" or "differential mortality" or "differential mortalities" or "age-specific death rate" or "age-specific death rates") or (incidence? or "secondary attack rate" or "incidence proportion" or "attack rate" or "cumulative incidence" or "incidence rate" or "person-time rate" or "secondary attack rates" or "incidence proportions" or "attack rates" or "cumulative incidences" or "incidence rates" or "person-time rates") or (prevalence? or "period prevalence" or "point prevalence" or "period prevalences" or "point prevalences" or morbidity or distribution)).tw.
Step 9: 7 AND 8
Step 10: limit 9 to yr="1980 -Current"
Result: 386

Web of Science
Step 1: TS=(meningitis)
Step 2: ALL=(China OR Chinese)
Step 3: ALL=(babies or baby or boy? or boyfriend or boyhood or girlfriend or girlhood or child? or girl? or infan* or kid? or minors or minors* or neonat* or neo-nat* or neo-nat* or newborn* or new-born* or paediatric* or peadiatric* or pediatric* or perinat* or preschool* or toddler? or underage? or under-age?)
Step 4: ALL=((mortality or mortalities or "case fatality rate" or "case fatality rates" or CFR or "case fatality ratio" or "case fatality ratios" or "crude death rate" or "death rate" or "crude mortality rate" or "mortality rate" or "crude death rates" or "death rates" or "crude mortality rates" or "mortality rates" or "excess mortality" or "excess mortalities" or "decline" or "mortality determinant" or "declines" or "mortality determinants" or "differential mortality" or "differential mortalities" or "age-specific death rate" or "age-specific death rates") or (incidence? or "secondary attack rate" or "incidence proportion" or "attack rate" or "cumulative incidence" or "incidence rate" or "person-time rate" or "secondary attack rates" or "incidence proportions" or "attack rates" or "cumulative incidences" or "incidence rates" or "person-time rates") or (prevalence? or "period prevalence" or "point prevalence" or "period prevalences" or "point prevalences" or morbidity or distribution or etiology or epidemic))
Step 5: #1 AND #2 AND #3 AND #4
Filters: Publication date from 1980/01/01 to 2022/08/09.
Result: 193

BIOSIS Previews
Step 1: TS=(meningitis)
Step 2: TS=(China OR Chinese)
Step 3: TS=(babies or baby or boy? or boyfriend or boyhood or girlfriend or girlhood or child? or girl? or infan* or kid? or minors or minors* or neonat* or neo-nat* or neo-nat* or newborn* or new-born* or paediatric* or peadiatric* or pediatric* or perinat* or preschool* or toddler? or underage? or under-age?)
Step 4: #1 AND #2 AND #3
Step 4: TS=((mortality or mortalities or "case fatality rate" or "case fatality rates" or CFR or "case fatality ratio" or "case fatality ratios" or "crude death rate" or "death rate" or "crude mortality rate" or "mortality

rate" or "crude death rates" or "death rates" or "crude mortality rates" or "mortality rates" or "excess mortality" or "excess mortalities" or "decline" or "mortality determinant" or "declines" or "mortality determinants" or "differential mortality" or "differential mortalities" or "age-specific death rate" or "age-specific death rates") or (incidence? or "secondary attack rate" or "incidence proportion" or "attack rate" or "cumulative incidence" or "incidence rate" or "person-time rate" or "secondary attack rates" or "incidence proportions" or "attack rates" or "cumulative incidences" or "incidence rates" or "person-time rates") or (prevalence? or "period prevalence" or "point prevalence" or "period prevalences" or "point prevalences" or morbidity or distribution or etiology or epidemic))
Step 5: #1 AND #2 AND #3 AND #4
Filter: Publication date from 1980/01/01 to 2022/08/09.
Result: 122

Cochrane
Step 1: MeSH descriptor: [meningitis] explode all trees
Step 2: (meningitis):ti,ab,kw
Step 3: #1 OR #2
Step 4: (China OR Chinese):ti,ab,kw
Step 5: (babies or baby or boy? or boyfriend or boyhood or girlfriend or girlhood or child? or girl? or infan* or kid? or minors or minors* or neonat* or neo-nat* or neo-nat* or newborn* or new-born* or paediatric* or peadiatric* or pediatric* or perinat* or preschool* or toddler? or underage? or under-age?):ti,ab,kw
Step 6: ((mortality or mortalities or "case fatality rate" or "case fatality rates" or CFR or "case fatality ratio" or "case fatality ratios" or "crude death rate" or "death rate" or "crude mortality rate" or "mortality rate" or "crude death rates" or "death rates" or "crude mortality rates" or "mortality rates" or "excess mortality" or "excess mortalities" or "decline" or "mortality determinant" or "declines" or "mortality determinants" or "differential mortality" or "differential mortalities" or "age-specific death rate" or "age-specific death rates") or (incidence? or "secondary attack rate" or "incidence proportion" or "attack rate" or "cumulative incidence" or "incidence rate" or "person-time rate" or "secondary attack rates" or "incidence proportions" or "attack rates" or "cumulative incidences" or "incidence rates" or "person-time rates") or (prevalence? or "period prevalence" or "point prevalence" or "period prevalences" or "point prevalences" or morbidity or distribution or etiology or epidemic)):ti,ab,kw
Step 7: #3 AND #4 AND #5 AND #6
Result: 11

CNKI
(SU=('xinshenger'+'yinger'+'yingyouer'+'youer'+'xiaoer'+'ertong') OR AB=('xinshenger'+'yinger'+'yingyouer'+'youer'+'xiaoer'+'ertong') OR TI=('xinshenger'+'yinger'+'yingyouer'+'youer'+'xiaoer'+'ertong') OR KY=('xinshenger'+'yinger'+'yingyouer'+'youer'+'xiaoer'+'ertong')) AND (SU=naomoyan' OR AB='naomoyan' OR TI='naomoyan' OR KY='naomoyan') AND (SU=('siwang'+'huanbing'+'bingsi'+'fabing'+'lihuan'+'fenbu'+'bingyin'+'liuxing'+'zhisilv'+'bingli') OR AB=('siwang'+'huanbing'+'bingsi'+'fabing'+'lihuan'+'fenbu'+'bingyin'+'liuxing'+'zhisilv'+'bingli') OR TI=('siwang'+'huanbing'+'bingsi'+'fabing'+'lihuan'+'fenbu'+'bingyin'+'liuxing'+'zhisilv'+'bingli') OR KY=('siwang'+'huanbing'+'bingsi'+'fabing'+'lihuan'+'fenbu'+'bingyin'+'liuxing'+'zhisilv'+'bingli'))
(SU=('新生儿'+'婴儿'+'婴幼儿'+'幼儿'+'小儿'+'儿童') OR AB=('新生儿'+'婴儿'+'婴幼儿'+'幼儿'+'小

