

Development and Independent Validation of a Mortality Prediction Model for HIV/PCP Inpatients Based on A Systematic Review and Meta-analysis

Jiayi Liu

Beijing Ditan Hospital

Yifan Guo

Beijing Ditan Hospital

Na Yang

The First Hospital of Lanzhou University

Linghang Wang

linghang.wang@ccmu.edu.cn

Beijing Ditan Hospital

Research Article

Keywords: HIV/PCP coinfection, inpatients mortality, related factors, meta-analysis, prediction model, clinical application

Posted Date: August 28th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10596459/v1>

License:   This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Additional Declarations: No competing interests reported.

Development and Independent Validation of a Mortality Prediction Model for HIV/PCP Inpatients Based on A Systematic Review and Meta-analysis

Jiayi Liu¹, Yifan Guo¹, Na Yang², Linghang Wang^{*1}

1 Department of Infectious Disease, Beijing Ditan Hospital, Capital Medical University, Beijing,
China

2 The First Hospital of Lanzhou University, Lanzhou, China

Email: Jiayi Liu - 18894452424@163.com; Yifan, Guo - gyf980923@163.com; Na, yang -
19909384972@163.com; Linghang, Wang - linghang.wang@ccmu.edu.cn

* Corresponding author

18 **Abstract**

19 **Background**

20 Early identification of mortality-associated factors in hospitalized patients with HIV/PCP is
21 important. This study aimed to explore predictors of mortality through a meta-analysis and to
22 develop a mortality risk prediction model for hospitalized patients with HIV/PCP coinfection.

23 **Method**

24 The literature on mortality-related factors of HIV/PCP coinfection inpatients was reviewed, and odds
25 ratios (ORs) with 95% confidence intervals (CIs) for relevant factors were extracted. We conducted a
26 meta-analysis to obtain pooled ORs. A risk stratification scoring system was then developed based on
27 meta-analytic findings and validated in an independent cohort of patients from Beijing Ditan
28 Hospital.

29 **Result**

30 A total of thirteen studies were included in the meta-analysis, and there were five mortality-
31 associated predictors were included in the final prediction model: serum albumin (ALB g/L, OR =
32 0.63, 95% CI 0.49–0.82), lactate dehydrogenase (LDH U/L, OR = 2.97, 95% CI 1.70–5.18), CD4⁺ T
33 cell count (cells/ μ L, OR = 0.36, 95% CI 0.20–0.66), requirement for mechanical ventilation (OR =
34 10.89, 95% CI 4.85–24.45) and pneumothorax (OR = 19.90, 95% CI 5.93–66.71). The prediction
35 scores were significantly higher in the death group than in the survival group (Mann-Whitney U test,
36 $P < 0.001$). The model showed good discrimination for mortality prediction, with an AUC of 0.891
37 (95% CI 0.860–0.918). The Hosmer-Lemeshow test yielded a χ^2 value of 6.700 ($P = 0.461$),
38 suggesting good model calibration. Decision curve analysis (DCA) showed that the prediction model

39 provided a higher net benefit than the "treat-all" and "treat-none" strategies across threshold
40 probabilities from 0.01 to 0.34, with a maximum net benefit of 0.25.

41 **Conclusion**

42 The prediction model possesses good prediction ability and clinical benefit.

43 **Keywords**

44 HIV/PCP coinfection, inpatients mortality, related factors, meta-analysis, prediction model, clinical
45 application

46 **Systematic Review Registration**

47 <https://www.crd.york.ac.uk/PROSPERO/view/CRD420251038025>, ID PROSPERO
48 [CRD420251038025].

49 **Background**

50 *Pneumocystis* pneumonia (PCP), caused by *Pneumocystis jirovecii*, is a severe lung infection that
51 commonly occurs in immunocompromised individuals, including those with malignancies, premature
52 infants, and severely malnourished patients previously[1,2]. Following the emergence of the
53 HIV/AIDS epidemic, the incidence of PCP peaked at 70%–80%, with a mortality rate reaching 40%.
54 Currently, the estimated annual incidence of HIV/PCP is 400,000, with a crude mortality rate of
55 15%[3]. The mortality rate of HIV/PCP ranges from 12.7%–19.3% and remained the leading cause of
56 deaths between 2013 and 2022 in China[4]. A systematic review found that approximately 6% of
57 HIV infected individuals in Ethiopia experienced PCP, which may be a conservative estimate[5].
58 Widespread ART application has reduced PCP incidence and mortality in HIV patients. However,
59 regions with poor healthcare infrastructure experience higher PCP incidence and mortality due to

inadequate screening[6-8]. Therefore, identifying factors related to mortality in HIV/PCP coinfection inpatients and establishing a clinically effective prediction model is essential.

