

From evidence to system-wide action: Adapting the APT-sepsis trial for China's maternal safety strategy

Yao Chen,¹ Dunjin Chen,¹ and Fang He^{1,2,*}

¹Department of Obstetrics and Gynecology; Guangdong Provincial Key Laboratory of Major Obstetric Diseases; Guangdong Provincial Clinical Research Center for Obstetrics and Gynecology; Guangdong Hong Kong Macao Greater Bay Area Higher Education Joint Laboratory of Maternal Fetal Medicine; The Third Affiliated Hospital, Guangzhou Medical University, Guangzhou 510182, China

²Department of Obstetrics, Guangzhou Women and Children's Medical Center, Guangzhou Medical University, Guangzhou 510623, China

*Correspondence: hefangjnu@126.com

Received: January 19, 2026; Accepted: April 22, 2026; Published Online: April 23, 2026; <https://doi.org/10.59717/j.xinn-med.2026.100218>

© 2026 The Author(s). This is an open access article under the CC BY license (<https://creativecommons.org/licenses/by/4.0/>).

Citation: Chen Y., Chen D. and He F. (2026). From evidence to system-wide action: Adapting the APT-sepsis trial for China's maternal safety strategy. *The Innovation Medicine* 4:100218.

Globally, a woman dies from pregnancy-related causes every two minutes. Sepsis is one of the major leading causes of these deaths, according to the World Health Organization. However, despite being largely preventable, it remains a critical burden, with the vast majority of infection-related mortality occurring in low- and middle-income countries (LMICs).¹ In the context of constrained health care resources, identifying pragmatic, scalable strategies for infection prevention and control has become an urgent global health priority. The Active Prevention and Treatment of Maternal Sepsis (APT-Sepsis) cluster-randomized controlled trial, published in the *New England Journal of Medicine* (NEJM) in 2025,² offers timely evidence to this end. The study demonstrated that, even without additional medical infrastructure, a structured, multicomponent behavioral and systems-level intervention reduced the risk of maternal infection-related mortality or severe morbidity by 32%. This article examines both the global significance of the APT-Sepsis trial—particularly its insights into the implementation of complex, multicomponent interventions in resource-limited settings—and the translation of these findings into actionable strategies within China's public health system.

EVIDENCE-BASED EVOLUTION: THE SECOND LEAP FROM SINGLE-DRUG PREVENTION TO SYSTEMATIC TREATMENT

The clinical approach to managing obstetric infections has followed a clear trajectory of evidence-based evolution in recent years. The Azithromycin Prevention in Labor Use Study (A-PLUS) trial, published in the *NEJM* in 2023, demonstrated that a single 2-gram oral dose of azithromycin during labor reduced the risk of maternal sepsis or mortality among women planning vaginal delivery.³ This landmark study established the value of azithromycin in infection prophylaxis and provided a practical, low-cost strategy for primary obstetric care.

The APT-Sepsis trial represents a pivotal second step—moving beyond single-drug prophylaxis to a comprehensive systems-level intervention. The study moved beyond pharmacologic measures by embedding antibiotic prophylaxis within an integrated “prevent-identify-treat” framework, which was operationalized through the implementation of the multicomponent FAST-M bundle (fluids, antibiotics, source control, transfer if required, and monitoring). This transition from isolated interventions to systemic reconfiguration underscores the importance of multidimensional strategies, positioning pharmacologic prophylaxis as the entry point and protocol-driven treatment as the foundation of comprehensive infection control (Figure 1).

CRITICAL APPRAISAL: INTERPRETING SUCCESS AND LIMITATIONS

The mortality paradox: A call for system integration

While APT-Sepsis significantly reduced composite infection-related outcomes, it did not significantly lower mortality or near-miss events. This unexpected finding does not indicate a failure of the intervention. Rather, it underscores the trial's scientific rigor and highlights the limits of system-level interventions alone.

The study demonstrated that this intervention model effectively disrupts most infection progression pathways, particularly those involving deep surgical sites, the perineum, or body cavities. However, once patients advance to critical states such as septic shock or multiple organ dysfunction, survival becomes primarily dependent on advanced life-support measures, including intensive care unit admission, hemodynamic monitoring, administration of vasoactive agents, and mechanical ventilation. This finding carries significant policy implications. System-level optimization cannot function in isolation; its

success hinges on seamless coordination across the continuum of care. If APT-Sepsis is to be implemented in primary care settings, parallel efforts must ensure a robust referral network spanning from community clinics to tertiary care facilities with advanced critical care capacity. Absent such integration, the intervention risks merely “shifting mortality risk upstream” rather than achieving a meaningful reduction. Health system development must be continuous and integrated—not fragmented.