儿'+'儿童') OR TI=('新生儿'+'婴儿'+'婴幼儿'+'幼儿'+'小儿'+'儿童') OR KY=('新生儿'+'婴儿'+'婴幼儿'+'幼儿'+'小儿'+'儿童')) AND (SU='脑膜炎' OR AB='脑膜炎' OR TI='脑膜炎' OR KY='脑膜炎') AND (SU=('死亡'+'患病'+'病死'+'发病'+'罹患'+'分布'+'病因'+'流行'+'致死率'+'病例') OR AB=('死亡'+'患病'+'病死'+'发病'+'罹患'+'分布'+'病因'+'流行'+'致死率'+'病例') OR TI=('死亡'+'患病'+'病死'+'发病'+'罹患'+'分布'+'病因'+'流行'+'致死率'+'病例') OR KY=('死亡'+'患病'+'病死'+'发病'+'罹患'+'分布'+'病因'+'流行'+'致死率'+'病例'))
Filters: Publication date from 1980/01/01 to 2022/08/09.
Result: 4473

Wanfang
((subject:(xinshenger) or subject:(yinger) or subject:(yingyouer) or subject:(youer) or subject:(xiaoer) or subject:(ertong)) and subject:(naomoyan)) and (subject:(siwang) or subject:(huanbing) or subject:(fabing) or subject:(lihuan) or subject:(fenbu) or subject:(bingyin) or subject:(liuxing) or subject:(zhisilv) or subject:(bingli))) and Date:1980-*
((主题:(新生儿) or 主题:(婴儿) or 主题:(婴幼儿) or 主题:(幼儿) or 主题:(小儿) or 主题:(儿童)) and 主题:(脑膜炎) and (主题:(死亡) or 主题:(患病) or 主题:(发病) or 主题:(罹患) or 主题:(分布) or 主题:(病因) or 主题:(流行) or 主题:(致死率) or 主题:(病例))) and Date:1980-* Result: 4413

VIP
(M=(xinshenger+yinger+yingyouer+youer+xiaoer+ertong)+R=(xinshenger+yinger+yingyouer+youer+xiaoer+ertong))*(M=naomoyan+R=naomoyan)*(M=(siwang+huanbing+bingsi+fabing+lihuan+fenbu+bingyin+liuxing+zhisilv+bingli)+R=(siwang+huanbing+bingsi+fabing+lihuan+fenbu+bingyin+liuxing+zhisilv+bingli))
(M=(新生儿+ 婴儿+婴幼儿+幼儿+小儿+儿童)+R=(新生儿+婴儿+婴幼儿+幼儿+小儿+儿童))*(M=脑膜炎+R=脑膜炎)*(M=(死亡+患病+病死+发病+罹患+分布+病因+流行+致死率+病例)+R=(死亡+患病+病死+发病+罹患+分布+病因+流行+致死率+病例))
Result: 3281

Data adjustment
Adjustments for hospitalization proportion, PCV use and access to care were considered. Proportion of in-hospital cases derived from patients with acute meningitis or encephalitis (AME) was applied to calculate incidence rate. Since the hospitalization rate study was conducted after introduction of PCV7, we then adjusted it to generate non-PCV incidence rate for meta-analysis. When estimating pneumococcal meningitis deaths, pooled raw CFR from meta-analysis was adjusted with potential access to care because children with pneumococcal meningitis might die at home, and some might be misdiagnosed on admission. We utilized the proportion of children seeking care for minor illnesses (such as stomachache or diarrhea) from CHNS as a proxy.

Table S1. PSRIMA 2020 checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	4-5
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	4-5
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	5-6
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	5 & Appendix S1
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Appendix S1
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	6
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	6
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	7
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	7
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	None
Effect	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used	7

measures		in the synthesis or presentation of results.	
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	7-8
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	7-8
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	7-8
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	7-8
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	7-8
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	8 & Table S7
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	None
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	7
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	8-9
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	8-9
Study characteristics	17	Cite each included study and present its characteristics.	Table S2-S6
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	None
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	9-12
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	9-12
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	9-12

	20c	Present results of all investigations of possible causes of heterogeneity among study results.	9-12
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Table S9
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	None
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	9-12
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	13
	23b	Discuss any limitations of the evidence included in the review.	14&17
	23c	Discuss any limitations of the review processes used.	16-17
	23d	Discuss implications of the results for practice, policy, and future research.	16-17
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	None
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	None
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	None
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	1&18
Competing interests	26	Declare any competing interests of review authors.	18
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	None

Table S2. Included studies after full text screening

Studies reporting on epidemiology of meningitis

1. Wu X, Dong BQ, Lin M, et al. Analysis of epidemiologic features of children with suspected meningitis in Nanning, Guangxi, 2000-2002. *Guangxi Prev Med* 2004; **10**(6): 324–6 (in Chinese).

2. Yang J, Dong B, Lin M, et al. Surveillance of acute encephalitis and meningitis in Guangxi autonomous region, China. *Dis Surveill* 2010; **25**(03): 190–4 (in Chinese).

3. Yang Y, Leng Z, Shen X, et al. Acute bacterial meningitis in children in Hefei, China 1990-1992. *Chin Med J (Engl)* 1996; **109**(5): 385–8.

4. Huang S. Clinical analysis of 108 cases purulent meningitis in infants [Master's Thesis]: Guangxi Medical University; 2013 (in Chinese).

5. Li Y, Yin Z, Shao Z, et al. Population-based surveillance for bacterial meningitis in China, September 2006-December 2009. *Emerg Infect Dis* 2014; **20**(1): 61-9.

6. Huang M. The etiology and clinical analysis of purulent meninggitis in children [Master's Thesis]: Chongqing Medical University; 2016 (in Chinese).

7. Huo L, Jiang C, Fan Y, Gao J, Wang H. Clinical features of hydrocephalus in 2067 cases of childhood purulent meningitis. *Chin J Pract Pediatr* 2018; **33**(7): 532–7 (in Chinese).

8. LI R, Wu S, Li L, Zhu L, Cui X. Analysis of distribution and drug resistance of pathogenic bacteria of meningitis infection in children. *Chinese Journal of Laboratory Pathologist* 2010; **2**(4): 205–8 (in Chinese).

9. Zhang L. The clinical manifestation and prognosis factor of purulent meningitis in 216 children [Master's Thesis]: Xuzhou Medical University; 2008 (in Chinese).

10. Dong B, Tang Z, Lin M, et al. Epidemiologic surveillance for bacterial meningitis in 140 000 children under 5 years of age in Nanning district, Guangxi province. *Zhonghua liu Xing Bing xue za zhi= Zhonghua Liuxingbingxue Zazhi* 2004; **25**(5): 391-5.

11. Chen Y, Liu L, Luo Y. Clinical analysis of 200 cases of purulent meningitis. *Chin J Med* 1999; **34**(7): 37 (in Chinese).