Although a few previous single-center studies have identified related risk factors in HIV/PCP coinfection inpatients, these studies were limited by small sample sizes or restricted geographic areas, leading to varied results and heterogeneous quality across studies[9,10]. Consequently, the mortality-associated factors and prediction models of mortality remain uncertain. This study aims to integrate multiple single-center studies by meta-analysis, develop and validate a mortality risk prediction model based on meta-analysis findings, and provide clinically useful information for risk stratification and prognostic assessment in hospitalized patients with HIV/PCP.

1 Methods

1.1 Literature searching and screening

We systematically searched the Cochrane Library, PubMed, Embase, Web of Science, WanFang Database, Chinese Biomedical Database (CBM), and China National Knowledge Infrastructure (CNKI) by a combination of MeSH terms and free-text words from inception to May 1, 2025. There were no language restrictions applied to the literature search. Additionally, we manually screened the reference lists of all included studies to identify additional relevant publications. Studies were selected for inclusion based on the following criteria: (a) hospitalized patients with HIV/PCP coinfection; (b) age ≥ 18 years; (c) HIV infection or AIDS was laboratory-confirmed; (d) PCP cases were diagnosed by microbiological and/or clinical criteria. Studies were excluded if they: (a) included outpatients with HIV/PCP coinfection; (b) were limited to specific subgroups (e. g., patients aged > 50 years only); (c) included participants aged < 18 years; (d) were conference abstracts, meta-analyses, animal studies, case reports, or reviews. There were two independent reviewers screened studies, and disagreements were resolved by discussion or consultation with a third reviewer. The

quality of the studies was assessed according to the Newcastle-Ottawa Scale (NOS). Only studies that scored ≥ 7 were included in the analysis.

1.2 Data extraction

Data were independently extracted from the included studies by two reviewers. The information extracted from studies included: first author, country of publication, year of publication, study design, sample size, number of deaths, reported mortality-associated factors, adjusted ORs, and corresponding 95% CIs. Any discrepancies were resolved through discussion or consultation with a third reviewer.

1.3 Meta-analysis

We extracted the ORs and 95% CIs for each related factor from the included studies and calculated pooled ORs using Review Manager 5.4. Heterogeneity across studies was assessed using the I^2 statistic. A fixed-effects model was applied when $I^2 \leq 50\%$ and $P > 0.10$, indicating low heterogeneity. Conversely, a random-effects model was employed when $I^2 > 50\%$ and $P \leq 0.10$, indicating substantial heterogeneity. The sources of heterogeneity were explored by sequentially excluding individual studies to identify potential contributors to the observed variation. Sensitivity analyses were conducted by a stepwise exclusion method. Publication bias was planned to be assessed using funnel plots when at least ten studies were available for a given factor. However, this assessment was not performed because fewer than ten studies were available for each identified factor.

1.4 Validation cohort

A total of 634 admissions diagnosed with HIV/PCP coinfection in Ditan Hospital between 2020 and 2025 were included in the validation cohort according to the same patient-level inclusion and

105 exclusion criteria used in the meta-analysis. We collected data on basic characteristics, initial
106 laboratory tests on admission, in-hospital procedures, discharge diagnoses, length of hospital stay,
107 history of present illness, and personal history from the electronic medical record (EMR).

108 **1.5 Model development**

109 We developed a scoring system based on the methods suggested by Jiang W et al.[11]. Pooled ORs
110 and 95% CIs of mortality-associated factors were obtained from meta-analysis. The pooled ORs were
111 then log-transformed to derive β coefficients. To generate an easy-to-use scoring system, each β
112 coefficient was multiplied by 10 and rounded to the nearest integer. The stratification and assignment
113 of scores for each related factor were determined based on literature review and clinical consensus.
114 These integers served as the matching scores assigned to each related factor stratum. The final
115 prediction score was calculated as the sum of the scores for all related factors.

116 **1.6 Model validation**

117 Model performance was evaluated in a cohort consisting of 634 admissions from Beijing Ditan
118 Hospital. However, there was a marked imbalance between the two groups, with 606 survivors and
119 28 deaths. To correct this imbalance, we introduced the synthetic minority oversampling technique
120 (SMOTE), proposed by Chawla, which generates synthetic samples by performing linear
121 interpolation between minority class instances and their nearest neighbors. SMOTE can effectively
122 reduce the imbalance ratio and improve the classification performance on the imbalanced
123 dataset[12,13].