Unimproved stillbirth rate: Indicating the need to advance the intervention window

In the secondary outcome analysis, there was no statistically significant difference in stillbirth rates between the APT-Sepsis intervention group and the control group (RR, 0.90; 95% CI, 0.73–1.10). This null finding is nonetheless informative. Infection remains one of the leading causes of stillbirth in low- and middle-income countries (LMICs).⁴ The APT-Sepsis intervention was implemented during the intrapartum period; however, most infection-related stillbirths—particularly those associated with chronic or subclinical intrauterine infections—occur during the second or third trimester, beyond the temporal scope of intrapartum interventions. Future strategies for maternal infection prevention may need to initiate earlier in pregnancy. For pregnancies complicated by infection, enhanced fetal surveillance methods (e.g., cardiotocography, fetal movement counting) should be incorporated into risk stratification protocols. Additionally, the development of artificial intelligence-driven early warning systems based on clinical data, vital signs, and inflammatory biomarkers (e.g., interleukin-6, procalcitonin) may enable timely detection of maternal-fetal compromise.

The evaluation method for complex interventions also needs optimization

The APT-Sepsis intervention employed a multicomponent, integrated approach encompassing improved hand hygiene compliance, optimized antibiotic use, and the FAST-M bundle sepsis identification and response protocol. Owing to its bundled design, isolating the individual effects of each component remains challenging—a phenomenon often referred to as the “black box” effect. The success of APT-Sepsis lay not only in its core intervention components, but also in the often-overlooked implementation strategies—such as provider training, team-based coordination, and quality feedback mechanisms. Therefore, when replicating this health system intervention in other settings, it remains uncertain whether all components must be retained or whether certain high-impact, low-cost elements can be prioritized. Examples include basic hand hygiene, inexpensive broad-spectrum antibiotics (e.g., azithromycin), and critical time thresholds within the FAST-M bundle. Future research should employ mixed-methods and process evaluation designs to assess the acceptability, feasibility, and interdependencies of individual components in real-world contexts. A detailed deconstruction of the bundled intervention is essential to guide its adaptation and implementation across diverse healthcare settings.

ADAPTATION TO CHINA: FINDING A BALANCE BETWEEN EVIDENCE AND NATIONAL CONDITIONS

The Lancet report on 70 years of maternal and child health in China highlighted remarkable achievements: the maternal mortality rate per 100,000 live births declined from 1500 to 16.9,⁵ driven by a powerful, government-led health system featuring a vast tertiary care network and near-universal

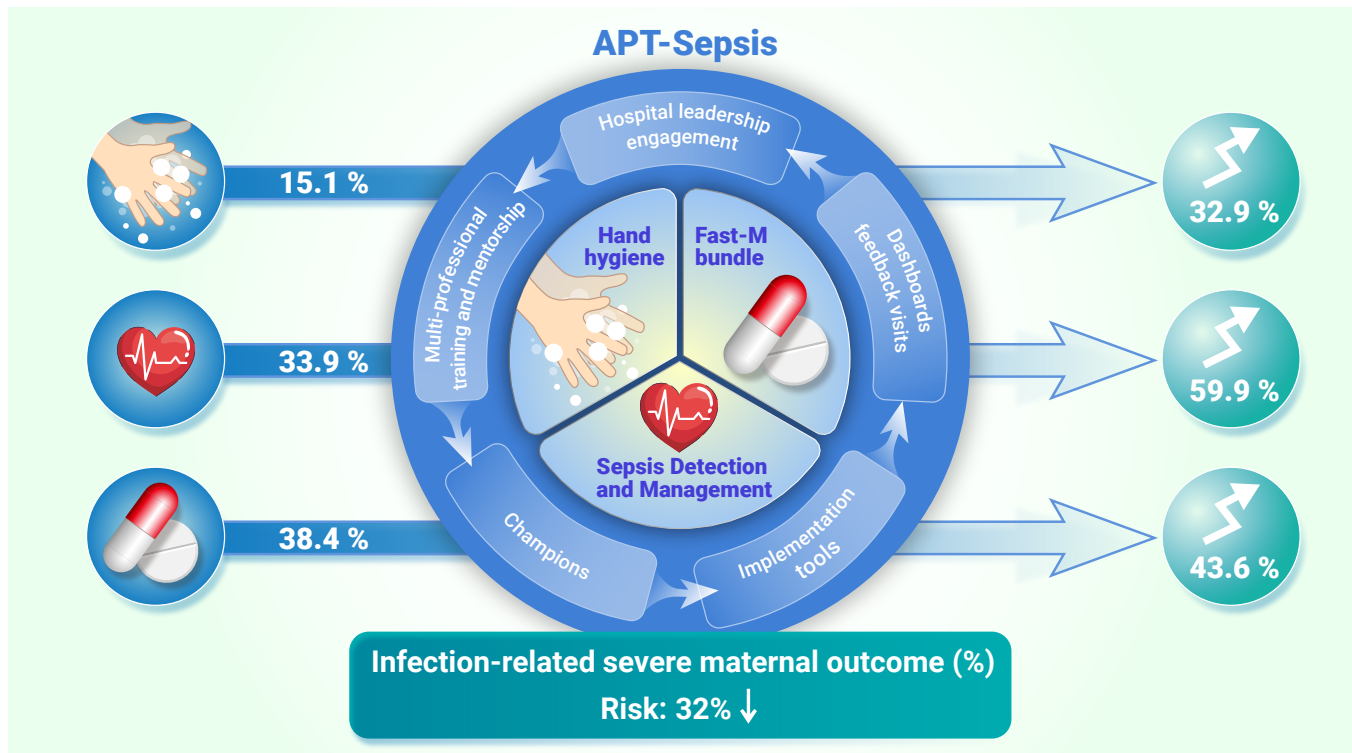


Figure 1. A multicomponent intervention to improve maternal infection outcomes APT-Sepsis: The Active Prevention and Treatment of Maternal Sepsis; FAST-M bundle: fluids, antibiotics, source identification and control, assessment of the need for transfer to a higher level of care, and monitoring of the woman and baby.