12. Feng H, Wang F, Zhang Y. Mortality rate and causes of deaths among children under 5 years old in Guizhou province, 1991–1995. *Chin J Public Health* 2017; **33**(10): 1469–73 (in Chinese).

13. He Z, Li X, Jiang L. Clinical analysis on 430 cases of infantile purulent meningitis. *SpringerPlus* 2016; **5**(1): 1994.

14. Le Y, Wang F, Gao W. Early diagnosis and treatment of purulent meningitis in infants: with analysis of 57 cases. *Journal of Liaoning Medical University* 1988; **9**(2): 140–2 (in Chinese).

15. Lv Z, Duan Q, Liu X, Yue S. Analysis of prognostic factors in 79 cases of pediatric purulent meningitis. *Shandong Medical Journal* 2001; **40**(20): 49–50 (in Chinese).

16. Zhang L. The study of clinical and pathogenic analysis and the value of S100B in early diagnosis of pediatric bacterial meningitis [Master's Thesis]: Fudan University; 2013 (in Chinese).

17. Zhang Y, Li M, Liu G, Song L, Zhang L, Xu A. Analysis of common pathogens and epidemiological characteristics of acute bacterial meningitis cases in Shandong Province. Paper presented at: The 9th forum on basic science & applied technology for prevention and control of infectious diseases. Inner Mongolia, China; 2018.

18. Zhang Y, Li M, Song L, et al. Sentinel surveillance and etiological analysis of acute bacterial meningitis in Shandong, 2006–2012. *Dis Surveill* 2014; **29**(1): 48–50 (in Chinese).

19. Zhao X, Cao W. Mortality surveillance of children younger than five years in Gansu, China in 2001–2005. *Maternal and child health care of China* 2011; **26**: 4354-6 (in Chinese).

20. Zou D, Liao J, Hu Y, Li B. Clinical analysis of 55 cases of purulent meningitis in infants. *The Journal of Practical Medicine* 2011; **27**(4): 639–42 (in Chinese).

Studies reporting on epidemiology of pneumococcal meningitis

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Table S3. Profile of included studies on incidence rate of meningitis

Meningitis type	Author-Year	Province	Study Design	Meningitis cases	Denominator (child-years)	Incidence rate (/100,000)
Probable bacterial meningitis	Yixing Li et al. 2014	Shandong	Surveillance	345	4102260	8.41
Probable bacterial meningitis	Yixing Li et al. 2014	Hubei	Surveillance	89	1280575	6.95
Probable bacterial meningitis	Yixing Li et al. 2014	Hebei	Surveillance	294	2563208	11.47
Probable bacterial meningitis	Yixing Li et al. 2014	Guangxi	Surveillance	436	1951656	22.34
Confirmed bacterial meningitis	Xinghua Wu et al. 2004	Guangxi	Surveillance	38	306947	12.38
Confirmed bacterial meningitis	Jinye Yang 2010	Guangxi	Surveillance	14	583333	2.40
Confirmed bacterial meningitis	Yonghong Yang et al. 1996	Anhui	Observational	46	234454	19.62
Pneumococcal meningitis	Mei Lin et al. 2004	Guangxi	Surveillance	4	307692	1.30
Pneumococcal meningitis	Xinghua Wu et al. 2004	Guangxi	Surveillance	3	306947	0.98
Pneumococcal meningitis	Kaile Chen et al. 2021	Jiangsu	Surveillance	33	722100	4.57

Table S4. Profile of included studies on mortality rate of meningitis

Meningitis type	Author-Year	Province	Start Year	End Year	Deaths	Denominator (child-years)	Mortality rate (/100,000) (95%CI)
All-cause meningitis	Xiaoxia Zhao et al. 2011	Gansu	2001	2005	7	74137	9.44
All-cause meningitis	Haizhe Feng et al. 2017	Guizhou	2004	2008	18	201715	8.92
All-cause meningitis	Haizhe Feng et al. 2017	Guizhou	2009	2009	108	358341	30.14
All-cause meningitis	Haizhe Feng et al. 2017	Guizhou	2010	2010	122	448996	27.17
All-cause meningitis	Haizhe Feng et al. 2017	Guizhou	2011	2011	104	444643	23.39
All-cause meningitis	Haizhe Feng et al. 2017	Guizhou	2012	2012	115	332185	34.62
All-cause meningitis	Haizhe Feng et al. 2017	Guizhou	2013	2013	17	220769	7.70
All-cause meningitis	Haizhe Feng et al. 2017	Guizhou	2014	2014	172	414359	41.51
All-cause meningitis	Haizhe Feng et al. 2017	Guizhou	2015	2015	14	304672	4.60
Confirmed bacterial meningitis	Xinghua Wu et al. 2004	Guangxi	2000	2002	7	306947	2.28
Pneumococcal meningitis	Mei Lin et al. 2004	Guangxi	2000	2002	1	307692	0.33

Table S5. Profile of included studies on case-fatality rate of meningitis

Author-Year	Start year	End year	Province	Data source	Study Design	Age strata	Meningitis Type	Case number	Death number
Xiaoling Shi et al. 2021	2017	2019	Qinghai	Hospital-based	Retrospective	0~1y	PM	80	19
Liang Zhu et al. 2020	2012	2017	Beijing	Hospital-based	Retrospective	0~1y	PM	32	11
Liang Zhu et al. 2020	2012	2017	Beijing	Hospital-based	Retrospective	3~5y	PM	30	8
Caiyun Wang et al. 2019	2013	2017	Multi-center	Hospital-based	Retrospective	0~1y	PM	64	16
Caiyun Wang et al. 2019	2013	2017	Multi-center	Hospital-based	Retrospective	1~3y	PM	39	7
Yan Zhang et al. 2018	2013	2016	Shandong	Hospital-based	Retrospective	1~3y	PM	4	0
Wenhui Wang et al. 2022	2014	2016	Shanxi	Hospital-based	Retrospective	3~5y	PM	26	11
Mei et al. 2004	2000	2002	Guangxi	Surveillance	Prospective	3~5y	PM	4	1
Shiqin Huang et al. 2013	2005	2012	Guangxi	Hospital-based	Retrospective	1~3y	BM	108	0
Lili Zhang et al. 2008	1986	2005	Jiangsu	Hospital-based	Retrospective	1~3y	BM	178	44
Ruirong Li et al. 2010	2010	2010	Jiangxi	Hospital-based	Retrospective	0~1y	BM	60	3
Liang Huoet al. 2018	2010	2016	Liaoning	Hospital-based	Retrospective	0~1y	BM	238	1
Mengyuan Huang et al. 2016	2006	2015	Chongqing	Hospital-based	Retrospective	0~1y	BM	203	0
Baiqing Dong et al. 2004	2000	2002	Guangxi	Surveillance	Prospective	3~5y	BM	38	7
Yan Zhang et al. 2018	2013	2016	Shandong	Hospital-based	Retrospective	1~3y	BM	194	0
Li Zhang et al. 2015	2001	2012	Shanghai	Hospital-based	Retrospective	0~1y	BM	36	1
Li Zhang et al. 2015	2001	2012	Shanghai	Hospital-based	Retrospective	1~3y	BM	20	1