124 The following software was used in this study: Review Manager (RevMan), SPSS 25.0, GraphPad
125 Prism 9, RStudio 4.5.0.

126 In this study, categorical variables were presented as numbers (percentages), and between-group

comparisons of survival and mortality were analysed by the Pearson chi-square test or Fisher's exact test. Continuous variables were expressed as median (interquartile range, IQR), and comparisons between two groups were performed by the Mann-Whitney U test.

2 Result

2.1 Literature Searching and Screening

A total of 3,191 records were initially retrieved from the databases. Thirteen studies[9,10,14-24] conducted in China, Spain, the United Kingdom, and the United States were ultimately included in the meta-analysis, which comprising 4,029 patients. The crude overall mortality rate across the included studies was 22%. Detailed information about the search strategy, literature screening flowchart is provided as **Additional file 1.docx**, and the basic characteristics and scoring results of the included studies is provided as **Additional file 2.docx**.

2.2 Model development

A total of 30 mortality-associated factors were identified across the included studies. After excluding factors that reported in only one study or showed inconsistent directions of association across studies, we finally identified 5 predictors associated with mortality across 9 studies: serum albumin[9,14,17,19,24] (ALB g/L, OR = 0.63, 95% CI 0.49–0.82), lactate dehydrogenase[19,24] (LDH U/L, OR = 2.97, 95% CI 1.70–5.18), CD4⁺ T cell count[19,24] (cells/ μ L, OR = 0.36, 95% CI 0.20–0.66), requirement for mechanical ventilation[16,17] (OR = 10.89, 95% CI 4.85–24.45) and pneumothorax[14,17] (OR = 19.90, 95% CI 5.93–66.71). The meta-analysis results are presented as forest plots in **Figure 1**. Detailed meta-analysis results are provided in **Additional file 3.docx**.

Related factors	OR (95% CI)	Heterogeneity
ALB	0.63 (0.49, 0.82)	$I^2=75\%$, $P<0.05$
LDH	2.41 (1.71, 3.39)	$I^2=0\%$, $P=0.63$
CD4+T cell	0.91 (0.83, 0.99)	$I^2=0\%$, $P=0.03$
Pneumothorax	19.98 (5.95, 67.07)	$I^2=28\%$, $P=0.24$
Mechanical ventilation	18.96 (7.86, 45.70)	$I^2=37\%$, $P=0.21$

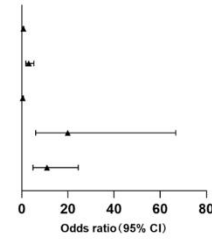


Figure 1. Results of Meta-analysis

The pooled ORs of related factors were logarithmically transformed and then multiplied by 10 to obtain integer scores. Stratified score assignment was then performed based on the included studies and clinical consensus, and the scoring strategy is presented in **Table 1**. For each admitted patient, the prognostic score can be calculated by summing the scores assigned to each risk factor.

2.3 Validation cohort

A total of 634 admissions with HIV/PCP coinfection from Ditan Hospital were included in the validation cohort, with ages ranging from 18 to 68 years. In the validation cohort, 606 survived (571 males and 35 females), and 28 died (26 males and 2 females). The causes of death included respiratory failure, heart failure, or arrhythmia. We extracted the initial laboratory data on admission for all patients, including ALB, LDH, CD4⁺ T cell count, as well as information on the occurrence of pneumothorax and the requirement for mechanical ventilation. The baseline characteristics of the validation cohort are presented as **Additional file 4.docx**. Prediction scores were significantly higher in the death group than in the survival group, as assessed using the Mann-Whitney U test ($P < 0.001$).

2.4 Model validation

Model performance was first evaluated in the original validation cohort. Given the marked imbalance between death and survival, SMOTE was performed in RStudio to reduce class imbalance in the

166 validation dataset. A total of 174 death samples were synthesized by an oversampling method. The
167 synthesized variables included ALB (g/L), LDH (U/L), CD4⁺ T cell count (cells/ μ L), presence of
168 pneumothorax, and mechanical ventilation status. The SMOTE procedure yielded a balanced dataset
169 of 606 survivors and 202 deaths, with a survival-to-death ratio of 3:1. The prognostic score was then
170 calculated for each sample according to the scoring system.