hospital delivery. The current challenge is shifting from mortality reduction to quality improvement, with sepsis emerging as a key target. APT-Sepsis provides a timely framework. Adapting this framework to China requires leveraging the country's systemic strengths while addressing its specific gaps, moving from technical adoption to strategic integration.

Primary prevention and early detection: Leveraging existing platforms

To improve maternal infection outcomes, a structured clinical pathway encompassing early risk identification, prevention, treatment, and system-level support is essential. Enhanced Risk Stratification: Integrate infection-specific markers (e.g., fever, tachycardia, inflammatory biomarkers) into China's established "Five-Color" pregnancy risk management system to trigger early screening protocols. Prophylaxis and Protocolized Care: Promote the cost-effective use of intrapartum azithromycin prophylaxis in primary settings, as supported by A-Plus trial evidence demonstrating a lower incidence of maternal sepsis (1.5% vs. 2.3%; RR, 0.65; 95% CI, 0.55–0.77).³ Complementing this preventive strategy, implement the time-bound FAST-M bundle across all tiers, with the "1-hour antibiotic" rule as a non-negotiable quality metric. Data-Driven Surveillance and Feedback: Utilize China's national maternal health information systems to monitor key performance indicators (e.g., bundle compliance times) and embed them within provider incentive schemes, mirroring APT-Sepsis's quality feedback mechanism.

Strengthening the critical care nexus: Closing the final gap

Specialized Capacity Building: Prioritize the development and standardization of Obstetric ICUs (OICUs) within the existing network of over 3,000 critical maternal care centers, ensuring capacity for advanced hemodynamic and respiratory support. Activating Integrated Networks: Formalize and accelerate the "green channel" referral system between primary facilities and tertiary OICUs, supported by real-time teleconsultation platforms to ensure seamless care transitions. Institutionalizing Multidisciplinary Learning: Standardize rapid-response MDT protocols for sepsis and strengthen tiered maternal mortality review systems to foster system-level learning and continuous quality improvement.

CONCLUSION: A BLUEPRINT FOR QUALITY-DRIVEN MATERNAL SAFETY

The APT-Sepsis trial demonstrates that, even in settings with constrained

medical resources, restructuring routine clinical practices can yield lifesaving outcomes. China's greatest value lies not in direct replication but in conceptual blueprint: the imperative for integrated, protocol-driven, and measurement-based care. Successfully adapting this blueprint requires a dual approach: first, scientifically deconstructing the intervention to identify core components for scalable implementation; and second, strategically embedding these components within China's formidable health system architecture. By doing so, China can translate global evidence into sustained action, turning the challenge of maternal sepsis into an opportunity to lead the next frontier of equitable, high-quality maternal healthcare.

REFERENCES

- Cresswell J.A., Alexander M., Chong M.Y.C., et al. (2025). Global and regional causes of maternal deaths 2009–20: A WHO systematic analysis. *Lancet Glob. Health* **13**:e626–e634. DOI:10.1016/s2214-109x(24)00560-6
- Lissauer D., Gadama L., Waitt C., et al. (2025). A multicomponent intervention to improve maternal infection outcomes. *N. Engl. J. Med.* Advance online publication. DOI:10.1056/NEJMoa2512698
- Tita A.T.N., Carlo W.A., McClure E.M., et al. (2023). Azithromycin to prevent sepsis or death in women planning a vaginal birth. *N. Engl. J. Med.* **388**:1161–1170. DOI:10.1056/NEJMoa2212111
- McClure E.M., Saleem S., Goudar S.S., et al. (2020). Stillbirth 2010–2018: A prospective, population-based, multi-country study from the Global Network. *Reprod. Health* **17**:146. DOI:10.1186/s12978-020-00991-y
- Qiao J., Wang Y., Li X., et al. (2021). A Lancet Commission on 70 years of women's reproductive, maternal, newborn, child, and adolescent health in China. *Lancet* **397**:2497–2536. DOI:10.1016/s0140-6736(20)32708-2

FUNDING AND ACKNOWLEDGMENTS

This work was supported by a grant from the National Natural Science Foundation of China (No.82571936). The funder had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

AUTHOR CONTRIBUTIONS

All authors contributed to the manuscript and approved the final version.

DECLARATION OF INTERESTS

The authors declare no competing interests.