Zufang Lv et al. 2001	1990	2000	Shandong	Hospital-based	Retrospective	0~1y	BM	65	8
Dongfang Zou et al. 2011	2006	2010	Guangdong	Hospital-based	Retrospective	0~1y	BM	55	4
Yanhua Chen et al. 1999	1993	1998	Beijing	Hospital-based	Retrospective	3~5y	BM	200	5
Yan Zhang et al. 2014	2006	2016	Shandong	Hospital-based	Retrospective	1~3y	BM	63	0
Yuan Le et al. 1988	1981	1987	Liaoning	Hospital-based	Retrospective	0~1y	BM	57	10
Zhihui He et al. 2016	2004	2013	Chongqing	Hospital-based	Retrospective	1~3y	BM	430	3

Table S6. Profile of included studies on etiology bacterial meningitis

Author-Year	Start year	End year	Province	Data source	Study Design	Age strata	Meningitis types	Specimen type	Method	Total positive cases	Denomina tor	Sp positive
Qian Huang et al. 2019	2013	2017	Qinghai	Hospital-based	Retrospecti ve	<5 years	SBM	CSF/Blood	Culture/P CR	24	145	12
Dongmei Tan et al. 2004	2000	2002	Guangxi	Surveillance	Prospective	<5 years	SBM	CSF	Culture	22	1212	3
Dongmei Tan et al. 204	2000	2002	Guangxi	Surveillance	Prospective	<5 years	SBM	Blood	Culture	39	1193	3
Junjie Zheng et al. 2020	2016	2020	Fujian	Hospital-based	Prospective	<5 years	SBM	CSF	Culture	53	5564	14
Huiping Wang et al. 2018	2013	2017	Yunnan	Hospital-based	Retrospecti ve	<3 years	PBM	CSF/Blood	Culture	25	1026	10
Luohui Liu et al. 2018	2014	2016	Guangdong	Hospital-based	Retrospecti ve	<1 year	PBM	CSF/Blood	Culture	6	72	-
Shiqin Huang et al. 2013	2005	2012	Guangxi	Hospital-based	Retrospecti ve	<3 years	PBM	Blood	Culture	8	68	1
Shiqin Huang et al. 2013	2005	2012	Guangxi	Hospital-based	Retrospecti ve	<3 years	PBM	CSF	Culture	11	97	3
Jun Yang et al. 2015	2010	2014	Guangdong	Hospital-based	Retrospecti ve	1 month~5 years	PBM	CSF/Blood	Culture	56	64	
Dalin Lu et al. 1992	1986	1989	Anhui	Hospital-based	Retrospecti ve	1 month~1 year	PBM	CSF	Culture	23	71	6
Dalin Lu et al. 1992	1986	1989	Anhui	Hospital-based	Retrospecti ve	1~3 years	PBM	CSF	Culture	2	11	-

Rong Mi et al. 2007	1992	2006	Beijing	Hospital-based	Retrospective	< 3 months	PBM	Blood	Culture	6	33	-
Dongfang Zou et al. 2011	2006	2010	Guangdong	Hospital-based	Retrospective	<1 year	PBM	CSF	Culture	14	55	8
Dongfang Zou et al. 2011	2006	2010	Guangdong	Hospital-based	Retrospective	<1 year	PBM	Blood	Culture	22	55	6
Jianre Ye et al. 2011	2008	2010	Zhejiang	Hospital-based	Retrospective	<3 years	PBM	CSF/Blood	Culture	27	72	4
Jing Gao et al. 2013	2009	2011	Jiangxi	Hospital-based	Retrospective	<5 years	PBM	CSF/Blood	Culture	19	86	6
Jieming Yu et al. 2018	2015	2017	Fujian	Hospital-based	Retrospective	1~3 months	PBM	Blood	Culture	10	53	-
Jieming Yu et al. 2018	2015	2017	Fujian	Hospital-based	Retrospective	1~3 months	PBM	CSF	Culture	4	53	-
Liwen Wu et al. 2018	2011	2016	Hunan & Chongqing	Hospital-based	Retrospective	1 month~1 year	PBM	CSF/Blood	Culture	109	317	13
Liwen Wu et al. 2018	2011	2016	Hunan & Chongqing	Hospital-based	Retrospective	1~3 years	PBM	CSF/Blood	Culture	16	47	11
Zhihui He et al. 2016	2004	2013	Chongqing	Hospital-based	Retrospective	1 month~3 years	PBM	Blood	Culture	22	146	5
Zhihui He et al. 2016	2004	2013	Chongqing	Hospital-based	Retrospective	1 month~3 years	PBM	CSF	Culture	5	420	2
Chi Li et al. 2018	2014	2016	Multi-center	Hospital-based	Retrospective	1 month~3 years	PBM	CSF/Blood	Culture	224	576	96
Xueqin Li et al. 2020	2015	2019	Henan	Hospital-based	Retrospective	<3 months	CBM	CSF	Culture	63	-	-

Liping Chen et al. 2021	2014	2019	Fujian	Hospital-based	Retrospective	1 month~3 years	CBM	CSF	Culture	28	-	13
Lei Shi et al. 2018	2012	2016	Henan	Hospital-based	Retrospective	1 month~1 year	CBM	CSF	Culture	26	-	3
Lei Shi et al. 2018	2012	2016	Henan	Hospital-based	Retrospective	1~3 years	CBM	CSF	Culture	19	-	-
Tao Huang et al. 2019	2014	2018	Tianjin	Hospital-based	Retrospective	1 month~1 year	CBM	CSF/Blood	Culture	50	-	10
Tao Huang et al. 2019	2014	2018	Tianjin	Hospital-based	Retrospective	1~5 years	CBM	CSF/Blood	Culture	16	-	5
Liyuan Wu et al. 2015	2009	2014	Sichuan	Hospital-based	Retrospective	3 months~1 year	CBM	CSF	Culture	12	-	4
Liyuan Wu et al. 2015	2009	2014	Sichuan	Hospital-based	Retrospective	1~3 years	CBM	CSF	Culture	5	-	5
Qiongling Peng et al. 2016	2011	2015	Guangdong	Hospital-based	Retrospective	<1 year	CBM	CSF/Blood	Culture	43	-	17
Qiongling Peng et al. 2016	2011	2015	Guangdong	Hospital-based	Retrospective	<3 years	CBM	CSF/Blood	Culture	18	-	10
Luona lin et al. 2016	2004	2015	Zhejiang	Hospital-based	Retrospective	<1 year	CBM	CSF/Blood	Culture	42	-	15
Yongqiang Xie et al. 2011	2005	2009	Guangdong	Hospital-based	Retrospective	1~3 months	CBM	CSF	Culture	55	-	5
Yongqiang Xie et al. 2011	2005	2009	Guangdong	Hospital-based	Retrospective	3 months~1 year	CBM	CSF	Culture	76	-	20
Yongqiang Xie et al. 2011	2005	2009	Guangdong	Hospital-based	Retrospective	1~3 years	CBM	CSF	Culture	76	-	26