171 The performance of the prediction model was evaluated on the oversampled dataset by the ROC
172 curve. The model achieved an AUC of 0.891 (95% CI 0.865–0.918, $P < 0.001$), indicating good
173 discriminative ability. The optimal cutoff score, based on the maximum Youden index was set at $> -$
174 12 points. At this cutoff, the model demonstrated a sensitivity of 76.7% and a specificity of 87.5%.
175 Calibration was assessed by the Hosmer–Lemeshow test, which showed good consistency between
176 predicted probability and observed mortality ($\chi^2 = 6.700$, $P = 0.461$). DCA showed that the prediction
177 model provided a superior net benefit compared with the “treat-all” strategy across threshold
178 probabilities ranging from 0.01 to 0.34, with a maximum net benefit of 0.25. The result of the
179 evaluation of the prediction model performance is presented in **Figure 2**.

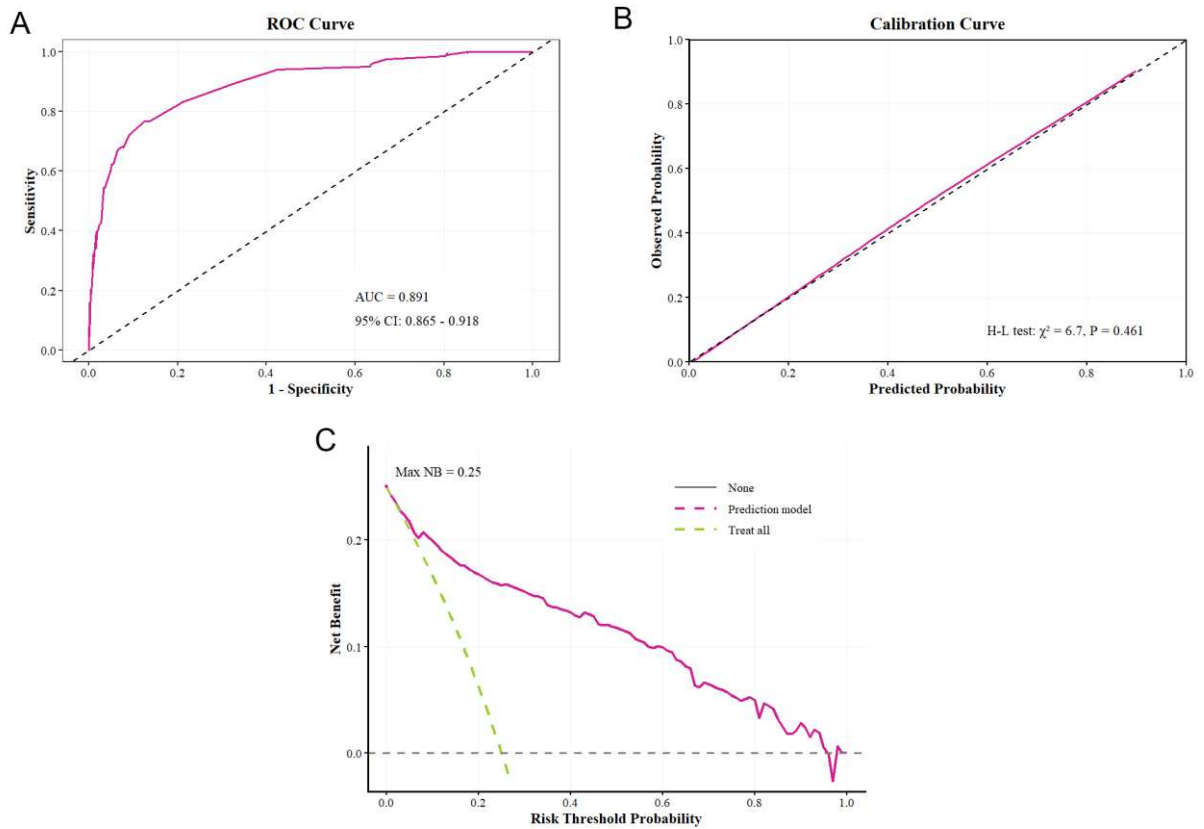


Figure 2. Evaluation of the prediction model performance.

(A) ROC curve of the prediction model for mortality risk. The AUC was 0.891 (95% CI 0.865-0.918). **(B)** Calibration curve, H-L test: $\chi^2 = 6.700$, $P = 0.461$. **(C)** Decision curve analysis (DCA), showing that the model provided a higher net benefit compared with the "treat-all" and "treat-none" strategies across threshold probabilities of 0.01 to 0.34, indicating favorable clinical utility.

3 Discussion

In this study, we identified five mortality-associated predictors in hospitalized patients with HIV/PCP coinfection through meta-analysis. Based on these predictors, we developed a mortality risk prediction model and further evaluated its performance in a validation cohort from Beijing Ditan Hospital.

ALB exerts antioxidant activity and can protect septic cells from oxidative stress. The release of cytokines and inflammatory factors can inhibit hepatic synthesis of ALB, leading to a reduction in ALB levels during acute or chronic inflammatory reactions. As an inflammatory marker, ALB can indirectly reflect the severity of the disease[25]. The meta-analysis conducted by Wang Y et al. revealed that ALB wasn't a related factor in non-HIV patients with PCP mortality. In contrast, a large number of studies on mortality-related factors in HIV/PCP coinfecting patients have demonstrated that lower ALB levels correlate with a higher risk of inpatient mortality[17,26,27]. LDH is a general intracellular enzyme involved in metabolism[28]. The detection of extracellular LDH in serum indicates cell death or aging. Elevated extracellular LDH levels are observed in various conditions, such as malignancies, hemolytic anemia, and ischemia[29]. Now, multiple single-center retrospective cohort studies have shown that elevated LDH levels are associated with an increased risk of mortality in coinfecting patients[9,26,27,30]. Pneumothorax is a common and potentially life-threatening complication in patients with HIV/PCP coinfection. Mediastinal pneumothorax is a rare but serious complication of PCP. Severe PCP and cough symptoms may contribute to pneumothorax formation, which can lead to increased morbidity and mortality[31]. A prospective cohort study showed that the incidence of pneumothorax was 1.2% in hospitalized patients with HIV/PCP coinfection and an inpatient mortality rate of 31% in those who developed pneumothorax compared to 6% in patients without pneumothorax[30]. Multiple studies have identified mechanical ventilation as an independent predictor of inpatient mortality among patients with concurrent infections, indicating that the requirement for mechanical ventilation often signifies critical illness and portends a poor prognosis[32].

There are two studies[9,10] previously developed mortality risk prediction models that demonstrated good clinical applicability in China. However, our model has several advantages over previous research findings. A key strength is that we identified related factors through systematic reviews and

meta-analysis rather than traditional single-center studies. This effectively replicates the advantages of a multicenter study and provides stronger evidence-based support. This approach substantially mitigates limitations commonly occurring in single-center studies. Second, we performed stratified scoring according to ORs based on studies and clinical consensus. This enables each patient to obtain a prediction score, facilitating individualized risk assessment. Third, we conducted an independent validation to further verify its generalizability. The results further confirmed the clinical value and practical utility of the prediction model.

However, this study also has limitations. First, differences existed in PCP diagnostic criteria across the studies included in the meta-analysis due to the limited number of available studies. Some studies employed etiological confirmation, while others included clinically diagnosed patients, which may have contributed to heterogeneity in pooled results. Although we addressed this through sensitivity analysis and random-effects models, a better result would be developed from original studies with more consistent diagnostic criteria. Second, the validation cohort was derived from a single-center population with a limited number of death events. Although multidimensional SMOTE was applied to augment the minority class through sample interpolation, synthetic data may not reflect real-world data. Consequently, further validation in a larger, more comprehensive cohort is essential to confirm the reliability and generalizability of this finding.

4 Conclusion

Based on a systematic review and meta-analysis, we developed a mortality risk prediction model for HIV/PCP coinfection inpatients, incorporating five factors: albumin, lactate dehydrogenase, CD4⁺ T cell count, pneumothorax, and mechanical ventilation. This prediction model demonstrates good discriminatory ability and can serve as a valuable clinical reference for assessing prognosis.

5 Abbreviations

238 PCP: *Pneumocystis pneumonia*; AIDS: acquired immunodeficiency syndrome; HIV: human
239 immunodeficiency virus; LDH: lactate dehydrogenase; ALB: serum albumin; CBM: Chinese
240 Biomedical Database; CNKI: China National Knowledge Infrastructure; NOS: Newcastle-Ottawa
241 Scale; EMR: electronic medical record; SMOTE: the synthetic minority oversampling technique.

242 **6 Declarations**

243 We declare that the research was conducted in the absence of any commercial or financial
244 relationships that could be construed as a potential conflict of interest.