Hong Li et al. 2009	1998	2002	Tianjin	Hospital-based	Retrospective	1 month~5 years	CBM	CSF	Culture	63	-	4
Chunfang Wu et al. 2015	2012	2014	Henan	Hospital-based	Retrospective	1 month~5 years	CBM	CSF/Blood	Culture	45	-	3
Lijun Du et al. 2014	2005	2014	Shanxi	Hospital-based	Retrospective	<3 months	CBM	CSF	Culture	94	-	2
Lijun Du et al. 2014	1994	2004	Shanxi	Hospital-based	Retrospective	<3 months	CBM	CSF	Culture	32	-	3
Lijun Du et al. 2014	1994	2004	Shanxi	Hospital-based	Retrospective	3 months~1 year	CBM	CSF	Culture	70	-	15
Lijun Du et al. 2014	2005	2014	Shanxi	Hospital-based	Retrospective	3 months~1 year	CBM	CSF	Culture	65	-	21
Lijun Du et al. 2014	2005	2014	Shanxi	Hospital-based	Retrospective	1~5 years	CBM	CSF	Culture	96	-	29
Lijun Du et al. 2014	1994	2014	Shanxi	Hospital-based	Retrospective	1~5 years	CBM	CSF	Culture	72	-	22
Jun Huang 2020	2014	2020	Guangdong	Hospital-based	Retrospective	1 month~1 year	CBM	CSF	Culture	30	-	3
Lingyun Guo 2016	2010	2014	Beijing	Hospital-based	Retrospective	1~2 months	CBM	CSF/Blood	Culture	43	-	1
Lingyun Guo 2016	2010	2014	Beijing	Hospital-based	Retrospective	3 months~1 year	CBM	CSF/Blood	Culture	115	-	58
Lingyun Guo 2016	2010	2014	Beijing	Hospital-based	Retrospective	1~3 years	CBM	CSF/Blood	Culture	66	-	37
Lingyun Guo 2016	2010	2014	Beijing	Hospital-based	Retrospective	3~5 years	CBM	CSF/Blood	Culture	37	-	22

Jinfeng Wu 2020	2012	2018	Chongqing	Hospital-based	Retrospective	1~3 months	CBM	CSF/Blood	Culture	40	-	1
Hongshi Chen 2014	2011	2013	Hainan	Hospital-based	Retrospective	1 month~1 year	CBM	CSF	Culture	57	-	7
Hongshi Chen 2014	2011	2013	Hainan	Hospital-based	Retrospective	1~5 years	CBM	CSF	Culture	8	-	4
Xiaoshan Peng 2021	2016	2018	Multi-center	Hospital-based	Retrospective	3 months~1 year	CBM	CSF	Culture	253	-	53

Table S7. Antimicrobial profile of *Streptococcus pneumoniae*

Antibiotics	Studies no.	Resistant isolates	Total specimens	Pooled resistant rate % (95%CI)
Ampicillin	1	10	10	100.00 (69.15-100.00)
Clindamycin	4	77	85	99.47 (68.55-100.00)
Tetracycline	4	79	72	96.28 (71.98-100.00)
Erythromycin	5	66	75	77.65 (44.75-99.14)
Penicillin	7	70	104	71.50 (43.78-93.36)
Sulfamethoxazole	4	54	62	71.13 (57.84-83.08)
Meropenem	2	15	23	65.18 (16.57-99.78)
Cefoxitin	1	12	19	63.16 (38.36-83.71)
Ciprofloxacin	2	16	29	50.51 (7.24-93.35)
Oxacillin	3	19	28	42.24 (3.83-86.33)
Cefepime	4	16	32	33.47 (2.88-73.05)
Cefotaxime	4	25	76	29.56 (4.03-63.88)
Ceftazidime	3	8	19	23.04 (0.00-70.28)
Chloramphenicol	4	7	76	6.71 (1.39-14.45)
Amoxicillin	2	3	53	4.41 (0.06-12.63)
Rifampicin	3	2	43	1.61 (0.00-9.53)
Levofloxacin	4	1	76	0.04 (0.00-3.49)
Moxifloxacin	2	0	27	0.00 (0.00-7.09)
Linezolid	3	0	37	0.00 (0.00-5.52)
Vancomycin	7	0	104	0.00 (0.00-0.95)
Clavulanic acid	1	0	10	0.00 (0.00-30.85)
Ceftriaxone	1	0	10	0.00 (0.00-30.85)
Imipenem	1	0	10	0.00 (0.00-30.85)
Teicoplanin	1	0	10	0.00 (0.00-30.85)
Gentamicin	1	0	10	0.00 (0.00-30.85)
Dalfopristin	1	0	14	0.00 (0.00-23.16)
Telithromycin	1	0	14	0.00 (0.00-23.16)

Table S8. Serotype distribution of detected *Streptococcus pneumoniae* in bacterial meningitis

	Coverage (%)		
	PCV7	PCV13	PPSV23
Xiaoyan Shi et al. 2018	74.36	91.67	100.00
Kaile Chen et al. 2021	84.00	96.00	100.00
Pooled coverage % (95%CI)	78.95 (69.03-88.87)	91.10 (80.05-100.00)	100.00 (97.12-100.00)

Table S9. Sensitive analysis of estimated pneumococcal meningitis burden using different proxies for access to care

	Model Used in the Present Study	Alternative Model[a]
Parameter	Source of Data	Source of Data
Incidence Rate (/100,000) (95%CI)	2.10 (0.59-7.46)	2.10 (0.59-7.46)
Population of Under-fives	77,883,888	77,883,888
CFR % (95%CI)	24.59 (19.35-30.28)	24.59 (19.35-30.28)
PCV Coverage (%)	1.68%	1.68%
Adjusted CFR % (95%CI)	33.94 (29.36-38.81)	50.54 (47.32-53.97)
Proxy for access to care (%)	85.71	60.33
Estimated Cases	1617.16 (454.35-5744.78)	1617.16 (454.35-5744.78)
Estimated Deaths	548.86 (474.80-627.62)	817.31 (765.24-872.78)

[a] In the present model, proxy for access to care was calculated using the item "Was medical care sought?" and that in the alternative model was calculated using the item "Saw local health workers or doctors".