245 **Ethical approval**

246 This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics
247 Committee of Beijing Ditan Hospital, Capital Medical University (No. DTEC-KY2019-016-001).
248 The requirement for informed consent was waived by the Ethics Committee of Beijing Ditan
249 Hospital due to the retrospective nature of the study, and all patient data were anonymized prior to
250 analysis.

251 **Consent for publication**

252 Not applicable.

253 **Data Availability Statement**

254 The data supporting our findings are derived from two parts. The meta-analysis was based on
255 previously published studies. All the data supporting the meta-analysis are provided in the
256 manuscript and Additional file. The external validation cohort was derived from the electronic
257 medical record (EMR) system of Beijing Ditan Hospital. Due to the sensitive nature of the patient
258 health information contained in these EMR data, and to mitigate re-identification risks associated

with the SMOTE-oversampled dataset, these specific hospital-derived datasets are not publicly available. However, the de-identified validation dataset may be available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

This study was supported by the "Research on Intelligent Identification of Key Infectious Diseases and Syndromes in Medical Institutions Based on the Implementation of Public Health Monitoring and Early Warning Functions" (No. 2025ZD01900402) and the National Major Science and Technology Project for the Control and Prevention of Major Infectious Diseases of China (No. 2017ZX10103004-018).

Author Contributions

JL contributed to literature search, data acquisition, statistical analysis, and drafting of the original manuscript; YG contributed to literature search and data acquisition; NY contributed to statistical analysis; LW conceived of the study, participated in its design, and revised the manuscript.

Acknowledgments

Not applicable.

References

- [1] Avino LJ, Naylor SM, Roecker AM. Pneumocystis jirovecii Pneumonia in the Non-HIV-Infected Population. Ann Pharmacother. 2016; 50:673-9.

280 [2] Huang YS, Yang JJ, Lee NY, Chen GJ, Ko WC, Sun HY, Hung CC. Treatment of *Pneumocystis jirovecii* pneumonia in HIV-
281 infected patients: a review. *Expert Rev Anti Infect Ther.* 2017; 15:873-92.

282 [3] Denning DW. Global incidence and mortality of severe fungal disease. *Lancet Infect Dis.* 2024; 24:e269.

283 [4] Xia H, Song J, Hu Y, Li L, Gao L, Ma P. Plasma IL-6 level predict the risk of in-hospital mortality in HIV-associated
284 *pneumocystis pneumonia*. *BMC Infect Dis.* 2025; 25:1823.

285 [5] Gelaw YM, Guracho YD, Robert-Gangneux F, Alene GD, Gangneux JP. The Burden of *Pneumocystis Pneumonia* Infection
286 among HIV Patients in Ethiopia: A Systematic Review. *Trop Med Infect Dis.* 2023; 8:114.

287 [6] Biała M, Ślabisz N, Knysz B. Fungal Infection in HIV-Infected Patients-Is It Still a Challenge. *J Clin Med.* 2025; 14:8570.

288 [7] Sati H, Alastruey-Izquierdo A, Perfect J, Govender NP, Harrison TS, Chiller T, Sorrell TC, Bongomin F, Oladele R,
289 Chakrabarti A, Wahyuningsih R, Colombo AL, Rodriguez-Tudela JL, Beyrer C, Ford N. HIV and fungal priority pathogens.
290 *Lancet HIV.* 2023; 10:e750-750e754.

291 [8] Siegel M, Masur H, Kovacs J. *Pneumocystis jirovecii* Pneumonia in Human Immunodeficiency Virus Infection. *Semin Respir*
292 *Crit Care Med.* 2016; 37:243-56.

293 [9] Wang X, Liu L, Wang W, Zhang Y, Chen H, Wang Z, Li J, Gao Y, Huang Y, Sun L, Zhang T, Li A. Mortality risk prediction
294 model in AIDS patients with *pneumocystis pneumonia* in China. *Front Cell Infect Microbiol.* 2024; 14:1485231.

295 [10] Wu L, Zhang Z, Wang Y, Hao Y, Wang F, Gao G, Yang D, Xiao J, Zhao H. A Model to Predict In-Hospital Mortality in
296 HIV/AIDS Patients with *Pneumocystis Pneumonia* in China: The Clinical Practice in Real World. *Biomed Res Int.* 2019;
297 2019:6057028.

298 [11] Jiang W, Wang J, Shen X, Lu W, Wang Y, Li W, Gao Z, Xu J, Li X, Liu R, Zheng M, Chang B, Li J, Yang J, Chang B.
299 Establishment and Validation of a Risk Prediction Model for Early Diabetic Kidney Disease Based on a Systematic Review and
300 Meta-Analysis of 20 Cohorts. *Diabetes Care.* 2020; 43:925-33.

301 [12] Luo YL, Gao XL, Wang JZ, Xiao MZ, Tao JX, Ouyang QN, Xiang C. [Prediction of the occurrence risk of progressive liver
302 fibrosis in patients with metabolic-associated fatty liver disease based on the SMOTE algorithm and nomogram]. *Zhonghua*
303 *Gan Zang Bing Za Zhi.* 2026; 34:115-23.

304 [13] Wang S, Dai Y, Shen J, Xuan J. Research on expansion and classification of imbalanced data based on SMOTE algorithm. *Sci*
305 *Rep.* 2021; 11:24039.

306 [14] Hao J, Li A, Tong Z. Nomograms for Death from *Pneumocystis jirovecii* Pneumonia in HIV-Uninfected and HIV-Infected
307 Patients. *Int J Gen Med.* 2022; 15:3055-67.

308 [15] Llibre JM, Revollo B, Vanegas S, Lopez-Nuñez JJ, Ornelas A, Marin JM, Santos JR, Marte P, Morera M, Zuluaga P, Tor J,
309 Clotet B. *Pneumocystis jirovecii* pneumonia in HIV-1-infected patients in the late-HAART era in developed countries. *Scand J*
310 *Infect Dis.* 2013; 45:635-44.

311 [16] Miller RF, Allen E, Copas A, Singer M, Edwards SG. Improved survival for HIV infected patients with severe *Pneumocystis*
312 *jirovecii* pneumonia is independent of highly active antiretroviral therapy. *Thorax.* 2006; 61:716-21.

313 [17] Radhi S, Alexander T, Ukwu M, Saleh S, Morris A. Outcome of HIV-associated *Pneumocystis pneumonia* in hospitalized
314 patients from 2000 through 2003. *BMC Infect Dis.* 2008; 8:118.

315 [18] Sage EK, Noursadeghi M, Evans HE, Parker SJ, Copas AJ, Edwards SG, Miller RF. Prognostic value of C-reactive protein in
316 HIV-infected patients with *Pneumocystis jirovecii pneumonia*. *Int J STD AIDS.* 2010; 21:288-92.

317 [19] Tang JY LX, Wu CY FDM. Clinical characteristics and risk factors for prognosis in patients with AIDS complicated with
318 *Pneumocystis jirovecii pneumonia*. *Modern Medicine and Health Research Electronic Journal.* 2023; 7:100-3.

319 [20] Tellez I, Barragán M, Franco-Paredes C, Petraro P, Nelson K, Del Rio C. *Pneumocystis jirovecii pneumonia* in patients with
320 AIDS in the inner city: a persistent and deadly opportunistic infection. *Am J Med Sci.* 2008; 335:192-7.

321 [21] Tian Q, Si J, Jiang F, Xu R, Wei B, Huang B, Li Q, Jiang Z, Zhao T. Caspofungin combined with TMP/SMZ as a first-line
322 therapy for moderate-to-severe PCP in patients with human immunodeficiency virus infection. *HIV Med.* 2021; 22:307-13.

323 [22] Walzer PD, Evans HE, Copas AJ, Edwards SG, Grant AD, Miller RF. Early predictors of mortality from *Pneumocystis jirovecii*
324 pneumonia in HIV-infected patients: 1985-2006. *Clin Infect Dis.* 2008; 46:625-33.

325 [23] Wang HW, Lin CC, Kuo CF, Liu CP, Lee CM. Mortality predictors of *Pneumocystis jirovecii pneumonia* in human
326 immunodeficiency virus-infected patients at presentation: Experience in a tertiary care hospital of northern Taiwan. *J Microbiol*
327 *Immunol Infect.* 2011; 44:274-81.

328 [24] Zhou J CRF, Han J YQE, Wang Y. Clinical features and prognostic risk factors in AIDS patients with *Pneumocystis carinii*
329 pneumonia. *Practical Preventive Medicine.* 2023; 30.

330 [25] Kumagai S, Arita M, Koyama T, Kumazawa T, Inoue D, Nakagawa A, Kaji Y, Furuta K, Fukui M, Tomii K, Taguchi Y,
331 Tomioka H, Ishida T. Prognostic significance of crazy paving ground glass opacities in non-HIV *Pneumocystis jirovecii*
332 pneumonia: an observational cohort study. *BMC Pulm Med.* 2019; 19:47.