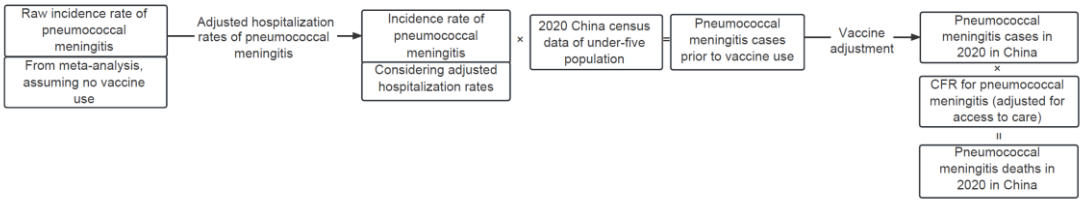

Figure S1. Flow chart of adjustments performed for estimates of pneumococcal meningitis burden.

Figure S2. Distribution of included studies in each province.

Deeper colors represent more included studies in this area. Multi-center studies are not listed.

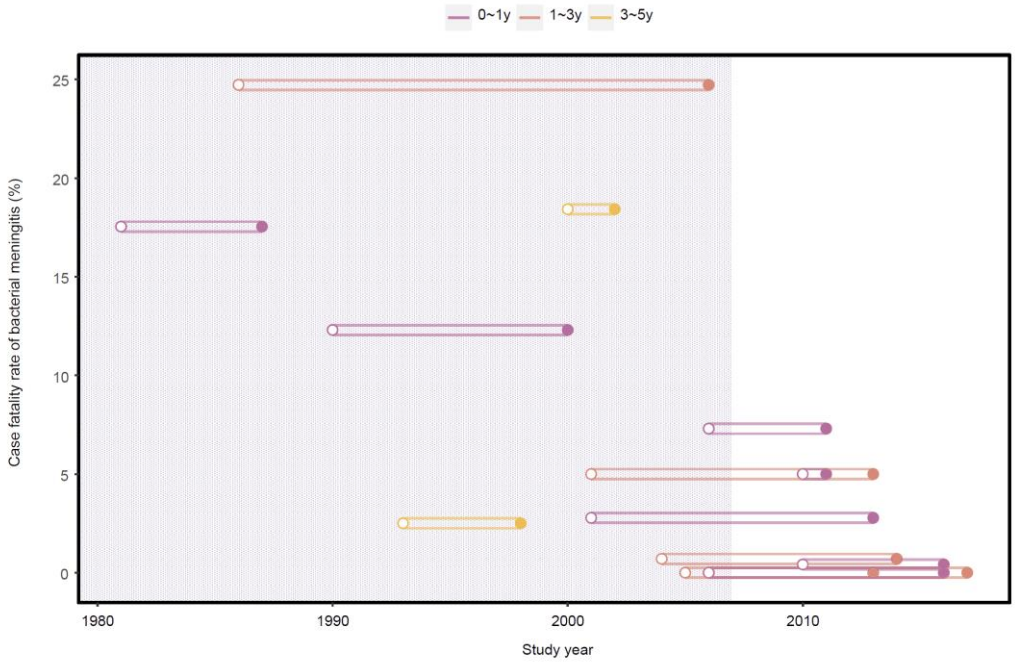

Figure S3. Distribution of case fatality rate of bacterial meningitis by time and age.
Hollow dots represent the start year of the study and solid dots represent the end year of the study. The dashed area represents time before year 2008.

Figure S4. Pooled proportion of different pathogens in confirmed bacterial meningitis cases by age strata.

The heights of bars represent pooled proportion of different pathogens and grey lines mark 20%, 40%, 60% respectively.

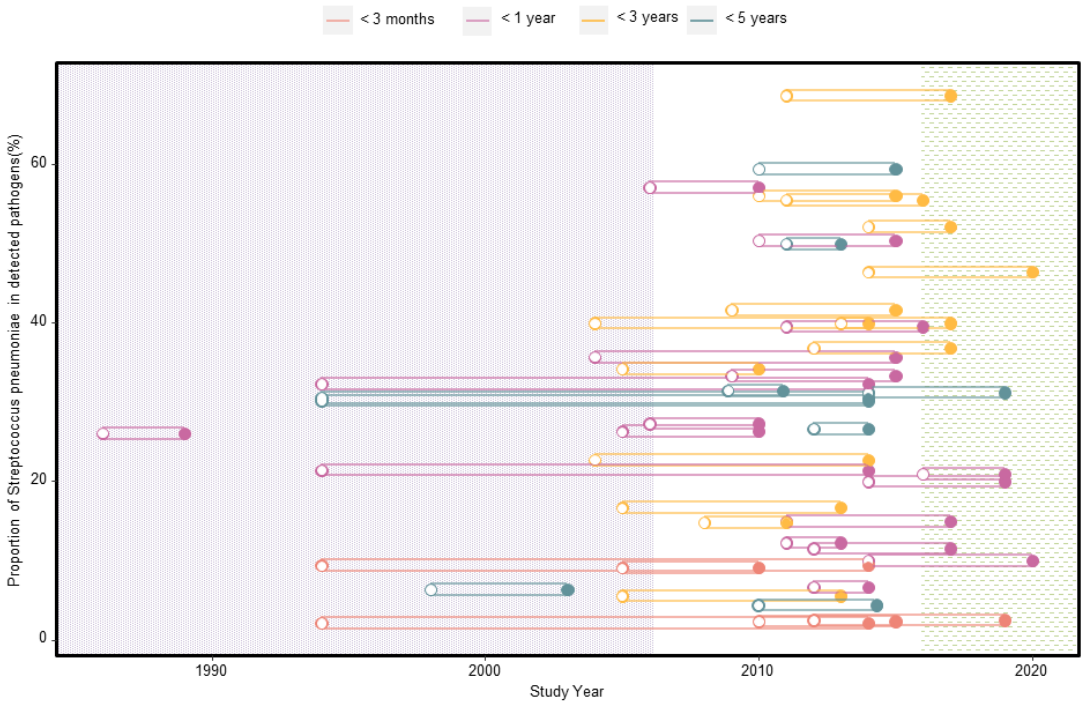

Figure S5. Distribution of proportion of *Streptococcus pneumoniae* in detected pathogens by time and age.

Hollow dots represent the start year of the study and solid dots represent the end year of the study. The dashed area represents time before year 2008.

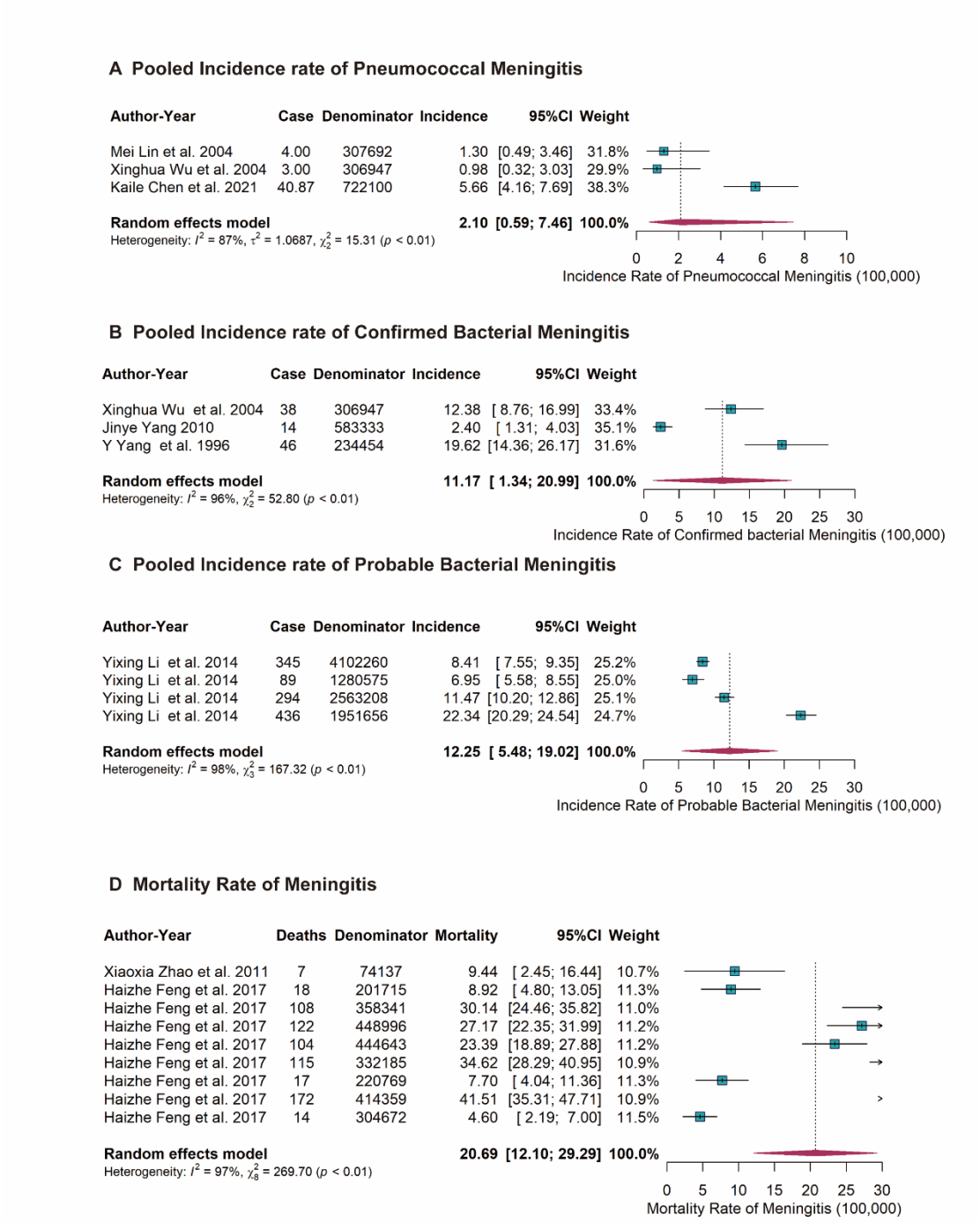

Figure S6. Forest plot of studies on incidence and mortality rate of meningitis.

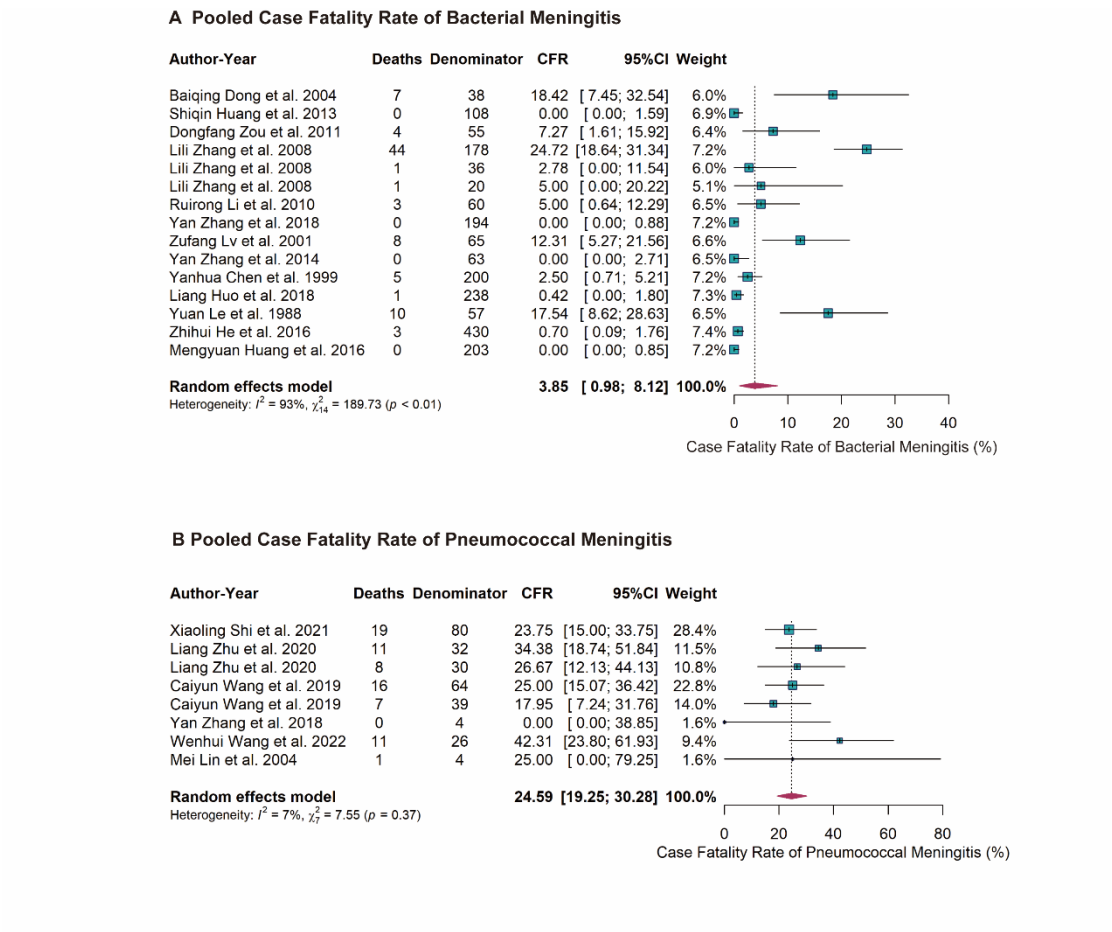

Figure S7. Forest plot of studies on case-fatality rate of meningitis.