333 [26] Li AX, Huang CY, Zhang HW, Zhang T, Wu H, Wang W. [Research on risk factors of short-term outcome in AIDS patients
334 with pneumocystis pneumonia]. *Zhonghua Yi Xue Za Zhi.* 2017; 97:833-7.

335 [27] Wang M, Dai X, Huang Y, Sun J, Dong X, Guo Y, Hu C, Zhou Q, Zhu B. The presence of *Pneumocystis jirovecii* DNA in
336 plasma is associated with a higher mortality rate in patients with AIDS-associated *Pneumocystis pneumonia*. *Med Mycol.* 2019;
337 57:582-7.

338 [28] Deng C, Li Y, Li Y. [Systemic review: the accuracy of lactic dehydrogenase in the diagnosis of pneumocystis pneumonia].
339 *Zhonghua Wei Zhong Bing Ji Jiu Yi Xue.* 2018; 30:322-6.

340 [29] Quist J, Hill AR. Serum lactate dehydrogenase (LDH) in *Pneumocystis carinii pneumonia*, tuberculosis, and bacterial
341 pneumonia. *Chest.* 1995; 108:415-8.

342 [30] Benfield TL, Helweg-Larsen J, Bang D, Junge J, Lundgren JD. Prognostic markers of short-term mortality in AIDS-associated
343 *Pneumocystis carinii pneumonia*. *Chest.* 2001; 119:844-51.

344 [31] Mada PK, Khan MH. *Pneumocystis jirovecii Pneumonia Complicated by Pneumomediastinum: A Case Report.* *Cureus.* 2024;
345 16:e58189.

346 [32] Helweg-Larsen J, Benfield TL, Eugen-Olsen J, Lundgren JD, Lundgren B. Effects of mutations in *Pneumocystis carinii*
 347 dihydropteroate synthase gene on outcome of AIDS-associated *P. carinii* pneumonia. *Lancet*. 1999; 354:1347-51.

348

349

350 **Figure 1.** Results of Meta-analysis

351 **Figure 2.** Evaluation of the prediction model performance. **(A)** ROC curve of the prediction model
 352 for mortality risk. The AUC was 0.891 (95% CI 0.865-0.918). **(B)** Calibration curve, H-L test: $\chi^2 =$
 353 6.700, P = 0.461. **(C)** Decision curve analysis (DCA), showing that the model provided a higher net
 354 benefit compared with the "treat-all" and "treat-none" strategies across threshold probabilities of 0.01
 355 to 0.34, indicating favorable clinical utility.

356 **Table 1.** Mortality risk stratification scoring model

Associated factors	Stratification	Score
ALB (g/L)	<21	0
	21-25	-5
	26-30	-10
	31-35	-15
	>35	-20
LDH (U/L)	<500	0
	501-725	9
	726-1000	18

	>1000	27
CD4 ⁺ T-cell count(cells/ul)	<20	0
	21-100	-10
	100-180	-20
	181-260	-30
	261-340	-40
	341-420	-50
	421-500	-60
	>500	-70
pneumothorax occurrence	0	0
	1	30
Requirement for mechanical	0	0
ventilation	1	30

357

358 Additional files

359 **Additional file 1.docx:** Detailed information about the search strategy and literature screening
360 flowchart. We searched 7 databases by a combination of MeSH terms and free-text words from
361 inception to May 1, 2025. We followed the PRISMA guidelines and presented the screening process
362 as a flowchart.

363 **Additional file 2.docx:** The basic characteristics and scoring results of the included studies. We
364 extracted first author, country of publication, year of publication, study design, sample size, sample
365 size and number of deaths, reported mortality-associated factors and score based on NOS of each
366 included study.

367 **Additional file 3.docx:** Detailed meta-analysis result for each related factor. This file provides forest
368 plots of the 5 related factors, including ALB, LDH, CD4⁺ T-cell count, pneumothorax, and
369 mechanical ventilation.

370 **Additional file 4.docx:** The Baseline Characteristics of Validation Cohort. This table presents the
371 baseline demographic and clinical characteristics of the validation cohort. Categorical variables are
372 presented as numbers (percentages) and comparisons between the two groups were performed by the
373 chi-square test or Fisher's exact test. Continuous variables are expressed as median (interquartile
374 range, IQR) and comparisons between the two groups were performed by the Mann–Whitney U test.

375

376