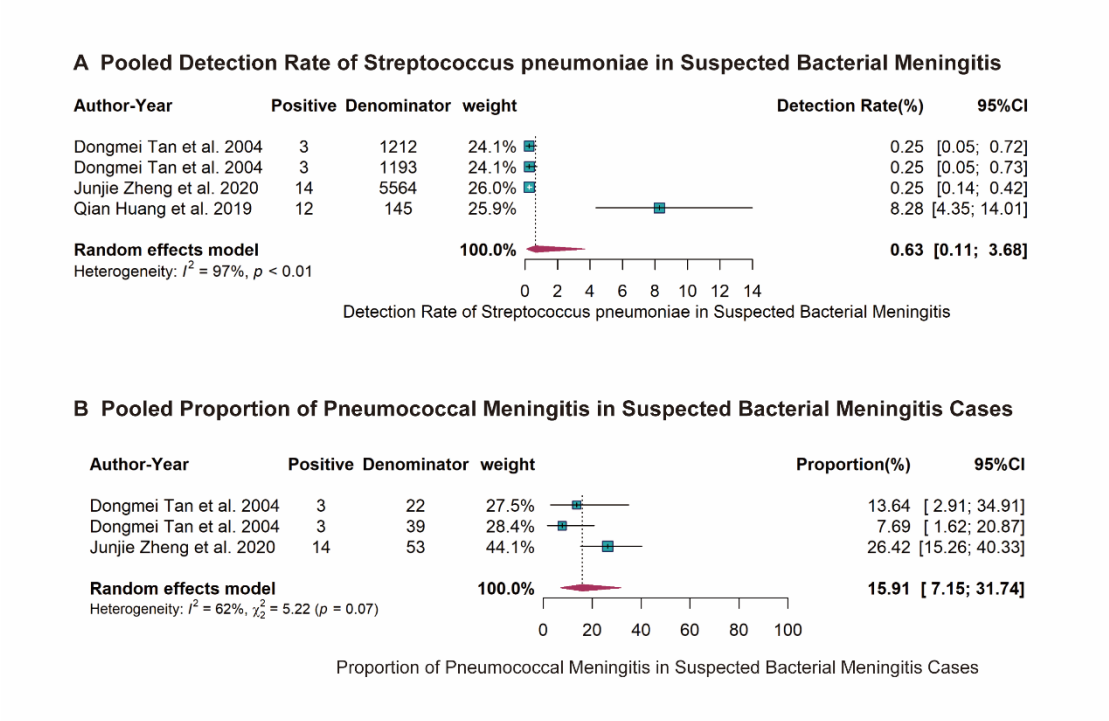

Figure S8. Forest plot of studies on positive rate and proportion of *Streptococcus pneumoniae* among suspected bacterial meningitis cases.

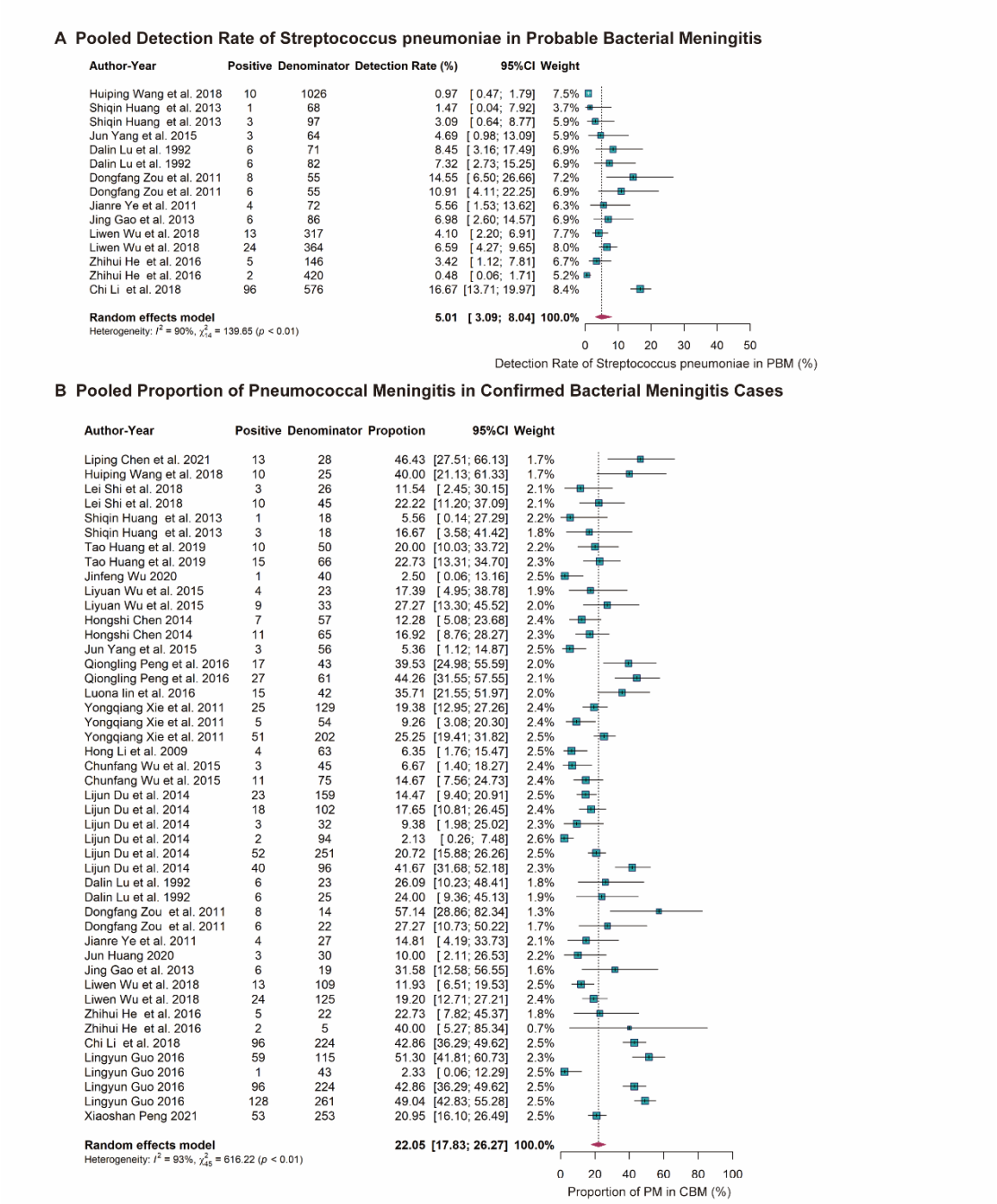

Figure S9. Forest plot of studies on *Streptococcus pneumoniae* positive rate in probable meningitis bacterial cases and proportion of pneumococcal meningitis in confirmed bacterial meningitis cases.